National Institute for Health and Care Excellence

Draft for consultation

Intrapartum care for women with existing medical conditions or obstetric complications and their babies

[C] Evidence reviews for heart disease

NICE guideline <TBC at publication>

Evidence reviews for women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions

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Draft for consultation

Developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Intrapartum care for women with cardiac disease – stratification of risk

Review question

What history, clinical examination and investigation is most useful to stratify the intrapartum risk for women with cardiac disease?

Introduction

The aim of this review is to examine cardiac disease symptoms, clinical observations and risk stratification tools for evidence of their value in identifying poor outcomes during intrapartum care and birth.

Summary of the protocol

See Table 1 for a summary of the population, intervention, comparison and outcomes (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the intrapartum period
Intervention	Recorded assessment of one or more of the following risk factors by at least a consultant cardiologist: Clinical history Intervention 1: • Family history Intervention 2: • Smoker Intervention 3: • Obstetric history Symptoms Intervention 4: • Breathlessness and severity, orthopnoea, paroxysmal nocturnal dyspnoea Intervention 5: • Palpitations Intervention 6: • Syncope Intervention 7: • Chest pain Clinical observations Intervention 8:

	• Pulse Intervention 9: • Blood pressure Intervention 10: • Jugular venous pressure Intervention 11: • Heart sounds Intervention 12: • Chest auscultation Intervention 13: • Pitting oedema Pre-pregnancy or antenatal cardiac function testing Intervention 14: • Echocardiogram Intervention 15: • Electrocardiogram (ECG) and ambulatory ECG Intervention 16: • Cardiopulmonary exercise testing (CPEX) Intervention 17: • Exercise testing Intervention 18: • Chest X-ray Intervention 19: • MRI Intervention 20: • Biomarkers – Brain Natriuretic Peptide (BNP) Risk assessment protocol Intervention 21: • Cardiac risk assessment protocols, tools or scoring systems for use at the onset of labour
Comparison	Each other
Outcomes	For the woman: • mortality • severe morbidity (ITU with organ support and organ transplant, or need for mechanical support) • mode of birth • women's satisfaction with labour and birth (including psychological wellbeing) For the baby: • mortality • severe morbidity (admission to a neonatal unit or encephalopathy)

	For studies evaluating cardiac risk assessment protocols, tools or scoring systems:
	• diagnostic accuracy of risk assessment protocols, tools or scoring systems to identify critical outcomes for the woman
	  ○ if reported dichotomously, sensitivity, specificity, positive and negative likelihood ratios
	  ○ if reported continuously, area under the ROC curve

BNP: brain natriuretic peptide; CPEX: cardiopulmonary exercise testing; ECG: electrocardiogram; ITU: intensive therapy unit; MRI: magnetic resonance imaging; ROC: receiver operator characteristic

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

There was no evidence identified for predictive accuracy of any individual risk factor or risk assessment protocol for any individual outcome of interest in this protocol. Thus, evidence from risk assessment protocols for combined outcomes of interest - cardiovascular events in the woman (defined by sustained symptomatic tachyarrhymia or bradyarrhymia requiring treatment, cardiac arrest or cardiac death, pulmonary oedema, a decline in New York Heart Association (NYHA) functional class compared with baseline, need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery, any cardiac failure (new onset or worsening) necessitating treatment or admission and bed rest, any thrombo-embolic complication, any myocardial infarction and/or any cerebrovascular accident, death from any cause or worsening of left ventricular ejection fraction) was considered for this review.

Seven cohort studies (3 prospective, 3 retrospective and one unspecified) were included in this review (see ‘Summary of clinical studies included in the evidence review’).

Six studies used CARdiac disease in PREGnancy (CARPREG) risk assessment (Balci 2014, Fu 2016, Lu 2015, Martins 2016, Pijuan-Domenech 2015, Tanous 2010); 4 studies used Zwangerschap bij Aangeboren HARtAfwijkingen pregnancy in congenital heart disease I (ZAHARA I) risk assessment (Balci 2014, Billebeau 2018, Fu 2016, Lu 2015); 5 studies used modified World Health Organization (WHO) risk assessment (Balci 2014, Billebeau 2018, Fu 2016, Lu 2015, Pijuan-Domenech 2015); 1 study used disease complexity risk assessment (Balci 2014) and 1 study used combined different risk assessment (Balci 2014).

Evidence from the studies included in the review is summarised below (see ‘Quality assessment of clinical studies included in the evidence review’). Predictive accuracy of individual risk factors (for example, family history, breathlessness) for cardiovascular events in the woman was not considered for this review.

All the risk assessment protocols were used to predict cardiovascular events for the woman which comprised of mixed critical and important outcomes. However, the outcome ‘cardiovascular events for the woman’ did not include the following important outcomes for the woman: mode of birth or women’s satisfaction with labour and birth. This outcome did not include any of the following critical outcomes for the baby: mortality or severe morbidity.

For studies evaluating cardiac risk assessment protocols, tools or scoring systems, evidence were reported continuously in area under the receiver operating characteristic (ROC) curve. There was no evidence reported dichotomously in sensitivity, specificity, positive and negative likelihood ratios.

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are provided in Appendix D.

Summary of clinical studies included in the evidence review

Table 2 provides a brief summary of the included studies.

Table 2: Summary of included studies

Study	Population	Intervention	Outcomes
Balci 2014 Prospective observational multicentre cohort study Netherlands	N=213 pregnancies in 203 women with structural CHD with ≤20 weeks gestation NYHA I: 99.5% Observed cardiac events: 22(10.3%)	• CARPREG[a] • Disease complexity[b] • Modified WHO[c] • ZAHARA I[d] • Total of all risk assessment protocol[e]	For the woman: • AUC for the risk of cardiovascular events
Billebeau 2018 Retrospective cohort study France	N=43 pregnancies in 36 women with cardiomyopathy NYHA >1: 22% Observed cardiac events: 15 (35%)	• Modified WHO[c] • ZAHARA I[d]	For the woman: • Number of cardiovascular events
Fu 2016 Retrospective cohort study China	N=730 pregnancies with congenital heart disease with ≥ 20 weeks gestation NYHA I-II: 99% Observed cardiac events: 68 (9.3%)	• CARPREG[a] • Modified WHO[c] • ZAHARA I[d]	For the woman: • AUC for the risk of cardiovascular events
Lu 2015 Retrospective cohort study	N=268 pregnancies in 190 women with congenital heart disease with ≥ 20 weeks gestation NYHA I-II: 97%	• CARPREG[a] • Modified WHO[c] • ZAHARA I[d]	For the woman: • AUC for the risk of cardiovascular events

Study	Population	Intervention	Outcomes
Taiwan	Observed cardiac events: 18 (6.7%)		
Martins 2016 Cohort study Brazil	N=132 pregnancies with heart conditions NYHA III: 0.03% Observed cardiac events: 30 (22.72%)	• CARPREG[a]	For the woman: • Number of cardiovascular events
Pijuan-Domenech2015 Prospective cohort study Spain	N=179 pregnancies in 164 women with heart disease NYHA I-II: 98.2% Observed cardiac events: 23 (13.4%)	• CARPREG[a] • Modified WHO[d]	For the woman: • AUC for the risk of cardiovascular events
Tauous 2010 Prospective cohort study Canada	N=66 pregnancies with congenital or acquired heart disease NYHA I-II: 97% Observed cardiac events: 8 (13%) Median GA: 13 weeks	• CARPREG[a]	For the woman: • Number of cardiovascular events

AUC: area under the receiver operator curve; BNP: brain natriuretic peptide; CARPREG: Cardiac disease in pregnancy; CHD: congenital heart disease; EF: ejection fraction; GA: gestational age; LVOT: left ventricular outflow tract; NYHA: New York Heart Association; ROC: receiver operating characteristic; WHO: World Health Organization; ZAHARA: Zwangerschap bij Aangeboren HartAfwijkingen pregnancy in CHD

[a] CARPREG: Risk points for women include one point each for i) Prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia); ii) NYHA functional class III/IV or cyanosis (SpO2 <90%); iii) Left heart obstruction (mitral valve area <2cm^2 or aortic valve area <1.5 cm^2 or peak LVOT gradient >30 mmHg (echocardiography); iv) Reduced systemic ventricular systolic function (EF <40%. The cardiovascular risks associated were 5%, 27% and 75% for 0 point, 1 point and ≥1 points respectively. The risk points for offspring were 0.75 point for left heart obstruction (mitral valve area < 2cm^2 or aortic valve area < 1.5 cm^2 or peak LVOT gradient > 30 mmHg (echocardiography)1 point each for i) NYHA functional class III/IV or cyanosis (SpO2<90%); ii) Smoking; iii) Heparin/warfarin during pregnancy; 3 points for multiple gestation. The higher the scores, the higher the risks of offspring complications.

[b] Disease complexity: there were 3 types of disease complexity: 1) Simple congenital heart disease (CHD): isolated aortic or mitral valve disease, small atrial septal defect, mild pulmonic stenosis, repaired atrial or ventricular septal defect, 2) Moderate complex CHD: atrioventricular septal defect, coarctation, Ebstein's anomaly, tetralogy of Fallot, 3) Complex CHD: cyanotic CHD, transposition of great arteries, Fontan procedure, truncus arteriosus

[c] Modified WHO classification: The cardiovascular risks associated were Class I: no detectable increased risk of maternal mortality and no/mild increase in morbidity, Class II: small increased risk of maternal mortality or moderate increase in morbidity, Class III: significantly increased risk of maternal mortality or severe morbidity and Class IV: extremely high risk of maternal mortality or severe morbidity.

[d] ZAHARA I: Risk points for woman include 0.75 point each for i) NYHA functional class III/IV; ii) Systemic atrioventricular valve regurgitation (moderate/severe); iii)Pulmonary atrioventricular valve regurgitation (moderate/severe), 1 point for cyanotic congenital heart disease (corrected and uncorrected), 1.5 point each for i) prior arrhymia; ii) cyanotic congenital heart disease (corrected and uncorrected), 2.5 points for left heart obstruction (peak LVOT gradient >50 mmHg or aortic valve area <1.0 cm^2)and 4.25 points for mechanical valve prosthesis. The cardiovascular risks associated were 2.9%, 7.5%, 17.5%, 43.1% and 70% for <0.5 point, 0.5 to 1.5 points, 1.51 – 2.5 points, 2.51-3.5 points and >3.51 points respectively. Risk points for offspring include 0.75 point each for i) cardiac medication before pregnancy; ii) cyanotic congenital disease (corrected and uncorrected), 1.75 points for twin or multiple gestation and 2.5 points for mechanical valve prosthesis. The offspring complication risks associated were 19.9%, 33.3%, 46.7% and 59.6% for <0.5 point, 0.5 to 0.99 point, 1 – 1.49 points and ≥ 1.5 points were 19.9%, 33.3%, 46.7% and 59.6% respectively.

[e] *A total of all other risk factors including total number of non-overlapping predictors of maternal cardiovascular events and offspring events (TPo) of ZAHARA I and CARPREG and from Khairy et al study (Maternal risk: severe pulmonary regurgitation or subpulmonary ventricular dysfunction and smoking history and Offspring risk: subaortic ventricular outflow tract gradient >30 mmHg).*

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question are presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Predictive accuracy of different risk assessment tools

<u>Outcomes for the woman</u>

Mortality and severe morbidity: cardiovascular events[a]

CARPREG

Very low quality evidence from 4 cohort studies (N=213, N=730, N=268, and N=179) of women with pre-existing cardiac disease reported that CARPREG did not accurately identify cardiovascular events.

[a]sustained symptomatic tachyarrhymia or bradyarrrhymia requiring treatment, cardiac arrest or cardiac death, pulmonary oedema, a decline in NYHA functional class compared with baseline, need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery, any cardiac failure (new onset or worsening) necessitating treatment or admission and bedrest, any thrombo-embolic complication, any myocardial infarction and/or any cerebrovascular accident, death from any cause or worsening of left ventricular ejection fraction.

Very low quality evidence from 1 cohort study (N=132) reported that women with pre-labour CARPREG score of 0, 1 and >1 developed 15%, 16% and 42% cardiovascular events, respectively.

Very low quality evidence from 1 cohort study (N=66) reported that women with pre-labour CARPREG score of 0, 1 and >1 developed 2%, 30% and 50% cardiovascular events, respectively.

Disease complexity

Very low quality evidence from 1 cohort study (N=213) reported that disease complexity had very poor to moderate accuracy to identify cardiovascular events.

Modified WHO criteria

Very low quality evidence from 4 cohort studies (N=213, N=730, N=268, and N=179) of women with a pre-existing cardiac condition reported that the modified WHO criteria had poor to excellent accuracy to identify cardiovascular events, however, there was serious imprecision.

Very low quality evidence from another cohort study (N=43) reported that women in pre-labour modified WHO group 1, 2/3 and 4 developed 33%, 37.5% and 30.8% cardiovascular events, respectively.

ZAHARA I

Very low quality evidence from 3 cohort studies (N=213, N=730, and N=268) of women with a pre-existing cardiac condition reported that ZAHARA I had very poor to good accuracy to identify cardiovascular events, however, there was serious imprecision.

Very low quality evidence from another cohort study (N=43) reported that women with pre-labour ZAHARA I score of 0-0.5, 0.51-1.5, 1.51-2.5, 2.51-3.5 and >3.5 developed 42.9%, 50%, 0%, 40% and 33% cardiovascular events, respectively.

A total of all risk assessment protocols

Very low quality evidence from 1 cohort study (N=213) reported that a total of all risk assessment protocols had very poor to moderate accuracy to identify cardiovascular events in the woman, however, there was serious imprecision.

Recommendations

C1. Risk assessment for women with heart disease should follow the principles of multidisciplinary team working (outlined in recommendation B1). Include a cardiologist with expertise in managing heart disease in pregnant women in the multidisciplinary team discussions.

C2. For women who present in the intrapartum period with previously undiagnosed heart disease, urgent multidisciplinary discussions are needed to try to ensure that the woman is offered the same level of care as a woman with an existing diagnosis of heart disease and, where possible, that their preferences are taken into account.

C3. Be aware that some women with heart disease are at low risk and management should be in line with the NICE guideline on intrapartum care for healthy women and babies, whereas others need individualised specialist care.

C4. For women with heart disease, reassess risk regularly during pregnancy and the intrapartum period using all of the following:

- comprehensive clinical assessment, including history and physical examination
- the modified WHO classification of risk[b], with the addition of Loeys Dietz syndrome
- NYHA functional class.

C5. Ensure that investigations are not withheld from women with heart disease because of pregnancy and that the results are reviewed and acted upon without delay.

Rationale and impact

Why the committee made the recommendations

The committee drew on their knowledge and experience to recommend that intrapartum care planning should start early in pregnancy for women with heart disease. Pregnancy and birth are associated with dramatic changes in the performance of the heart and the circulation. Early risk assessment is needed to plan for birth and agree any additional management. Women who present in the intrapartum period with a previously unrecognised heart problem pose a particular challenge. Urgent multidisciplinary discussions are needed to ensure that they are offered comparable intrapartum care to women with an existing diagnosis.

The committee agreed that multidisciplinary care should include a cardiologist with expertise in managing heart conditions during pregnancy because they were concerned that not all pregnant women with heart disease have appropriate cardiac referrals. Only a few cardiologists in the UK have an interest in managing heart disease in pregnancy and the MBBRACE-UK report identified deficient care when non-specialist cardiologists had given inappropriate advice. The benefit of specialist cardiology advice also includes encouraging women with low-risk conditions towards vaginal birth with no medical intervention, in line with the NICE guideline on intrapartum care for healthy women and babies .

Based on the available evidence and their knowledge and experience, the committee agreed that risk assessment should include diagnostic classification, cardiac functional capacity and clinical assessment. For some women this can mean reassurance that no additional precautions are needed, for others a full discussion of the risks and a comprehensive plan will be required. The committee recognised the importance of thorough clinical assessment as raised in the CEMACH reports and the need to provide prompt investigation identified in the 2016 MBBRACE-UK report.

Based on their knowledge and experience, the committee recommended that the woman's clinical condition is reassessed regularly during pregnancy and the intrapartum period. Many changes in performance of the heart and circulation occur gradually during pregnancy, but the intrapartum period and early postpartum period (including the first hours and days after birth) sees changes that can trigger a deterioration in cardiac function and therefore it is vital that investigations are undertaken and acted upon promptly.

[b] The WHO classification of risk from contraceptive use and pregnancy in cardiovascular disease modified to classify pregnancy risk associated with specific cardiovascular conditions (Thorne et al. 2006). The committee adapted the modified classification of risk outlined in Thorne et al. 2006, based on their clinical experience to clarify the intrapartum risk associated with heart disease, including the addition of Loeys Dietz syndrome.

Impact of the recommendations on practice

The committee agreed that the recommendations will reduce variation in practice and encourage best practice that already exists in many areas of the country. In some areas there may be more referrals to tertiary level services for specialist advice from a cardiologist with expertise in managing heart conditions during pregnancy. However, specialist advice should better determine which women need additional intervention and provide reassurance for those women whose heart condition would not affect their birth plans.

The committee believed that cardiac investigations are not rapidly available in all areas of the UK and this is reinforced by delays to investigations being identified by MBRRACE-UK in some cases of maternal death. There is variation in access to echocardiography, an investigation that can be crucial to making a diagnosis when symptoms of heart disease develop in the intrapartum period. A plan to ensure urgent access to echocardiography (including out of hours) for pregnant women with heart disease should be considered.

The recommendation that vaginal birth is safe for women with mild heart disease may reduce unnecessary medical intervention.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Mortality for the woman or the baby, severe maternal morbidity (admission to the intensive treatment unit (ITU) with organ support and transplant, or need for mechanical support) and severe morbidity for the baby (admission to the neonatal unit or encephalopathy) were identified as critical outcomes because the committee considered these to be the best outcomes to evaluate antenatal and intrapartum management for cardiac conditions in labour and birth. Mode of birth was considered important as this outcome could help the clinicians' decision for the best planning for women with cardiac conditions. Women's satisfaction with labour and birth was also regarded as important as this outcome was likely to reflect the overall impact of service delivery for women with cardiac conditions.

The quality of the evidence

Quality In Prognostic Studies (QUIPS) checklist was used to assess the quality of each study. 4 cohort studies were appraised as having low risk of bias whereas the other 3 were identified as moderate risk of bias. The common limitation of these studies were that they were descriptive studies and did not analyse predictive accuracy value of the assessment tool. The outcome considered in all the studies was composite comprising cardiovascular mortality, arrhythmia necessitating treatment, heart failure necessitating treatment, thromboembolic events such as pulmonary embolism, valve thrombosis, deep venous thrombosis, vascular events such as stroke, myocardial infarction or dissection, need for urgent or invasive cardiovascular intervention up to 6 months postpartum or endocarditis. This outcome was considered to be an indirect outcome of interest and thus, the evidence was downgraded by 1 level. The confidence interval was also wide and the evidence was downgraded by a further level because of this. The review protocol was deliberately set to be broad in recognition of the lack of evidence available to inform the corresponding intrapartum care review in the NICE guideline on intrapartum care for healthy women and babies (CG190) and to capture any relevant evidence that might have been available from test-and-

treat trials, randomised controlled trials (RCTs) or observational studies for the wide range of cardiac conditions and components of clinical and risk assessment. Overall, the available evidence was of very low quality.

Benefits and harms

The broad spectrum of cardiac disease means that an individual risk assessment for women is an important step. The committee considered that the care of women with low-risk cardiac conditions should not be over medicalised and could be managed in line with the NICE guideline on intrapartum care for healthy women and babies (CG190). The committee believed that the benefit of early assessment (in the early stages of pregnancy and for some women in the preconception period) was a key feature of high-quality care and that during the intrapartum phase there should be implementation of a pre-arranged plan and prompt re-assessment if the women has developed new symptoms.

The committee described how the principles of multidisciplinary team (MDT) working should be followed during risk assessment for women with cardiac disease. The committee explained that a cardiologist with expertise in managing heart disease during pregnancy should be included in the core multidisciplinary team as failure to properly manage the condition could lead to fatal consequences for the woman.

The committee agreed that intrapartum care for women who have no antenatal care should be managed in the same way as for women who develop a new cardiac condition during the intrapartum period. They recognised however that this may not always possible due to the clinical urgency with which the woman may need to be treated.

In the presence of an antenatal diagnosis of a cardiac condition, the committee agreed that based on the evidence, risk stratification should proceed in accordance with the WHO classification as modified in Thorne 2006. In addition, the committee used their clinical experience to adapt the modified classification of risk outlined in Thorne et al. 2006. These adaptations included the addition of Loeys Dietz syndrome as it is a relatively new diagnosis that was not widely recognised when Thorne 2006 was published. It was also agreed that this should be coupled with an assessment of functional status (NYHA class). The committee believed that the benefit of using both assessments would be to provide 2 opportunities to identify women at high risk and that the combination of a diagnostic class and a functional status measure would provide a safety net for a woman who may have a low-risk diagnosis but still be troubled by symptoms and also an asymptomatic woman whose cardiac lesion is of high concern.

The committee acknowledged that when women with extremely high-risk cardiac lesions become pregnant it can be the cause of very significant concern and stress to the clinicians involved. The importance of sharing this burden in an MDT and of referral for the best available opinion is essential, and in accordance with reports on maternal deaths in the UK and GMC guidance.

The committee believed that the value of taking a thorough medical history and careful physical examination could not be over-emphasised. The application of these elements does not appear to have been tested in the published literature but the committee remained convinced that these are key elements of clinical medicine in the UK. They noted the emphasis placed on these elements in investigations of maternal mortality and the multiple reports on maternal deaths in the UK which have highlighted the need for clinical rigour in these basic medical skills. The recent MBRRACE-UK surveillance report published in 2018

draws specific attention to elements of the medical history which should be explored, including family history and specific enquiry for symptoms that strongly suggest a cardiac origin for the problem (orthopnoea, paroxysmal nocturnal dyspnoea and a cough productive of pink frothy sputum). A thorough, basic physical examination, coupled with an open mind to consider cardiac pathologies had been overlooked in a number of the women who died.

The committee found that the literature did not provide any evidence concerning the hierarchy or usefulness of different cardiac investigations in the risk assessment process but they believed that following history taking and physical examination, basic investigations (12-lead ECG and plain chest X-ray) followed by targeted advanced diagnostic tests could further the risk assessment and planning process.

The committee concurred with the conclusions of the MBRRACE-UK surveillance report published in 2018 that the absence of a diagnosis in the presence of significant symptoms would be an important clinical red flag and the progression of a pregnancy would add a time-critical element to the need for referral and investigations.

The recommendations developed by the committee are consistent with those in condition-specific NICE cardiac disease guidelines that make recommendations for pregnant women with suspected myocardial ischaemia and heart failure (for example, NICE guidance on chest pain of recent onset [CG95], cardiovascular disease: risk assessment and reduction, including lipid modification [CG181] and chronic heart failure in adults: management [CG108]).

The committee highlighted the dynamic profile of haemodynamics in women who are pregnant or who have just given birth. This can lead to changes in previously stable conditions and presentation of previously unrecognised problems as well as the occurrence of new conditions which may or may not be specific to pregnancy. This changing physiology mandates frequent reassessment and re-evaluation.

The committee also emphasised in their discussion that all the investigations which were required to stratify the risk should be performed in a timely manner regardless of the pregnancy. The committee gave their views that late or inadequate risk assessment for these women could put both the woman and the baby at detrimental risks. They also suggested to review and take appropriate action promptly.

Cost effectiveness and resource use

No clinical evidence was identified for this review and the committee made a qualitative assessment of cost effectiveness.

The committee agreed that it would be cost effective to start planning early in pregnancy as dramatic changes to the performance of the heart and circulation can occur. Planning for birth and the need for additional management would be important to improve outcomes. Similarly the committee agreed that multidisciplinary involvement was needed to minimise the risk of adverse outcomes. They recommended that the multidisciplinary care included the relevant levels of experience and expertise and that this could reduce NHS costs associated with birth by encouraging vaginal births without medical intervention where appropriate.

The committee also believed that risk assessment, including diagnostic classification, cardiac functional capacity and clinical assessment would promote cost effective care particularly in cases where reassurance could be obtained that no additional precautions were necessary.

The committee acknowledged that there was some variation in practice and that the recommendations could potentially lead to more referrals to tertiary level services in some areas which would have a resource impact. However, they also thought that specialist advice could reduce costs by providing assurance to some women where their heart condition did not affect their birth plan and thereby reducing unnecessary medical intervention. Overall the committee did not think that their recommendations would have a significant resource impact for the NHS.

Other factors the committee took into account

Despite the uncertainty evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding stratification of risk for women with heart disease.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Review question

What is the appropriate management of anticoagulation for women with valvular disease in planning for childbirth?

Introduction

The aim of this review is to determine appropriate intrapartum anticoagulant management for women with bioprosthetic or mechanical valves.

Summary of the protocol

See Table 3 for a summary of the population, intervention, comparison and outcomes (PICO) characteristics of this review.

Table 3: Summary of the protocol (PICO) table

Population	Women with congenital or acquired valvular heart disease and with bioprosthetic (group 1) or mechanical (group 2) heart valves who are pregnant and beyond 24 weeks of gestation, including those in the intrapartum period
Intervention	**Group 1 – bioprosthetic valves:** Intervention 1: • Aspirin (and other antiplatelet agents; clopidogrel, ticagrelor or dipyridamole) Intervention 2: • Low-molecular-weight heparin (LMWH; dalteparin, enoxaparin, or tinzaparin) **Group 2 – mechanical valves:** Intervention 1: • Aspirin (and other antiplatelet agents; clopidogrel, ticagrelor or dipyridamole) Intervention 2: • Oral anticoagulants (warfarin, acenocoumarol, phenindione) Intervention 3: • Low-molecular-weight heparin (dalteparin, enoxaparin, or tinzaparin) Intervention 4: • New anticoagulants (direct factor Xa inhibitors: rivaroxaban, apixaban; direct thrombin inhibitors: dabigatran)

	Intervention 5: • Unfractionated heparin Intervention 6: • Different treatment regimens according to stage of pregnancy and consisting of combinations of the above drugs, some also including vitamin K antagonist Intervention 7: • Suspension of anticoagulation during the intrapartum period Intervention 8: • Bridging anticoagulation postpartum
Comparison	**Group 1 – bioprosthetic valves:** Comparison 1: • No anticoagulation **Group 2 – mechanical valves:** Comparison 1: • Low-molecular-weight heparin (dalteparin, enoxaparin, or tinzaparin) Comparison 2: • Warfarin
Outcomes	**For both types of prosthetic valves:** For the woman: • mortality • major morbidities (any thromboembolic events - pulmonary embolism, valve thrombosis, stroke or intracranial haemorrhage), obstetric haemorrhage (antenatal or postpartum), cardiovascular compromise (as defined by study), new maternal arrhythmia, infective endocarditis, myocardial infarction) • admission to a HDU or ITU • women's satisfaction with labour and birth (including psychological wellbing) • epidural haematoma • unplanned general anaesthesia • duration of hospital stay For the baby: • mortality (intrauterine death or neonatal death) • major neonatal morbidity (preterm birth, fetal anticoagulation, fetal haemorrhage, intracerebral or intracranial bleeding) • admission to a neonatal unit

1 *HDU: high dependency unit; ITU: intensive therapy unit; LWMH: low molecular weight heparin*

2 For further details see the full review protocol in Appendix A. The search strategies are
3 presented in Appendix B.

Clinical evidence

Included studies

Sub-question 1: Bioprosthetic heart valves

No clinical evidence was identified for this review.

Sub-question 2: Mechanical heart valves

One systematic review of case series and cohort studies and 5 prospective cohort studies were included in this review (see 'Summary of clinical studies included in the evidence review').

Of these, 2 studies compared low-molecular-weight heparin (LMWH) with unfractionated heparin (UFH) (Khader 2016, Xu 2016) whereas 2 studies compared LMWH with first-trimester heparin followed by warfarin until before birth when it was replaced by heparin (Vause 2017, Xu 2016). Three studies looked at the comparison of low and high dose of warfarin (Ayad 2016, Soma-Pillay 2011, Xu 2016). Studies examined warfarin in comparison with LMWH in 2 studies (Vause 2017, Xu 2016) or UFH in 1 study (Xu 2016) or unspecified heparin in 1 study (Xu 2016) or heparin followed by warfarin followed by heparin in 3 studies (Khamoushi 2011, Vause 2017, Xu 2016).

Evidence from the studies included in this review is summarised below (see 'Quality assessment of clinical studies included in the evidence review').

Data was reported on the critical outcomes for the woman, mortality, major morbidities (as major thromboembolic event or major antenatal haemorrhagic event). Data was also reported on the following critical outcomes for the baby, mortality. One study reported outcomes as poor maternal outcome and poor fetal outcome which comprised of mixed critical and important outcomes for the woman and the baby, respectively. Evidence was not available for the following outcomes for the woman: admission to a high dependency unit (HDU), intensive treatment unit (ITU) (important outcome) or women's satisfaction with labour and birth (important outcome), epidural haematoma (important outcome), unplanned general anaesthesia (important outcome) and duration of hospital stay (outcomes of limited importance). Evidence was also not available for the following outcomes for the baby: major neonatal morbidity (critical outcome) and admission to a neonatal unit (important outcome).

There was no evidence available for the following interventions: aspirin, new anticoagulants and suspension of anticoagulation during the intrapartum period.

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in Appendix D.

Summary of clinical studies included in the evidence review

Table 4 provides a brief summary of the included studies.

Table 4: Summary of included studies

Study	Population	Intervention	Comparison	Outcome	Comments
Ayad 2016 Prospective cohort study Egypt	N=100 women with mechanical heart valves	• Warfarin throughout pregnancy	Different doses of warfarin • ≤5 mg • >5 mg	For the baby: • Live birth	
Khader 2016 Prospective cohort study Egypt	N=40 women with mechanical heart valves	• UFH (15.000 IU/12 hr) before 6 weeks gestation until 12 hours before birth	• Enoxaparin (1 mg/kg bd) before 6 weeks until 36 weeks gestation; then unfractionated heparin (15.000 IU/12 hour) was given until 12 hours before birth	For the woman: • Maternal death • Antepartum haemorrhage (APH) • Postpartum haemorrhage (PPH) • Thrombotic complications For the baby: Live birth	

Study	Population	Intervention	Comparison	Outcome	Comments
Khamoushi 2011 Prospective cohort study Iran	N= 49 pregnancies in 44 women	• Warfarin throughout pregnancy, heparin at time of delivery	• IV injections of UFH during 6th-12th gestational week, warfarin until the 36th gestational week followed by heparin for the last two weeks of pregnancy and at time of delivery	For the woman: • Prosthetic valve dysfunction in third trimester or after delivery	
Soma-Pillay 2011 Prospective cohort study South Africa	N=62 women with mechanical heart valves	• Subcutaneous unfractionated heparin until 12 weeks gestation, then warfarin was given (INR 2.5 to 3.5) until 36 weeks gestation when subcutaneous unfractionated heparin was restarted, until the morning of labour	Different doses of warfarin • ≤5 mg • 5.1 to 7.4 mg • ≥7.5 mg	For the baby: • Pregnancy loss (Miscarriages and stillbirths)	Data from 5.1 to 7.4 mg and ≥7.5 mg were combined and analysed as ≥5 mg. This outcome was assessed as indirect.

Study	Population	Intervention	Comparison	Outcome	Comments
Vause 2017 Prospective population-based cohort study UK	N=53 women with mechanical heart valves	• Warfarin throughout pregnancy • LMWH throughout pregnancy • First trimester LMWH with subsequent warfarin until early third trimester, converting to heparin before birth • Other	Each other	For the woman: • Poor maternal outcome (maternal death or serious morbidity – admission to intensive care for >1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intra-abdominal bleeding, vaginal haematoma, wound haematoma) For the baby: • Poor fetal outcome (any pregnancy loss [miscarriage or termination of pregnancy], stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit)	The outcomes were assessed as indirect.

Study	Population	Intervention	Comparison	Outcome	Comments
Xu 2016 Systematic review Multiple countries	N = 2113 pregnancies from 51 studies of women with mechanical heart valves of four anticoagulation regimens	• a regimen of a vitamin K antagonist (VKA) throughout pregnancy • a heparin (H)/VKA regimen, which includes use of VKAs except for adjusted doses of unfractionated or low molecular weight heparin (LMWH) during 6-12 weeks of pregnancy • an LMWH regimen of adjusted LMWH doses throughout pregnancy • an unfractionated heparin (UFH) regimen of adjusted doses of UFH throughout pregnancy	Comparative data provided for H/VKA versus LMWH only	For the woman: • Maternal death (any maternal antenatal death from any cause) • Maternal major thrombotic event (included fatal thromboembolism, prosthetic valve thrombosis requiring thrombolysis or emergency surgery, documented evidence of central nervous system embolization, documented evidence of peripheral limb and visceral embolization requiring surgery, and any other related events requiring hospitalization) • Maternal major antenatal haemorrhagic event (major haemorrhagic events in the antenatal period, including death due to haemorrhage, intracranial bleeding or documented cardiac tamponade requiring intervention, haemorrhage requiring transfusion, and any other related events requiring inpatient treatment) For the baby: • Intrauterine fetal or neonatal mortality (spontaneous abortion, therapeutic abortion, stillbirth and neonatal death)	The data from this study is indirect because it does not specifically pertain to the intrapartum period. Total number of pregnancies in each anticoagulation were unclear as the study reported only number available for each outcome.

H: heparin; INR: international normalised ratio; IU: international unit; IV: intravenous; LMWH: low-molecular-weight heparin; UFH: unfractionated heparin; VKA: vitamin K antagonists

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F)

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Sub-question 2: Mechanical heart valves

Unfractionated heparin alone versus low-molecular-weight heparin ± unfractionated heparin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=227) of women with mechanical heart valves reported that there is no clinically important difference between UFH and LMWH for mortality.

Very low quality evidence from 1 prospective cohort study (N=40) of women with mechanical heart valves showed that there is no event of mortality in either women receiving UFH or those receiving LMWH followed by UFH.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=180) of women with mechanical heart valves showed that there is a clinically important harmful effect of UFH compared with LMWH for the risk of major thromboembolic event.

However, very low quality evidence from 1 prospective cohort study (N=40) of women with mechanical heart valves showed no major thromboembolic event in either women receiving UFH or those receiving LMWH followed by UFH.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=212) of women with mechanical heart valves showed that there is no clinically important difference between UFH and LMWH for the risk of major antenatal haemorrhagic event.

Very low quality evidence from 1 prospective cohort study (N=40) of women with mechanical heart valves showed no clinically important difference between women receiving UFH and those receiving LMWH followed by UFH for the risk of major antenatal haemorrhagic event.

Major morbidity: postpartum haemorrhagic event

Very low quality evidence from 1 prospective cohort study (N=40) of women with mechanical heart valves showed that there is no clinically important difference between UFH and LMWH followed by UFH for the risk of postpartum haemorrhagic event.

Outcomes for the baby

Mortality

Very low quality evidence from 1 systematic review (n=167) of women with mechanical heart valves reported that there is a clinically important harmful effect of UFH compared with LMWH for mortality of babies.

However, very low quality evidence from 1 prospective cohort study (N=40) of women with mechanical heart valves showed no clinically important difference between UFH and LMWH followed by UFH for mortality of babies.

Heparin followed by warfarin followed by heparin versus low-molecular-weight heparin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=461) of women with mechanical heart valves showed no clinically important difference between heparin followed by warfarin followed by heparin and LMWH for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=450) of women with mechanical heart valves showed no clinically important difference between heparin followed by warfarin followed by heparin and LMWH for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=427) of women with mechanical heart valves showed that there is a clinically important beneficial effect of heparin followed by

warfarin followed by heparin compared with those receiving LMWH for the risk of major antenatal haemorrhagic event.

Poor maternal outcome[c]

Very low quality evidence from 1 prospective cohort study (n=50) of women with mechanical heart valves showed no clinically important difference between heparin followed by warfarin followed by heparin and LMWH for the risk of poor maternal outcome.

Outcomes for the baby

Mortality

Very low quality evidence from 1 systematic review (n=438) of women with mechanical heart valves showed that there may be a clinically important harmful effect of heparin followed by warfarin followed by heparin compared with LMWH for mortality of babies, but there is uncertainty around the estimate.

Poor fetal outcome[d]

Very low quality evidence from 1 prospective cohort study (n=50) of women with mechanical heart valves showed no clinically important difference between heparin followed by warfarin followed by heparin and LMWH for the risk of poor fetal outcome.

Low-dose warfarin (≤5 mg/day) ± unfractionated heparin versus high-dose warfarin (>5 mg/day) ± unfractionated heparin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=673) of women with mechanical heart valves showed that there is no clinically important difference between low-dose warfarin and high-dose warfarin for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=386) of women with mechanical heart valves showed that there is a clinically important beneficial effect of low-dose warfarin compared with high-dose warfarin for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=771) of women with mechanical heart valves showed that there is no clinically important difference between low-dose warfarin and high-dose warfarin for the risk of major antenatal haemorrhagic event.

Outcomes for the baby

Mortality

[c] Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for > 1day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)

[d] Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit.

Very low quality evidence from 1 systematic review (n=474) of women with mechanical heart valves showed that there is no clinically important difference between low-dose warfarin and high-dose warfarin for mortality of babies.

However, very low quality evidence from 1 prospective cohort study (N=98) of women with mechanical heart valves showed that there may be a clinically important beneficial effect of low-dose warfarin compared with high-dose warfarin for mortality of babies.
Very low quality evidence from 1 prospective cohort study (N=62) of women with mechanical heart valves showed that there is no clinically important difference between low-dose warfarin followed by UFH and high-dose warfarin followed by UFH for mortality of babies.

Low-molecular-weight heparin versus warfarin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=507) of women with mechanical heart valves showed that there is no clinically important difference between LMWH and warfarin for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=537) of women with mechanical heart valves showed that there may be a clinically important harmful effect of LMWH compared with warfarin for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=637) of women with mechanical heart valves showed that there is a clinically important harmful effect of LMWH and warfarin for the risk of major antenatal haemorrhagic event.

Poor maternal outcome[e]

Very low quality evidence from 1 prospective cohort study (n=44) of women with mechanical heart valves showed that there is no clinically important difference between LMWH and warfarin for the risk of poor maternal outcome.

Outcomes for the baby

Mortality

Very low quality evidence from 1 systematic review (n=637) of women with mechanical heart valves showed that there is a clinically important beneficial effect of LMWH compared with warfarin for mortality of babies.

Poor fetal outcome[f]

Very low quality evidence from 1 prospective cohort study (n=44) of women with mechanical heart valves showed that there is no clinically important difference between LMWH and warfarin for the risk of poor fetal outcome.

[e] Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for > 1day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)

[f] Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit

Unfractionated heparin versus warfarin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=508) of women with mechanical heart valves showed that there is no clinically important difference between UFH and warfarin for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=491) of women with mechanical heart valves showed that there is a clinically important harmful effect of UFH compared with warfarin for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=653) of women with mechanical heart valves showed that there is a clinically important harmful effect of UFH compared with warfarin for the risk of major antenatal haemorrhagic event.

Outcomes for the baby

Mortality

Very low quality evidence from 1 systematic review (n=608) of women with mechanical heart valves showed that there is a clinically important harmful effect of UFH compared with warfarin for mortality of babies.

Heparin (unspecified[g]) versus warfarin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=621) of women with mechanical heart valves showed that there is no clinically important difference between heparin and warfarin for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=604) of women with mechanical heart valves showed that there is a clinically important harmful effect of heparin compared with warfarin for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=751) of women with mechanical heart valves showed that there is a clinically important harmful effect of heparin compared with warfarin for the risk of major antenatal haemorrhagic event.

Outcomes for the baby

Mortality

[g] Unspecified: LMWH or UFH or their combination strategy

Very low quality evidence from 1 systematic review (n=706) of women with mechanical heart valves showed that there is no clinically important difference between heparin and warfarin for mortality of babies.

Heparin followed by warfarin followed by heparin versus warfarin

Outcomes for the woman

Mortality

Very low quality evidence from 1 systematic review (n=742) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for mortality.

Major morbidity: major thromboembolic event

Very low quality evidence from 1 systematic review (n=761) of women with mechanical heart valves showed that there is a clinically important harmful effect of heparin followed by warfarin followed by heparin compared with warfarin alone for the risk of major thromboembolic event.

Major morbidity: major antenatal haemorrhagic event

Very low quality evidence from 1 systematic review (n=868) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for the risk of major antenatal haemorrhagic event.

Poor maternal outcome[h]

Very low quality evidence from 1 prospective cohort study (n=12) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for the risk of poor maternal outcome.

Prosthetic valve dysfunction: 3rd trimester or after birth

Very low quality evidence from 1 prospective cohort study (N=49) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for the risk of prosthetic valve dysfunction at 3rd trimester or after birth.

Outcomes for the baby

Mortality

Very low quality evidence from 1 systematic review (n=879) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for mortality of babies.

Poor fetal outcome[i]

[h] Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for >1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident or bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)

[i] Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit

Very low quality evidence from 1 prospective cohort study (n=12) of women with mechanical heart valves showed that there is no clinically important difference between heparin followed by warfarin followed by heparin and warfarin alone for the risk of poor fetal outcome.

Recommendations

C6. When pregnancy is confirmed, involve women with mechanical heart valves in multidisciplinary discussion of plans for anticoagulation during the intrapartum period (see recommendation B1). Explain that they will need individualised anticoagulation depending on their current treatment.

C7. For women with mechanical heart valves who are taking warfarin in the third trimester, switch anticoagulation to low-molecular-weight heparin by 36^{+0} weeks of pregnancy or 2 weeks before planned birth (if this is earlier than 36^{+0} weeks). Consider doing this by:

- stopping warfarin and 24 hours later starting low-molecular-weight heparin using a twice daily regimen at a dose based on the most recent weight available
- checking anti-Xa levels 3 to 4 hours after at least 3 doses of low-molecular-weight heparin, aiming for a peak level between 1 and 1.4 IU/ml
- checking anti-Xa levels weekly or fortnightly if the last test gave a peak level of 1 to 1.4 IU/ml, and at least weekly if not (checking adherence).

C8. For women with mechanical heart valves, stop therapeutic low-molecular-weight heparin 24 hours before a planned caesarean section and consider aiming to perform the caesarean section as near to 24 hours after stopping as possible and no later than 30 hours after stopping.

C9. For women with mechanical heart valves who are having an induction of labour, a senior obstetrician should be involved in:

- deciding when to stop low-molecular-weight heparin in order to:
  - minimise the risk of maternal haemorrhage or valve thrombosis
  - enable the option of regional analgesia
- reviewing the progress of induction and the need for anticoagulation every 12 hours, aiming for a low level of heparin at the time of active labour.

C10. For women with mechanical heart valves, carry out a further senior review (involving at least an obstetrician and an anaesthetist) of the risk of haemorrhage and valve thrombosis 3 to 4 hours after birth. Based on this review, consider 1 of the following options:

- therapeutic low-molecular-weight heparin
- prophylactic low-molecular-weight heparin
- no low-molecular-weight heparin.

Aim to restart therapeutic low-molecular-weight heparin as soon as possible after the 3- to 4-hour review.

C11. For women with mechanical heart valves, consider delaying restarting warfarin until at least 7 days after birth and closely supervise anticoagulation when doing so.

C12. For women who are taking warfarin and who present in established labour:

- check the international normalised ratio (INR) immediately and consult a haematologist
- stop anticoagulation immediately until the woman has had an assessment by an obstetrician, which should happen within 2 hours

- carry out a senior review (including at least a senior obstetrician, haematologist and a consultant obstetric anaesthetist) to discuss the mode of birth most likely to give the lowest risk of bleeding for the woman and the baby
- consider reversal of anticoagulation.

C13. For women with bioprosthetic valves, continue any antiplatelet treatment (for example, low-dose aspirin) throughout the intrapartum period.

Rationale and impact

Why the committee made the recommendations

The evidence looked at the effects of different anticoagulants throughout pregnancy on maternal and neonatal outcomes rather than their effects during labour. The evidence was also limited to women with mechanical heart valves. Therefore, the committee based recommendations on their experience and advice from a cardiac specialist.

They noted that a woman with a mechanical heart valve is prone to thrombosis if she has inadequate anticoagulation, but is vulnerable to excessive bleeding with too much anticoagulation. Either can lead to devastating fatal incidents for the woman and her baby. It is therefore important that planning for the management of anticoagulation during the intrapartum period starts when pregnancy is confirmed. The committee agreed that a woman with a mechanical heart valve should be switched to low-molecular-weight heparin by 36 weeks of pregnancy, or 2 weeks before planned birth, because heparin has a shorter half-life than warfarin and reduces the risk of serious medical problems for the baby.

The committee acknowledged that continuous infusion of unfractionated heparin continues to be used in some centres. However, they did not make a recommendation on this because use of unfractionated heparin has declined in the UK, with fewer professionals being familiar with how to achieve and maintain adequate anticoagulation. They agreed, based on the once daily dosing of warfarin, that low-molecular-weight heparin should be started 24 hours after stopping warfarin. Monitoring of anti-Xa level and dose adjustments are needed to ensure that an appropriate level of anticoagulation is achieved. Anti-Xa levels should not be checked until after at least the third dose because stable anti-Xa levels are unlikely before this. For women who have a planned caesarean section, the risk of an epidural haematoma can be reduced by stopping low-molecular-weight heparin 24 hours before. For women having an induction of labour, the decision of when to stop low-molecular-weight heparin should balance the risk of valve thrombosis against the possibility of having regional analgesia. A senior obstetrician should be involved in this decision and review the progress of induction.

For a woman presenting in labour on warfarin, the committee agreed that anticoagulation be stopped immediately to minimise the risks of excessive bleeding for the woman and baby during labour. The committee recommended that obstetric assessment should occur within 2 hours, recognising that although assessment was urgent it would not always be possible to do this immediately. The committee agreed that the international normalised ratio (INR) be checked immediately and a haematologist consulted. The INR determines the degree of anticoagulation in the woman and baby and indicates how they should be managed. A haematologist would advise how to reverse anticoagulation if this was needed. Senior review, involving a senior obstetrician, haematologist and consultant obstetric anaesthetist, should ensure the safest birth for the woman and baby.

Impact of the recommendations on practice

The committee believed that these recommendations reflect modern UK practice and the growing clinical confidence in low-molecular-weight heparin over unfractionated heparin. Anti Xa assays are essential for the monitoring and titration of low-molecular-weight heparin and the committee recognised that access to this test may need to be improved.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The following outcomes were prioritised for the review.

Mortality for the woman and the baby were considered as critical outcomes because mortality would be an extreme adverse outcome for either the woman or the baby if anticoagulation during labour was in appropriate. Major morbidities for the woman (any thromboembolic events including pulmonary embolism, valve thrombosis, stroke or intracranial haemorrhage; obstetric haemorrhage including antenatal and postpartum bleeding; cardiovascular compromise; new maternal arrhythmia; infective endocarditis; or myocardial infarction) as well as major morbidity for the baby (preterm birth, fetal anticoagulation, fetal haemorrhage, intracerebral or intracranial bleeding) were regarded as outcomes of critical importance because these complications can lead to major interventions or life-long and devastating consequences.

Women's satisfaction with labour and birth was considered to be an important outcome to emphasise that care should be centred on the women. Admission to HDU or ITU, epidural haematoma and unplanned general anaesthesia were agreed as important outcomes for the woman as they indirectly reflect inappropriate anticoagulation during labour. Similarly, admission to a neonatal unit was considered to be an important outcome for the baby because improper anticoagulation for a woman during labour could lead to prolonged labour resulting in neonatal asphyxia or the direct effect of anticoagulant on the baby through the placenta, either of which would result in the baby being admitted to ITU.

The quality of the evidence

The evidence in this review was based on a systematic review of cohort studies and case series or individual prospective cohort studies. It should be noted that all studies assessed the effects of anticoagulants throughout pregnancy, not just during labour. However, the evidence was not downgraded because this reflects current clinical practice. The quality of each study was appraised using the AMSTAR and Newcastle-Ottawa checklists for systematic reviews and cohort studies, respectively. The GRADE quality of all evidence was very low.

Benefits and harms

The committee highlighted that inadequate anticoagulation for women with a mechanical heart valve could cause thrombosis, however too much anticoagulation could lead to excessive bleeding: and either situation could cause fatality in the woman and her baby. Therefore the committee recommended close collaboration within an MDT and an individualised plan during pregnancy for how to manage the intrapartum period for women with mechanical heart valves because this would increase the chances of an uncomplicated and successful birth.

The committee recommended a 2-week gap between stopping warfarin and the birth of the baby for women with mechanical heart valves who take warfarin during pregnancy. In the interim, anticoagulation should be covered by heparin. The committee also emphasised the need for close monitoring of anti-Xa levels and that the heparin dose should be adjusted accordingly. The committee explained that anti-Xa level reflects the anticoagulant effect of heparin and should be kept between 1-1.4 IU/ml. They elaborated that the benefit of switching to heparin in the near term is to have better control over intrapartum bleeding compared to continuing warfarin, while reducing the risk of thrombosis in women with mechanical heart valves. The committee also highlighted that the fetus will be more anticoagulated than the woman if the woman is taking warfarin. Thus, the committee recommended that switching to heparin 2 weeks before planned birth would allow time for the fetus to gain normal coagulation back which would in turn mean that vaginal birth could be considered.

The committee elaborated that if a caesarean section is planned for a woman with mechanical heart valves, then LMWH, used in therapeutic doses, should be withheld 24 hours before a caesarean section to reduce the risk of epidural haematoma. Also, the caesarean section should be performed between 24-30 hours after stopping anticoagulation. If induction of labour was planned for a woman with mechanical heart valves, it was suggested to seek a senior obstetrician's opinion on when to stop heparin. The decision would be on the balance of benefits (having an option of regional analgesia) and risks (valve thrombosis) of stopping heparin. Progress of labour should be monitored closely and appropriate action taken promptly.

The committee agreed that if a woman on warfarin presents in labour, caesarean section may be the best option for the baby though it might not be the best option for the woman and therefore it was recommended that consideration should be given by a senior obstetrician, haematologist and a consultant obstetric anaesthetist as to which mode of birth would be most appropriate to balance the benefits and risks for both the woman and the baby.

The emphasis of the recommendations on close monitoring and appropriate titration to achieve the target of anti-Xa levels between 1 and 1.4 IU/ml, together with close collaboration between an obstetrician, a haematologist, a cardiologist and an obstetric anaesthetist during the intrapartum period would increase the chances of an uncomplicated and successful birth.

For a woman presenting in labour and who is taking warfarin, the risk of excessive bleeding during labour for both the woman and the baby can be minimised by stopping the anticoagulation immediately, followed by an urgent assessment by an obstetrician. The committee agreed that to determine the degree of anticoagulation in the woman and baby the international normalised ratio (INR) should be checked promptly. The INR should be reviewed by a haematologist, who could also advise on how to reverse anticoagulation if necessary.

Regarding women with bioprosthetic valves, the committee recommended continuing anti-platelet therapy throughout labour on the balance of the associated benefits and risks.

Cost effectiveness and resource use

No clinical evidence was identified for this review and the committee made a qualitative assessment of cost effectiveness.

The recommendations aimed to balance the risks of too much or too little anticoagulation, either of which could result in the death of the woman or the baby. Given the potential loss of

life the committee considered that the recommendations intended to mitigate the risks of too much or too little anticoagulation were likely to be cost effective.

The committee considered that the recommendations largely reflected current practice and, therefore, they did not anticipate a significant resource impact to the NHS.

Other factors the committee took into account

Despite the low quality of the evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding the management of anticoagulation for women with mechanical heart valves.

Intrapartum care for women with cardiac disease – mode of birth

Review question

Which women with cardiac disease should be offered elective caesarean section or assisted second stage for reasons specific to cardiac disease?

Introduction

The aim of this review is to examine outcomes for the woman and baby following elective caesarean section for reasons related to a cardiac condition compared with outcomes following a planned vaginal birth.

Summary of the protocol

See Table 5 for a summary of the population, intervention, comparison and outcomes (PICO) characteristics of this review.

Table 5: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the intrapartum period
Intervention	Elective caesarean section
Comparison	Vaginal birth
Outcomes	For the woman: • mortality • major morbidity • women's satisfaction with labour and birth (including psychological wellbeing) • emergency caesarean section For the baby: • mortality • major morbidity

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

One retrospective cohort study was included for this review (see 'Summary of clinical studies included in the evidence review').

There were 2 comparisons in this study: planned caesarean section for cardiac reasons versus planned vaginal birth and planned caesarean section for any reason versus planned vaginal birth (Ruys 2015).

Evidence from the studies included in the review is summarised below (see 'Quality assessment of clinical studies included in the evidence review').

For the comparison of planned caesarean section for cardiac reasons versus planned vaginal birth, data was reported for the following outcomes for the woman, mortality (critical outcome), major morbidity: postpartum heart failure, postpartum haemorrhage (critical outcome) and emergency caesarean section for obstetric or cardiac reasons (important outcome). Data was also reported for the critical outcome mortality of the baby. There was no evidence identified for the following important outcome for the woman, women's satisfaction with labour and birth. There was no evidence identified for the following critical outcome for the baby, major morbidity.

For the comparison of planned caesarean section for any reason versus planned vaginal birth, data was reported for the following outcome for the woman, emergency caesarean section for cardiac reasons (important outcome). There was no evidence identified for the following maternal outcomes: mortality (critical outcome), major morbidity (critical outcome) and women's satisfaction with labour and birth (important outcome). There was no evidence identified for any outcomes for the baby: mortality (critical outcome) and major morbidity (critical outcome).

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in Appendix D.

Summary of clinical studies included in the evidence review

Table 6 provides a brief summary of the included studies.

Table 6: Summary of included studies

Study	Population	Intervention/ Comparison	Outcomes	Comments
Ruys 2015 Retrospective cohort study Registry data from 28 countries	N=1262 pregnancies among women with structural or ischaemic heart disease from the European Registry on Pregnancy and Heart Disease between 2007 and 2011	Comparison 1: • Planned caesarean section for cardiac reasons (n=172) • Planned vaginal birth (n=869) Comparison 2: • Planned caesarean section for any reason (both cardiac and obstetric) (n=393) • Planned vaginal birth (n=869)	Comparison 1: For the woman: • Mortality • Major morbidity: ○ Postpartum heart failure ○ Postpartum haemorrhage[1] • Emergency caesarean section for obstetric or cardiac reasons For the baby: • Mortality Comparison 2:	Cardiac reasons for emergency caesarean section are only provided for women in planned caesarean section group, but not for women in planned vaginal birth group that went on to have emergency caesarean section for cardiac reasons. Outcomes are presented by

Study	Population	Intervention/ Comparison	Outcomes	Comments
			For the woman: • Emergency caesarean section for cardiac reasons	planned caesarean section/vaginal birth rather than performed caesarean section/vaginal birth.

[1]*Postpartum haemorrhage is defined in the paper as >500 mL in vaginal births and as >1000 mL in caesarean sections, or as requiring transfusion*
N: total number of participants

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Planned caesarean section for cardiac reasons versus planned vaginal birth

Outcomes for the woman

Mortality

Very low quality evidence from 1 retrospective cohort study (n=1041) of women with structural or ischaemic heart disease showed a clinically important higher number of maternal deaths in the group of women planning an elective caesarean section for cardiac reasons compared to women planning a vaginal birth. The causes of death were not reported.

Major morbidity: postpartum heart failure

Very low quality evidence from 1 retrospective cohort study (n=1041) of women with structural or ischaemic heart disease showed a clinically important higher number of postpartum heart failure events in the group of women planning an elective caesarean section for cardiac reasons compared to women planning a vaginal birth.

Major morbidity: post-partum haemorrhage

Very low quality evidence from 1 retrospective cohort study (n=1041) of women with structural or ischaemic heart disease showed no clinically important difference in postpartum haemorrhage between women planning an elective caesarean section for cardiac reasons and women planning a vaginal birth.

Emergency caesarean section

Very low quality evidence from 1 retrospective cohort study (n=1041) of women with structural or ischaemic heart disease showed no clinically important difference in emergency caesarean section (for either cardiac or obstetric reasons) between women planning an elective caesarean section for cardiac reasons and women planning a vaginal birth. The reasons for emergency caesarean section were not reported.

Outcomes for the baby

Mortality

Very low quality evidence from 1 retrospective cohort study (n=1041) of women with structural or ischaemic heart disease showed no clinically important difference in mortality of the baby between women planning an elective caesarean section for cardiac reasons and women planning a vaginal birth. The causes of death were not reported.

Planned caesarean section for any reason (obstetric or cardiac reasons) versus planned vaginal birth

Outcomes for the woman

Emergency caesarean section

Very low quality evidence from 1 retrospective cohort study (N=1262) of women with structural or ischaemic heart disease showed a clinically important higher number of emergency caesarean sections for cardiac reasons in the group of women planning an elective caesarean section (for either cardiac or obstetric reasons) compared to women planning a vaginal birth. The cardiac reasons for emergency caesarean section in the group of women planning an elective caesarean section were: heart failure (n=13), arrhythmia (n=5), acute coronary syndrome (n=1), ischaemic cerebral event (n=1), unknown (n=5). The reasons for emergency caesarean section in the group of women planning a vaginal birth were not reported.

Recommendations

C14. Offer an individualised birth plan covering all three stages of labour to women with heart disease following multidisciplinary discussion (outlined in recommendation B1). Consider including a cardiologist with expertise in managing heart disease in pregnant women in the multidisciplinary team discussions.

C15. Offer planned birth (caesarean section or induction of labour) for women with mechanical heart valves in order to minimise the time off anticoagulation.

C16. Consider planned caesarean section for women with:

- any disease of the aorta assessed as high risk
- pulmonary arterial hypertension
- NYHA class III or IV heart disease.

Explain the risks and benefits of caesarean section. If the woman chooses not to have a caesarean section, offer an assisted second stage of labour without active pushing.

C17. For women with heart disease who have planned a caesarean section, offer an individualised emergency care plan in case they present in early labour, with new symptoms or with obstetric complications.

C18. Throughout pregnancy, manage pulmonary arterial hypertension in consultation with a specialist centre for this condition.

Rationale and impact

Why the committee made the recommendations

Evidence was very limited so the committee drew on their knowledge and experience to make recommendations. They agreed that risk assessment is necessary to understand how well the woman's heart is functioning and is likely to cope with the exertion of labour and the circulatory changes that take place after birth. Women should have advice from a team with experience of intrapartum care for women with heart conditions. This will usually involve doctors from at least 3 specialties (obstetrics, cardiology and anaesthesia) in formulating an individualised birth plan. In this way the woman's wishes for labour and birth can be discussed in relation to the specific risks of her condition.

In order to minimise the time without anticoagulation, elective caesarean section or induction of labour should be offered for women with mechanical heart valves. The risks of valve thrombosis cannot be overstated but this needs to be balanced against the risks of bleeding around the time of birth.

Planned caesarean section should be considered for women with high-risk aortic disease or the most severe cardiac conditions, but the committee recognised that some of these woman may prefer to plan for a vaginal birth. When this is the woman's preference she should be fully informed of the risks and be offered an assisted second stage of labour without active pushing to try and reduce the risk of aortic dissection, aortic rupture or acute heart failure.

When an elective caesarean section is proposed, emergency plans should still be made and shared with the intrapartum care team in case the woman presents in early labour, with new symptoms or with an obstetric complication.

In the UK, the management of pulmonary arterial hypertension is concentrated in a small number of specialist centres. Pulmonary arterial hypertension is a life-threatening condition that requires expert management. The MDT planning for a woman with pulmonary hypertension must include a respiratory physician from one of these centres.

Although the exertion of labour and the fluid shifts at birth may be detrimental to some heart conditions this is not true for all women. The committee considered that many women with mild heart disease can be reassured that a normal vaginal birth is safe.

Impact of the recommendations on practice

It is thought that the recommendations largely reflect current UK practice. The committee recognised that most women with more severe heart disease are already managed in large obstetric-led units by clinical teams with experience in this area. By attempting to define the conditions which pose the highest risk, the recommendations may result in further centralisation of specialist services.

Women with pulmonary hypertension are already offered care in specialist centres. Pregnancy and childbirth hold such serious risks for women with this condition and the committee agreed that liaison with specialist respiratory physicians was essential.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The following outcomes were prioritised for this review.

Mortality and major morbidity for either the woman or the baby were prioritised as critical outcomes as these are extreme adverse outcomes which could result from inappropriate planning for mode of labour. Women's satisfaction with labour and birth was considered as an important outcome to emphasise the fact that women's values, wishes and expectations should be taken into account when planning mode of birth. Emergency caesarean section was also regarded as an important outcome because this was a good indicator of unsuitable planning for mode of birth.

The quality of the evidence

No experimental comparative studies were identified. One retrospective cohort study was identified. The quality was assessed with GRADE and was rated as very low. The population studied was heterogeneous with different underlying cardiac diagnoses, and there was no stratified analysis by severity of disease or by cardiac condition. Moreover, in the planned vaginal birth group there was a higher percentage of women with NYHA class 1 and a lower percentage with NYHA class 2, 3 and 4 compared to the group planning a caesarean section for cardiac reasons, although the study did not mention whether the difference was statistically significant. The study showed that there was a statistically significant difference in NYHA class, type of heart disease, pre-eclampsia and anticoagulation between the planned vaginal birth group and group planning a caesarean section (for either cardiac or obstetric reasons). Therefore, there was high risk of selection bias. The study authors did not adjust for any important factors in the comparison of planned caesarean section versus planned vaginal birth, therefore there was high risk of comparability bias.

Benefits and harms

Based on their clinical expertise, the committee suggested that all women with cardiac conditions should have an individualised birth plan after multidisplinary discussion involving a cardiologist with expertise in managing cardiac conditions during pregnancy. This expertise would also be available during labour in an obstetric unit.

The committee agreed that a planned caesarean section or induction of labour should be considered for women with mechanical heart valves because this would make management of anticoagulation easier, with the potential to minimise the length of time off anticoagulation.

The committee expressed their view that if the woman was confirmed to have a cardiac condition of WHO class 1 or NYHA functional class I, the pregnancy could be considered as low risk and it could be managed in line with the NICE guideline on (CG190). The committee agreed that there was no evidence to guide how long a woman with a cardiac condition should actively push during the second stage of labour and that where possible they would want to proceed as for a woman without a cardiac condition to give the woman a chance of a vaginal birth. Current practice for women having a vaginal birth would be to set a time limit of perhaps 1 or 2 hours if a woman had a low-risk cardiac disease, but for some women (for example, multiparous women) labour might progress easily and then the obstetrician should use clinical judgement in deciding how long active pushing should continue without further intervention (instrumental birth or emergency caesarean section).

The committee considered 3 groups of women to be at greater risk of poor outcomes due to active pushing in the second stage of labour. These were: women with any disease of the aorta assessed as high risk because of the risk of aortic dissection; women with pulmonary arterial hypertension; and women with a functional status of NYHA class III or IV. The committee agreed that such women should be offered a planned caesarean section because an active second stage of labour might be detrimental to their cardiac condition. However, the committee recognised that this might be unacceptable to some women who wished to have a vaginal birth. The committee provided clarification to specify that such women should not actively push at all, and instead be offered assistance in the form of an instrumental birth in the second stage of labour. The committee noted that women should be made aware of the greater chance of an emergency caesarean section in such circumstances.

The committee discussed particular cardiac conditions where recommendations were needed. Women with pulmonary arterial hypertension were considered to be at very high risk of catastrophic outcomes. Therefore advice should be sought from one of the specialist centres in the UK as there is a lower mortality rate for women with this condition when such centres are consulted about care throughout pregnancy and birth.

Cost effectiveness and resource use

Clinical evidence was limited and the committee made a qualitative assessment of cost effectiveness.

The committee's recommendations were intended to facilitate a choice of vaginal birth in women with mild heart disease where it would be considered safe. They reasoned that this could reduce the costs associated with unnecessary intervention. However, the recommendations also reflected that there were some women in whom a vaginal birth would be contraindicated on safety grounds.

Pulmonary hypertension is a life-threatening condition and the committee reasoned that a specialist setting and expert management would be cost effective in that context.

The committee considered that the recommendations largely reflected current practice and they did not anticipate that they would have a significant resource impact to the NHS. They acknowledged that their recommendations might lead to a further centralisation of services for those heart conditions which are thought to pose the highest risk. Other factors the committee took into account

Despite the low quality of the evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding the mode of birth for women with heart disease.

Intrapartum care for women with cardiac disease – fluid management

Review question

Which women with cardiac conditions need additional haemodynamic monitoring or management during childbirth: input–output chart of fluid balance with a urinary catheter or urometer; invasive monitoring using an arterial line and central venous pressure; cardiac output monitoring; fluid restriction?

Introduction

The aim of this review is to determine which women with cardiac disease who are in the peripartum period require more specialist haemodynamic monitoring to avoid issues with circulating blood volume.

Summary of the protocol

See Table 7 for a summary of the population, intervention, comparison and outcomes (PICO) characteristics of this review.

Table 7: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the intrapartum period
Intervention	Fluid monitoring using one or more of: Intervention 1: • input–output chart of fluid balance with a urinary catheter or urometer (hourly monitoring) Intervention 2: • invasive monitoring using an arterial line and/or central venous pressure Intervention 3: • cardiac monitoring (ECG, pulmonary artery thermodilution via a pulmonary artery floatation catheter (PAFC), lithium dilution cardiac output (LiDCO), pulse contour analysis systems (PiCCO and FloTrac), oesophageal Doppler and other ultrasound Doppler techniques (USCOM),thoracic bioreactance based techniques (NICOM), trans-thoracic and trans-oesophageal echo)
Comparison	Comparison 1: • No haemodynamic monitoring (for milder groups, WHO 1 and 2) Comparison 2: • Invasive versus non-invasive monitoring (ECG, input-output, oxygen saturation, non-invasive blood pressure (NIBP; for more severe groups, WHO 3 and 4)
Outcomes	For the woman: • mortality

	• major morbidity (pulmonary oedema, renal impairment, acute kidney injury, infection, complications of central venous) cannulation (haematoma, pneumothorax, or air embolus), or inotropic and mechanical heart support) • unexpected admission to intensive treatment unit (ITU) • women's satisfaction with labour and birth (including psychological wellbeing) • emergency caesarean section For the baby: • mortality • major morbidity (respiratory distress, or encephalopathy)

ECG: Electrocardiogram; WHO: World Health Organization

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

No clinical evidence was identified for this review.

See the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are provided in Appendix D.

Summary of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so there are no evidence tables in Appendix E). No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so no quality assessment was undertaken and there are no GRADE tables in Appendix G).

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

No clinical evidence was identified for this review.

Recommendations

C19. During pregnancy, plan the management of fluid balance during the intrapartum period for women with heart disease with the multidisciplinary team (outlined in recommendation B2). The team should include a cardiologist with expertise in managing heart disease in pregnant women. Multidisciplinary discussion should include:

- how the condition affects fluid balance
- optimum fluid balance and how this might be achieved
- plans for risk assessment and monitoring.

C20. Identify women with heart disease for whom fluid balance is critical to cardiac function. These include women with:

- severe left-sided stenotic lesions (for example, aortic stenosis and mitral stenosis)
- hypertrophic cardiomyopathy
- cardiomyopathy with systolic ventricular dysfunction
- pulmonary arterial hypertension
- Fontan circulation and other univentricular circulations
- NYHA class IV heart disease.

C21. For women with heart disease in whom fluid balance is critical for optimal cardiac function, offer tailored monitoring and clinical review during the intrapartum period, and consider escalation as follows:

- hourly monitoring of fluid input and output (with at least 4-hourly assessment by a senior healthcare professional), blood pressure, pulse, respiratory rate and oxygen saturation
- continuous electrocardiogram (ECG) and pulse oximetry with interpretation by trained staff
- continuous intra-arterial blood pressure monitoring
- cardiac output monitoring with non-invasive techniques, or serial echocardiography by trained staff.

C22. Offer standard fluid management during the intrapartum period for women with WHO 1 and NYHA class I heart disease.

C23. Consider standard fluid management during the intrapartum period for women with WHO 2 to 3, or NYHA class II to III heart disease after a multidisciplinary discussion (outlined in recommendation B1).

Research recommendations

Is point of care, focused echocardiography superior to standard care (clinical evaluation, JVP/CVP) for prediction of fluid responsiveness in peripartum women with cardiac disease?

Rationale and impact

Why the committee made the recommendations

In the absence of evidence, the committee used their knowledge and experience to make recommendations for haemodynamic monitoring for women with heart disease during birth. Risk assessment and planning of intrapartum monitoring needs specialist multidisciplinary input. Discussions should take place during pregnancy and involve the woman so that she knows how her condition might be affected by changes in blood pressure, and blood volume, and fluid shifts during labour and birth and the type of monitoring needed to manage this. For women with mild heart disease, management of fluid balance does not mean a change from standard care. For those with more severe conditions standard care may still be suitable but decisions need to be based on specialist assessment of the type and severity of the condition and the woman's views. There are some heart conditions in which fluid balance is critical to cardiac function and frequent monitoring and assessment by an experienced clinician are needed as a minimum. For these conditions more invasive monitoring may also be needed.

Impact of the recommendations on practice

The committee agreed that specialist planning for intrapartum monitoring to identify the monitoring needs of women with different heart conditions together with stepped escalation of monitoring intensity would reduce variation in practice. It would allow NHS resources to be directed more effectively to reduce morbidity and mortality associated with fluid management during the intrapartum period for women with cardiac conditions and their babies. Women's experience of labour and birth would be improved through their involvement in management discussions and because they would receive a level of intervention appropriate to their needs taking their priorities for birth into account where possible.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Mortality for the woman and the baby were considered to be critical outcomes because poor assessment of cardiac function during labour among women with cardiac conditions could increase maternal and neonatal deaths. Major morbidity for the woman (pulmonary oedema, renal impairment, acute kidney injury, infection or complications of central venous cannulation such as haematoma, pneumothorax, air embolus; inotropic and mechanical

heart support) and major morbidity for the baby (respiratory distress or encephalopathy) were also regarded as critical outcomes as inappropriate management for women with cardiac conditions in labour could expose the women and their babies to life-threatening complications.

Unexpected admission to ITU for the woman was considered to be an important outcome because although relatively subjective it is a good and common indicator of medical or obstetric emergencies. In addition, women's satisfaction with labour and birth, including psychological wellbeing, was agreed to be an important outcome to highlight that care in labour should centre on the woman.

The quality of the evidence

No clinical evidence was identified for this review.

Benefits and harms

Fluid balance is of vital importance to women with cardiac disease, and fluid overload or hypovolaemia is to be avoided. In those heart conditions most affected by fluid changes, the consequences of mistakes in fluid balance can be death or severe morbidity from heart failure leading to pulmonary oedema (fluid in the lungs) and inadequate blood supply to the vital organs. Invasive monitoring is also associated with serious harms for the woman. The committee agreed that as a minimum, and consistent with other recommendations, best practice would be the definition of an intrapartum fluid monitoring and management plan during the antenatal period drawing upon multidisciplinary expertise and involving the woman. This is because for some heart conditions achieving fluid balance is critical to ensuring optimal heart function and the woman's wellbeing, but for others, fluid management is not as important. Therefore risk assessment is dependent on the diagnosis and may affect the woman's birth plans, for example, some cardiac conditions would require monitoring that necessitates birth in theatre or ITU and not on the labour ward.

The benefits of achieving optimal fluid balance during the intrapartum period are in attaining the best possible cardiac function for the woman during the physiologically and haemodynamically stressful period of labour and birth, and in minimising the risk of potential harms of imbalances and complications arising from these and impaired cardiac function. The committee recognised that there is a stratification of monitoring invasiveness that would correlate with the type and severity of the cardiac condition and the increasing expertise needed to perform and interpret assessments as the basis for clinical decisions.

The committee discussed which heart conditions would be of most concern, acknowledging that the recommendations would only be relevant to those in which fluid management is important. It was concluded that these would not precisely match the WHO or NYHA functional classification but there were several conditions where achieving euvolaemia would be critical to optimal cardiac function and that an individualised approach was key. The fluid balance of women with pulmonary arterial hypertension is of particular concern because of the likelihood of poor outcomes and must be managed in conjunction with a national pulmonary hypertension unit.

During the intrapartum period, women with heart conditions are at risk of pulmonary oedema and therefore it is vital that monitoring is tailored individually and results interpreted by trained staff, including a senior clinician.

The committee wanted to minimise intervention where possible, agreeing that women with the least severe heart conditions as defined by WHO 1 and NYHA class I would not require

additional fluid management because observations regarding fluid balance would be performed routinely and escalated if necessary as part of standard care.

The committee agreed that broad recommendations for women with WHO 2 or 3, and NYHA class II or III heart conditions should not be made as a woman's individual capacity to cope with haemodynamic shifts during the intrapartum period would vary, as would her priorities regarding the birth plan. Hence an individualised approach to management would be more appropriate incorporating the woman's views as well as advice from the obstetrician and anaesthetist providing care.

Cost effectiveness and resource use

No clinical evidence was identified for this review and the committee made a qualitative assessment of cost effectiveness.

The committee considered that standard care was all that was required for women with mild heart disease and even, subject to specialist assessment, for some women with more severe conditions. They considered that their recommendations would help prevent over-medicalisation and unnecessary intervention in the intrapartum period.

However, the committee also recognised that the increased resource use of more intensive monitoring and senior clinical input was likely to be cost effective when fluid balance is critical to cardiac function.

The committee considered that the recommendations would reduce variation in practice and that NHS resources would be better targeted as a result. They did not anticipate that the recommendations would have a significant resource impact for the NHS.

Other factors the committee took into account

Because of the lack of evidence, the committee chose to make a research recommendation about how the woman's fluid balance should be assessed to guide fluid management. See Appendix L for further details.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Review question

What is the most appropriate method of diagnosis for women with suspected cardiomyopathy in labour?

Introduction

The aim of this review is to identify whether biomarker or clinical indications of cardiomyopathy are predictive of the condition to the extent that they necessitate urgent – rather than routine – referral to a cardiologist.

Summary of the protocol

See

Table **8:** **Summary of the protocol (PIRO) table**

Population	Any of: • pregnant women with suspected cardiomyopathy • women in labour with suspected cardiomyopathy • women in the postpartum period with suspected or confirmed cardiomyopathy up to 6 months postpartum
Index test	Biomarkers/enzymes: Index test 1 • Brain natriuretic peptide (BNP) Clinical history or observation: Index test 2 • Orthopnoea Index test 3 • Breathlessness at rest Index test 4 • Pulmonary oedema Index test 5 • Tachycardia Index test 6 • Hypotension Index test 7 Systemic oedema
Reference standard/ Target condition	Reference standard 1 • Peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation (by a cardiologist) Reference standard 2 Maternal mortality due to peripartum cardiomyopathy

Outcomes	For diagnostic comparisons: • sensitivity • specificity • positive and negative likelihood ratios For prognostic comparisons: measures of association (risk ratios, odds ratios or hazard ratios) between prognostic factors and peripartum cardiomyopathy defined as above or related maternal mortality

1 For a summary of the population, index test, (diagnostic) reference standard and outcomes
2 (PIRO) characteristics of this review.

3 **Table 8: Summary of the protocol (PIRO) table**

Population	Any of: • pregnant women with suspected cardiomyopathy • women in labour with suspected cardiomyopathy • women in the postpartum period with suspected or confirmed cardiomyopathy up to 6 months postpartum
Index test	Biomarkers/enzymes: <u>Index test 1</u> • Brain natriuretic peptide (BNP) Clinical history or observation: <u>Index test 2</u> • Orthopnoea <u>Index test 3</u> • Breathlessness at rest <u>Index test 4</u> • Pulmonary oedema <u>Index test 5</u> • Tachycardia <u>Index test 6</u> • Hypotension <u>Index test 7</u> Systemic oedema
Reference standard/ Target condition	<u>Reference standard 1</u> • Peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation (by a cardiologist) <u>Reference standard 2</u> Maternal mortality due to peripartum cardiomyopathy

Outcomes	For diagnostic comparisons: • sensitivity • specificity • positive and negative likelihood ratios For prognostic comparisons: measures of association (risk ratios, odds ratios or hazard ratios) between prognostic factors and peripartum cardiomyopathy defined as above or related maternal mortality

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

Three studies (two prospective and one retrospective case-control studies) were included in this review (see 'Summary of clinical studies included in the evidence review').

All studies included women who first presented with symptoms of heart failure during their pregnancy or within 9 months post-partum (Haghikia 2013, Fett 2011, Karaye 2016). The outcomes of these women were compared with those from women with normal cardiac function.

Evidence from the studies included in the review is summarised below (see 'Quality assessment of clinical studies included in the evidence review').

Data was reported on the following index tests, BNP, orthopnoea, pulmonary oedema, tachycardia or systemic oedema to diagnose peripartum cardiomyopathy. Echocardiogram plus expert clinical interpretation was used as a reference standard. There was no evidence identified for the following index tests: breathlessness at rest and hypotension.

There was no evidence identified for any prognostic index test to predict peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation or maternal mortality due to peripartum cardiomyopathy.

See also the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in Appendix D.

Summary of clinical studies included in the evidence review

Table 9 provides a brief summary of included studies.

Table 9: Summary of included studies

Study	PPCM women	Control women	Index test	Definition of cardiomyopathy
Fett 2011 Retrospective case-control study N=57 USA	n=47 women with idiopathic first onset heart failure during last month of pregnancy up to 6 months postpartum	n= 10 earlier pregnancies of women with PPCM or their friends or relatives	• Orthopnoea • Palpitation • Ankle oedema • Weight gain • Unexplained cough	Heart Failure Left ventricular ejection fraction of ≤ 45% by echocardiogram
Haghikia 2013 Prospective case-control study N=115 Germany	n=69 women with idiopathic peripartum cardiomyopathy	n=19 healthy postpartum women with normal cardiac function (defined by LVEF > 55%)	• NTproBNP at baseline	Left ventricular ejection fraction of ≤ 45%
Karaye 2016 Prospective case-control N=131 South Africa	n=54 women with cardiomyopathy near end of pregnancy and within 9 months postpartum control Note - Serum K+ and Na+ levels were significantly lower in PPCM	n=77 women in 9-month postpartum period with no history of cardiac disease or hypertension and with normal ECG	• Heart rate assessed by using ECG	Left ventricular ejection fraction < 50% by echocardiogram

N: total number of participants; ECG: echocardiogram; K+: potassium, Na+: Sodium; NTproBNP: N-terminal prohormone of brain natriuretic peptide; PPCM: peripartum cardiomyopathy; LVEF: left ventricular ejection fraction

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question is presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Diagnostic index tests for peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation (by a cardiologist)

BNP

Very low quality evidence from one prospective case control study (n=88) found that there is a statistically significant increase in NTproBNP levels among women with peripartum cardiomyopathy compared with the control group at the time of diagnosis of peripartum cardiomyopathy. The uncertainty around the result and its clinical significance could not be estimated.

Orthopnoea

Very low quality evidence from a retrospective case-control study (N=57) reported that orthopnoea was very useful for 'ruling in' (very serious imprecision) and 'ruling out' (no serious imprecision) peripartum cardiomyopathy. Sensitivity was 96% (95% CI: 85-99) and specificity was 100% (95% CI: 69-100).

Pulmonary oedema: unexplained cough

Very low quality evidence from a retrospective case-control study (N=57) reported that unexplained cough was moderately useful for 'ruling in' (serious imprecision) and not useful for 'ruling out' (serious imprecision) peripartum cardiomyopathy. Sensitivity was 72% (95% CI: 58-84) and specificity was 90% (95% CI: 56-100).

Tachycardia: heart rate ≥100 beats per minute

Very low quality evidence from one prospective case-control study (N=131) suggested that tachycardia (detected by electrocardiogram) was not useful for 'ruling in' (no serious imprecision) and not useful for 'ruling out' (no serious imprecision) peripartum cardiomyopathy. Sensitivity was 67% (95% CI: 53-79) and specificity was 78% (95% CI: 67-87).

Tachycardia: palpitation

Very low quality evidence from one retrospective case-control study (n=56) reported that palpitation was very useful for 'ruling in' (very serious imprecision) but not useful for 'ruling out' (serious imprecision) peripartum cardiomyopathy. Sensitivity was 77% (95% CI: 62-88) and specificity was 100% (95% CI: 63-100).

Systemic oedema: ankle oedema

Very low quality evidence from a retrospective case-control study (N=57) reported that ankle oedema was not useful for 'ruling in' (no serious imprecision) but moderately useful for 'ruling out' (very serious imprecision) peripartum cardiomyopathy. Sensitivity was 96% (95% CI: 86-100) and specificity was 30% (95% CI: 7-65).

Systemic oedema: weight gain in last month of pregnancy (>2 pounds per week)

Very low quality evidence from a retrospective case-control study (N=57) reported that weight gain of more than 2 pounds per week in last month of pregnancy was not useful for 'ruling in' (serious imprecision) and not useful for 'ruling out' (serious imprecision) peripartum cardiomyopathy. Sensitivity was 69% (95% CI: 83-92) and specificity was 70% (95% CI: 35-93).

Recommendations

See the recommendations in the Intrapartum care for women with cardiac disease - management for women with peripartum cardiomyopathy section.

Research recommendations

See the research recommendations in the Intrapartum care for women with cardiac disease - management for women with peripartum cardiomyopathy section.

Rationale and impact

See the rationale and impact in the intrapartum care for women with cardiac disease - management for women with peripartum cardiomyopathy section.

The committee's discussion of the evidence

See The committee's discussion of the evidence for the review question about management of peripartum cardiomyopathy.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Review question

What is the optimal management for women with peripartum cardiomyopathy in labour?

Introduction

The aim of this review is to compare standard management of cardiomyopathy to standard management plus either bromocriptine or cabergoline; these are the pharmaceutical interventions around which there is most important clinical disagreement.

Summary of the protocol

See Table 10: Summary of the protocol (PICO) table for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 10: Summary of the protocol (PICO) table

Population	Pregnant women who develop symptoms of cardiac failure (secondary to cardiomyopathy) before, during or up to 48 hours after labour
Intervention	Intervention 1: • Bromocriptine in addition to standard care Intervention 2: • Cabergoline in addition to standard care
Comparison	Comparison 1: • Standard care
Outcomes	For the woman: • mortality • recovery of ventricular function measured by left ventricular ejection fraction (at 6 weeks to 1 year) • major morbidity • women's satisfaction with labour and birth (including psychological wellbeing) • women's health related quality of life For the baby: • mortality • major morbidity

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

C Clinical evidence

2 Included studies

3 One randomised controlled trial was included in this review (see 'Summary of clinical studies
4 included in the evidence review').

5 This study compared bromocriptine plus standard treatment with standard treatment alone in
6 women with peripartum cardiomyopathy (Sliwa 2010).

7 Evidence from the studies included in the review is summarised below (see 'Quality
8 assessment of clinical studies included in the evidence review').

9 Data was reported on the critical outcomes of the woman, mortality, recovery of ventricular
10 function (measured by left ventricular ejection fraction (LVEF) < 35%) and major morbidity
11 (New York Heart Association (NYHA) III/IV class at 6 months follow-up; adverse events
12 including thromboembolism at 6 month follow-up) as well as the critical outcome of the baby,
13 mortality. There was no evidence identified for other outcomes for the woman, major morbidity
14 (important outcome), women's satisfaction with labour and birth (important outcome) and
15 women's health related quality of life (of limited importance outcome). There was no evidence
16 identified for the important outcome of the baby, major morbidity.

17 There was no evidence identified for the following intervention, cabergoline in addition to
18 standard care.

19 See also the study selection flow chart in Appendix C.

2 Excluded studies

21 Studies not included in this review with reasons for their exclusions are provided in Appendix
22 D.

2 Summary of clinical studies included in the evidence review

24 Table 11 provides a brief summary of included studies.

25 **Table 11 Summary of included studies**

Study	Population	Intervention/Comparison	Outcomes
Sliwa 2010 RCT South Africa	N=20 women with new-onset symptomatic peripartum cardiomyopathy and a LV ejection fraction (LVEF) <35%	• Bromocriptine (2.5 mg bd for 2 weeks followed by 2.5 mg od for 6 weeks) in addition to standard treatment (n=10) • Standard treatment which included frusemide and enalapril ± carvedilol and warfarin (n=10)	For the woman: • Mortality • LVEF <35% at 6 months follow-up • NYHA class III/IV at 6 months follow-up For the baby: • Mortality

26 *N: Total number of participants in each study; bd: twice daily; od: once daily; LVEF: left ventricular ejection*
27 *fraction; n: total number of participants; NYHA: New York Heart Association; mg: milligrams*

28 See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this
29 review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profiles for this review question are presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Bromocriptine plus standard treatment versus standard treatment alone

Outcomes for the woman

Mortality

Very low quality evidence from one randomised controlled trial (N=20) reported that there was no clinically important difference between bromocriptine plus standard treatment and standard treatment alone for maternal mortality at 6 months follow-up.

Recovery of ventricular function measured by left ventricular ejection fraction

Very low quality evidence from one randomised controlled trial (n=15) reported that there was no clinically important difference between bromocriptine plus standard treatment compared with standard treatment alone for left ventricular ejection fraction < 35% at 6 months follow-up.

Major morbidity: NYHA III/IV class

Very low quality evidence from one randomised controlled trial (n=15) reported that there was no clinically important difference between bromocriptine plus standard treatment or standard treatment alone for the risk of having NYHA class III or IV at 6 months follow-up.

Major morbidity: adverse events including thromboembolism

Moderate quality evidence from one randomised controlled trial (N=20) reported that there was no adverse event including thromboembolism in either the bromocriptine plus standard treatment or standard treatment alone at 6 months follow-up.

Outcomes for the baby

Mortality

Moderate quality evidence from one randomised controlled trial (N=20) reported that there was no neonatal death in either bromocriptine plus standard therapy or standard therapy alone at 6 months follow-up.

Recommendations

C24. Take a cardiac-specific history and suspect heart failure if there is not another likely cause of any of the following symptoms:

- breathlessness when lying down (ruling out aortocaval compression) or at rest
- unexplained cough, particularly when lying down or which produces frothy pink sputum
- paroxysmal nocturnal dyspnoea – being woken from sleep by severe breathlessness and coughing which may be productive of pink frothy sputum, and is improved by moving to an upright position
- palpitation (awareness of persistent fast heart rate at rest).

C25. Consider heart failure in the intrapartum period if there are any of the following symptoms and signs:

- pale, sweaty, agitated with cool peripheries
- heart rate persistently greater than 110 beats per minute at rest
- respiratory rate persistently greater than 20 breaths per minute at rest
- hypotension (systolic blood pressure <100mmHg)
- oxygen saturation less than 95% on air
- elevated jugular venous pressure
- added heart sound or murmur
- reduced air entry, basal crackles and wheeze, on listening to the chest.

C26. If any of the symptoms or signs in recommendations C24 and C25 suggest heart failure, a consultant should review the woman's condition without delay.

C27. When there is a clinical suspicion of heart failure in any woman in the intrapartum period:

- establish peripheral venous access
- measure urea and electrolytes, and perform a full blood count
- measure arterial blood gases
- perform an ECG
- perform a chest X-ray.

C28. If clinical suspicion of heart failure in the intrapartum period cannot be ruled out by the investigations in recommendation C27, arrange:

- review by a cardiologist (with interim review by a healthcare professional with expertise in this area if a cardiologist is not immediately available)

- a transthoracic echocardiogram by a trained technician or cardiologist
- measurement of N-terminal pro-brain natriuretic peptide (NT-proBNP) levels.

C29. Consider early birth for women with heart failure due to cardiomyopathy, depending on the severity of the condition and how well the condition has responded to treatment.

C30. Optimise treatment for heart failure as soon as possible after birth even if the woman is breastfeeding.

C31.If clinical suspicion of heart failure persists after birth, consider cardiac MRI scan.

Research recommendations

Can near patient BNP testing diagnose cardiomyopathy?

Is there a role for bromocriptine in the management of peripartum cardiomyopathy?

Rationale and impact

Why the committee made the recommendations

Although most of recommendations were based on the committee's experience because of the limited evidence, there was some evidence to inform the recommendations on heart rate and using NT-proBNP levels. The committee agreed that symptoms and signs suggesting heart failure should be assessed initially by a member of the obstetric team and if present, confirmed by a consultant. When clinical examination raises the suspicion of heart failure, imaging and blood tests are required to assist review by a cardiologist or the most senior available physician to make a definitive diagnosis. This recommendation arises from evidence from the confidential enquiry into maternal mortality in the UK, that the diagnosis may be missed or delayed.

The committee made recommendations to support prompt and accurate diagnosis of heart failure because it is difficult to distinguish between the symptoms and signs of the normal physiological changes of late pregnancy and the pathological symptoms and signs of heart failure. A basic but thorough history and examination are key to identifying women who are at risk and the committee wanted to stress the importance of these.

Although heart failure in the intrapartum period is rare, it is an important cause of maternal mortality. Prompt medical management is needed to stabilise the woman's immediate condition but a change to the obstetric management may also be necessary to improve or limit worsening of her heart condition.

Impact of the recommendations on practice

The recommendations largely reflect current best practice. The committee agreed they should reinforce practice as well as improving postnatal prescribing and encouraging these women to breastfeed.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

This section includes the committee's discussion of the evidence for the review question about diagnosis of peripartum cardiomyopathy.

For the review about diagnosis of cardiomyopathy, the committee prioritised maternal mortality from cardiac failure and major maternal morbidity caused by cardiomyopathy as the most important target conditions for detection or prediction. The sensitivity and specificity of symptoms and signs of heart failure were considered against the gold standard investigation for the diagnosis of peripartum cardiomyopathy, namely echocardiography.

For the review about management of cardiomyopathy, clinical outcomes for the woman and the baby were prioritised for review.

Mortality for the woman and the baby were considered as critical outcomes because poor management of cardiomyopathy could lead to unnecessary maternal and neonatal deaths. Recovery of maternal ventricular functions at 6 weeks to 1 year postpartum, measured by left ventricular ejection fraction, was also regarded as a critical outcome to assess the functional improvement of cardiomyopathy by the intervention.

Major morbidity for the woman and the baby were considered to be important outcomes as they are good indicators of inadequate management of cardiomyopathy during labour. Women's satisfaction of labour and birth was regarded as an important outcome to highlight that care should be centred on the woman.

The quality of the evidence

For the review about diagnosis of cardiomyopathy, 3 case-control studies with moderate to high risk of bias were included. Other limitations were that the definitions varied and the assessment of cardiac function in the control group was not reported. There were also wide confidence intervals around likelihood ratio estimates and lack of adjustment for confounders in prognostic studies. Overall, the GRADE assessment of the evidence was that it was of very low quality.

For the review about management of cardiomyopathy, 1 randomised study with moderate risk of bias was included. A Cochrane checklist for randomised trials was used to assess the quality of the evidence. The reasons for downgrading the evidence were lack of allocation concealment and lack of blinding to care providers. Moreover, the 95% confidence interval for relevant point estimates were very wide and the evidence was appraised as imprecise. Overall, the GRADE assessment of the evidence ranged from very low to moderate.

Benefits and harms

In the experience of the committee, a pregnant woman with orthopnoea, paroxysmal nocturnal dysnoea, palpitation or unexplained cough particularly with a pink frothy sputum would suggest heart failure. These were also highlighted in a recent MBRRACE-UK report as important symptoms and signs in pregnant women which should always be fully investigated. The diagnostic evidence for orthopnoea did not contradict this view, but only partially supported it. Similarly for breathlessness, the more certain evidence was that not being breathless was a useful indication that the woman did not have heart failure.

The committee also discussed that a persistent respiratory rate of more than 20 breaths per minute would be a useful indicative sign of heart failure for clinicians. Based on their clinical judgement, they also agreed that a persistently raised heart rate of 110 beats per minute would be a useful indicative sign for clinicians. One of the difficulties in identifying heart failure lies in drawing a distinction between the symptoms and signs of normal physiological pregnancy and labour and those due to peripartum cardiomyopathy. For example, the committee acknowledged that the most common cause of breathlessness and tachycardia would probably be maternal anxiety. However, anxiety is likely to be ameliorated with reassurance and there is a discernible difference between anxiety-related high respiratory and heart rates and persistent signs indicative of cardiomyopathy. Although the confidence intervals were wide for the available evidence for unexplained cough as an indicator of heart failure, this evidence was moderately useful in the detection of peripartum cardiomyopathy. The committee did not consider signs of systemic oedema (ankle oedema or weight gain) to be sufficiently discriminatory to include in their recommendations.

Thus, the committee made a recommendation that if a woman presented with any symptom or sign indicative of heart failure, a prompt review should be performed by a consultant. Once clinically confirmed, investigations to confirm the diagnosis, assess the severity of heart failure and support the further management should follow. These would include ECG, arterial blood gases, chest X-ray, urea and electrolytes and full blood counts Additionally, emergency management such as peripheral venous assess should be in place. On the other hand, if clinical suspicion of heart failure cannot be ruled out by subsequent investigations, a review by a cardiologist or a healthcare professional with expertise in this area should be arranged. At the same time, transthoracic echocardiogram with interpretation by a trained technician or cardiologist as well as measurement of NT-proBNP levels should be arranged. Meanwhile, treatment for heart failure should be initiated. It should be noted that angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor blockers (ARBs) and spironolactone are contraindicated in pregnancy (NICE guidance on hypertension in pregnancy: diagnosis and management [CG107]).

The committee also suggested considering early birth for women with heart failure depending on the severity of the condition and treatment responsiveness. They recommended continuing heart failure treatment with medication compatible with breastfeeding in the postpartum period. If the heart failure persisted after the birth, a cardiac MRI scan should be performed.

The committee provided additional detail to justify the recommendations. Echocardiography was recognised in the MBRRACE-UK report on maternal deaths to be an important tool in the assessment of a critically sick pregnant or postpartum woman to make diagnoses and prevent inappropriate treatment, and therefore a recommendation was made to use it to identify suspected heart failure. Its particular usefulness in distinguishing critical presentations of peripartum cardiomyopathy was noted, although it requires skilled interpretation by an operator familiar with the normal cardiac changes of pregnancy. Although the evidence for NT-proBNP testing was not conclusive and of very low quality, the committee recognised that this was a commonly used test to identify heart failure outwith the obstetric setting and concluded that it could be useful to identify heart failure due to peripartum cardiomyopathy with expert interpretation.

The MBRRACE-UK surveillance report published in 2018 found that only 17% of women who died of cardiac conditions were known to have pre-existing cardiac problems and that one third of women who died of myocardial disease or cardiomyopathy had peripartum cardiomyopathy. Delays in diagnosis and missed diagnosis were highlighted in fatalities due to peripartum cardiomyopathy. Therefore, although cardiomyopathy is rare, it is an important

cause of maternal mortality and there is a need for clinical alertness to rule it out or seek prompt diagnostic confirmation to permit management.

The committee agreed with conclusions from the MBRRACE-UK surveillance report published in 2018 that pregnancy can make the differential diagnoses of critical illness more complex and that a balance between appropriate clinical suspicion and a conclusive diagnosis is necessary. The committee made recommendations in support of this to explain the steps that should be taken when symptoms and signs noticed from the clinical history raise initial suspicion of heart failure due to peripartum cardiomyopathy and to clarify that initial clinical suspicion should trigger review including clinical examination and further investigations by a senior clinician with final diagnosis being undertaken by a cardiologist or the most senior available physician to avoid delays if the cardiologist is not immediately available.

Cost effectiveness and resource use

There was limited evidence for these reviews and the committee made a qualitative assessment of cost effectiveness.

Heart failure is an important cause of maternal mortality and often occurs in women who were not known to have a pre-existing heart condition. The recommendations are intended to mitigate the risks of maternal mortality and morbidity and the committee believed that the potential impact in reducing adverse outcomes made it likely that they were cost effective. They considered it important that imaging and blood tests be undertaken when a clinical examination raises the suspicion of heart failure as, otherwise, the diagnosis may be missed or delayed.

The committee considered that the recommendations largely reflect current best practice. Furthermore, they noted that heart failure in the intrapartum period is rare. Therefore, they did not anticipate that the recommendations would have a significant impact on NHS resources.

Other factors the committee took into account

For the review about diagnosis of cardiomyopathy, the limited evidence prompted the committee to make a research recommendation to examine the value of BNP for diagnosing cardiomyopathy. See Appendix L for further details.

For the review about management of cardiomyopathy, the current evidence was limited to studies with a very small sample size. Therefore, the committee decided to make a research recommendation to evaluate the effectiveness and safety of bromocriptine in the management of peripartum cardiomyopathy. See Appendix L for further details.

Intrapartum care for women with cardiac disease – anaesthesia

Review question

Is regional or general anaesthesia safer for women with cardiac disease for peripartum surgical procedures including caesarean section?

Introduction

The aim of this review is to examine outcomes for the woman and baby comparing regional with general anaesthesia. This is important because women with cardiac disease may not be able to tolerate acute changes in heart rate and blood pressure which can occur with use of both regional and general anaesthesia.

Summary of the protocol

See Table 12 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 12: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the intrapartum period
Intervention	General anaesthesia
Comparison	Regional anaesthesia (spinal, epidural, or CSE)
Outcomes	For the woman: • mortality • major morbidity (including perioperative cardiovascular collapse, stroke, hypotension, cardiac arrest, hypertension, intracranial haemorrhage, or myocardial infarction) • women's satisfaction with labour and birth (including psychological wellbeing) • need for a high dependency unit (HDU) or intensive treatment unit (ITU) • re-admission to hospital within 6 weeks of birth • duration of hospital stay For the baby: • mortality • major neonatal morbidity (including ischaemic encephalopathy) • unexpected admission to a neonatal unit

CSE: sombined spino-epidural

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

C Clinical evidence

2 Included studies

3 One systematic review of case series was included in the review (see 'Summary of clinical
4 studies included in the evidence review').

5 The systematic review compared regional anaesthesia with general anaesthesia in women
6 with pulmonary arterial hypertension (Bédard 2009).

7 Evidence from the studies included in the review is summarised below (see 'Quality
8 assessment of clinical studies included in the evidence review').

9 Data were reported on the critical outcome for the woman, mortality. There was no evidence
10 identified for the following outcomes for the woman: major morbidity (critical outcome),
11 women's satisfaction with labour and birth (critical outcome), need for a high dependency
12 unit (HDU) or intensive treatment unit (ITU) (important outcome), re-admission to hospital
13 within 6 weeks of birth (important outcome) and duration of hospital stay (outcome of limited
14 importance). There was no evidence identified for the following important outcomes for the
15 baby: mortality, major neonatal morbidity and unexpected admission to a neonatal unit.

16 See also the study selection flow chart in Appendix C.

17 Excluded studies

18 Studies not included in this review with reasons for their exclusions are provided in Appendix
19 D.

20 Summary of clinical studies included in the evidence review

21 Table 13 provides a brief summary of included studies.

22 **Table 13: Summary of included studies**

Study	Population	Intervention/comparison	Outcomes	Comments
Bédard 2009 Systematic review of case reports/case series Various countries	N=53 pregnant women with pulmonary arterial hypertension (PAH) giving birth by caesarean section	• Regional anaesthesia (n=30) • General anaesthesia (n=23)	For the woman: • Mortality	Analysis does not account for confounders – univariate analysis is conducted. Significant risk of publication bias for included studies, due to the nature of case reports.

23 *N: total number of participants in each study*

24 See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this
25 review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question is presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Regional anaesthesia versus general anaesthesia

Women with pulmonary hypertension

Outcomes for the woman

Mortality

Very low quality evidence from a systematic review of case reports/case series (N=53) reported a statistically significant association between women undergoing general anaesthesia and maternal mortality in comparison to women undergoing regional anaesthesia. The clinical significance of this finding could not be determined.

Recommendations

See the recommendations in the Intrapartum care for women with cardiac disease - risks and benefits of central neuraxial analgesia compared with systemic analgesia section.

Research recommendations

See the research recommendations in the Intrapartum care for women with cardiac disease - risks and benefits of central neuraxial analgesia compared with systemic analgesia section.

Rationale and impact

See the rationale and impact in the Intrapartum care for women with cardiac disease - risks and benefits of central neuraxial analgesia compared with systemic analgesia section.

The committee's discussion of the evidence

See The committee's discussion of the evidence for the review question about analgesia for women in labour with heart disease.

Intrapartum care for women with cardiac disease – analgesia

Review question

What are the risks and benefits of central neuraxial analgesia compared with systemic analgesia, inhaled analgesia or no analgesia for women with cardiac disease who are in labour?

Introduction

The aim of this review is to compare different analgesic techniques and their effects on outcomes for women and babies. This is important because painful contractions at any time during labour and pushing during the second stage of labour result in additional demands on the woman's cardiovascular system that can be ameliorated by providing effective analgesia.

Summary of the protocol

See Table 14 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 14: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the intrapartum period
Intervention	Interventions 1: • Systemic analgesia (using the opioids pethidine, morphine, diamorphine or remifentanil; or ketamine) Intervention 2: • Inhaled analgesia (nitrous oxide, or sevoflurane) Intervention 3: Non-pharmacological analgesia (Transcutaneous electrical nerve stimulation, acupuncture, water papules, birthing pools, reflexology, aromatherapy, hypnobirthing, or homeopathy)
Comparison	Central/regional neuraxial analgesia (spinal, epidural, or combined spinal epidural)
Outcomes	For the woman: • mortality • major morbidity (respiratory arrest, pulmonary oedema, or haematoma) • adequacy of analgesia (women's perception of pain (pain scores), need for a top up or second technique) • blood pressure (hypertension or hypotension) • mode of birth For the baby: • neonatal mortality

	• fetal morbidity (respiratory depression and fetal distress (heart rate changes or abnormalities))

For further details see the full review protocol in Appendix A. The search strategies are presented in Appendix B.

Clinical evidence

Included studies

No clinical evidence was identified for this review.

See the study selection flow chart in Appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusion are provided in Appendix D.

Summary of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so there are no evidence tables in Appendix E). No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

No clinical evidence was identified for this review (and so no quality assessment was undertaken and there are no GRADE tables in Appendix G).

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

E Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

F Evidence statements

No clinical evidence was identified for this review.

R Recommendations

C32. During pregnancy, prepare a plan for managing anaesthesia and analgesia for women with heart disease involving a multidisciplinary team (outlined in recommendation B1). Consider including a haematologist for women on an anticoagulation regimen.

C33. Consider offering the same advice about anaesthesia and analgesia in labour to women with WHO 1 or WHO 2 heart disease as described in the NICE guideline on intrapartum care for healthy women and babies.

C34. Consider regional anaesthesia for women with WHO 3 and WHO 4 heart disease, unless this is contraindicated.

C35. Consider collaborative working in the intrapartum period between an obstetric anaesthetist and a cardiac anaesthetist for women with WHO 3 and WHO 4 heart disease.

C36. When using regional anaesthesia for women with heart disease, aim to preserve cardiovascular stability by, for example, using a combined spinal–epidural technique with a low-dose spinal component and cautious epidural top-up.

C37. Offer close intrapartum monitoring of the heart and circulation to all women with WHO 3 and WHO 4 heart disease; this will usually include continuous invasive intra-arterial pressure monitoring and may include central venous pressure monitoring and advanced cardiac output monitoring.

C38. Offer cardio-stable low-dose regional analgesia to women with WHO 3 or WHO 4 heart disease when pain during labour and birth may affect their heart.

C39. Consider regional analgesia for women who have been on low-molecular-weight heparin and who have not had a prophylactic dose for at least 12 hours, or a therapeutic dose for at least 24 hours.

R Rationale and impact

W Why the committee made the recommendations

Evidence identified was very limited so the committee made recommendations based on their knowledge and experience. The committee wanted to promote the best medical opinion while also taking into account women's needs and wishes. Regional anaesthesia offers several benefits over general anaesthesia that are still relevant even when a woman has a heart condition.

The committee was aware that the type of anaesthesia that women with heart conditions receive can vary according to the attending anaesthetist's experience and technical expertise. Therefore obstetric anaesthetists and cardiac anaesthetists should collaborate to provide the most cardio-stable anaesthetic option for the women. They agreed that information and advice should be shared with the woman so the best outcomes can be achieved. Women with WHO 1 or WHO 2 heart disease should be given the same advice as described in the NICE guideline on intrapartum care for healthy women and babies.

Based on knowledge of the physiological consequences of pain and the evidence that regional anaesthesia provides the most complete pain relief in labour, the committee agreed that to minimise the risks of labour without adversely affecting the woman's heart condition, women with WHO 3 and WHO 4 heart disease should be offered regional anaesthesia for labour. These women have critical heart failure and life threatening heart disease and need to be carefully monitored to avoid serious mortality and morbidity.

Women who have not had a prophylactic dose of low-molecular-weight heparin for 12 hours or a therapeutic dose for at least 24 hours could be considered for regional analgesia as, the committee agreed, after this time the risk of bleeding from regional analgesia is considered to be very low.

Impact of the recommendations on practice

Most pregnant women with severe heart disease are already offered care in large obstetric-led units with links to cardiac centres. Therefore, these recommendations reinforce current practice and are unlikely to lead to a change. The recommendation that women with WHO 1 and WHO 2 heart disease should be treated as healthy women may reduce unnecessary change in routine intrapartum practice.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

This section includes the committee's discussion of the evidence for the review question about anaesthesia for women in labour with heart disease.

For the review about anaesthesia, maternal mortality and major morbidity (including perioperative cardiovascular collapse, stroke, hypotension, cardiac arrest, hypertension, intracranial haemorrhage or myocardial infarction) and women's satisfaction with labour and birth (including psychological wellbeing) were agreed as critical to decision making because these most closely relate to anaesthetic technique. Other outcomes for the woman, admission to HDU or ITU and re-admission to hospital within 6 weeks and outcomes for the baby, mortality, major morbidity (including ischaemic encephalopathy) and unexpected admission to a neonatal unit might reflect local policy and are less likely to be associated with the effects of anaesthesia and therefore were regarded as important to decision making.

For the review about analgesia, maternal mortality, major morbidity (such as respiratory arrest, pulmonary oedema or haematoma) and adequacy of analgesia were regarded as outcomes critical to decision making as they were extreme outcomes which could result from poor analgesic technique. Other outcomes for the woman, blood pressure (hypertension or

hypotension) were considered as important as they were relatively subjective and would vary widely. Outcomes for the baby, neonatal mortality and fetal morbidities (respiratory depression, fetal distress and heart rate changes or abnormalities) were selected as important outcomes as these outcomes were indirect but serious if there was prolonged labour due to inadequate or complicated analgesia.

The quality of the evidence

For the review about anaesthesia, only 1 study of very low quality evidence was available to inform the committee's decision making. This was a systematic review of case series of women with pulmonary arterial hypertension. It suggested a statistically significantly association between mortality and general anaesthesia. However, the univariate analysis did not account for confounding factors and there was a significant risk of publication bias from inclusion of case report studies. Hence the committee did not find the evidence helpful to inform their decision making and decided to make recommendations based on their clinical experience.

For the review about analgesia, no clinical evidence was identified.

Benefits and harms

The committee emphasised the importance of the woman's preference while maximising safety. For women with an underlying cardiac condition, a pain management plan during the peripartum period should be prepared by an MDT, and for women on an anticoagulation regimen, a haematologist should also be involved in the planning.

The committee agreed that many women with cardiac conditions can physiologically cope with pain and should therefore be offered all the different pain management options (analgesia or anaesthesia) recommended in the NICE guideline on intrapartum care for healthy women and babies (CG190), including non-pharmacological pain relief and no pain relief.

The committee was aware of clear evidence from general obstetric populations that in the non-elective situation, regional anaesthesia is safer than general anaesthesia in terms of mortality and severe morbidity. This is because in the emergency situation, airway complications are more likely to arise. They elaborated that the anaesthetist is less likely to fully assess the airway or have less help and equipment to manage a difficult airway in such a situation. As a result, the woman is more likely to regurgitate or aspirate. Evidence that regional anaesthesia is also safer in the elective situation was not available. The committee agreed that the increased risk of emergency general anaesthesia was present in women with heart disease but they were reluctant to extrapolate the lack of evidence of an increased risk in elective situations to inform recommendations for the elective situation because of differences in the clinical profiles of healthy women and those with heart conditions.

The committee agreed that maintenance of haemodynamic control during anaesthesia was more important than the anaesthetic technique itself. There was little evidence to suggest that a general or regional anaesthetic technique was better than another in achieving this. However regional anaesthesia has several advantages in other respects. The most important of these was that most women prefer to be awake and experience the birth of their child. The committee noted that even when women were very ill and might die, regional anaesthesia would be the preferred option where possible to allow them to see their baby. Other important considerations were quicker recovery from regional anaesthesia and better post-

operative pain relief, as well as reduced bleeding and risk of postpartum haemorrhage. The committee further noted that general anaesthesia tended to be reserved for women with particularly severe conditions likely to require intensive care post-operatively and for women having an obstetric emergency. The committee concluded that regional anaesthesia should be offered to women with WHO 3 or WHO 4 heart disease unless there were specific contraindications.

When considering the type of regional technique to produce anaesthesia the committee concluded that a combined spinal-epidural technique was preferable to either epidural or spinal. This is because in order to provide anaesthesia of sufficient intensity and duration, a spinal was most likely to produce cardiovascular instability. On the other hand de novo epidural anaesthesia, which is rarely undertaken nowadays, has a slow onset of action and requires much higher doses of local anaesthetic which if misplaced could cause cardiovascular catastrophe.

The committee recognised that anaesthetists' skills and experience in giving general or regional anaesthesia would vary. For example, most cardiac anaesthetists might prefer administering general anaesthetic whereas the majority of obstetric anaesthetists would have greater experience of regional techniques. The only absolute contraindication to regional anaesthesia would be if the woman was taking an anticoagulant, declined, or was allergic to local anaesthetics.

The committee agreed that shared involvement from an obstetric and a cardiac anaesthetist would be restricted to women with WHO 3 or WHO 4 heart disease, for example, unstable heart failure or worsening pulmonary hypertension, where the woman is likely to require adult intensive care post-operatively. Thus, the committee suggested having close cardiac monitoring during labour for these women with continuous invasive intra-arterial pressure monitoring, central venous pressure monitoring or advanced cardiac output monitoring.

For women with a cardiac condition in WHO category 3 or 4 the physiological effects of labour pain can cause haemodynamic compromise and have detrimental consequences. Therefore, for women with cardiac conditions for which the absence of pain is particularly beneficial, low-dose regional (either epidural or combined spinal-epidural) pain relief should be considered. The committee shared their knowledge and experience that the effects of pain in the haemodynamic system include increased myocardial work, increased oxygen consumption and tachycardia. In cardiac conditions with poor ventricular function and low cardiac output these physiological effects of pain are poorly tolerated and they have serious risks for women in labour. Therefore, it is important to ensure that effective pain relief is provided for these women during labour. Regional analgesia gives overwhelmingly better pain relief during labour than systemic or inhaled analgesia. However, regional analgesia can cause hypotension that can potentially jeopardise the haemodynamic function of a woman with a cardiac condition, therefore, when regional pain relief is given a low-dose technique ensuring cardiovascular stability should be used.

The committee recognised that special consideration should be given to women on anticoagulation medication who are at an increased risk of spinal or epidural haematoma if regional pain relief is used. They agreed that if such women wish to have regional pain relief, or if they require effective pain relief due to their cardiac condition, it can be given provided if 24 hours have elapsed since the previous therapeutic dose of the anticoagulant, or 12 hours since the previous prophylactic dose, because after this time the risk of bleeding is considered to be low. The committee also recognised the importance of having a

haematologist in the MDT preparing a pain relief plan with the woman. If regional pain relief is used, the plan for should include consideration of the removal of the epidural catheter.

The committee also noted that when systemic pain relief is used, pethadine is not usually suitable for women with cardiac conditions because of side effects that can be dangerous for people with these conditions and alternatives should be used.

Cost effectiveness and resource use

There was limited evidence for these reviews and the committee made a qualitative assessment of cost effectiveness.

For women with WHO 1 or WHO 2 heart disease the committee recommended the same advice as in the NICE guideline on intrapartum care for healthy women and babies (CG190).

The committee considered that the recommendation to consider regional anaesthesia for women with WHO 3 and WHO 4 would be cost effective because it costs less than general anaesthesia and can provide the most complete pain relief without adversely affecting the woman's heart condition.

The committee noted that most pregnant women with severe heart disease will already be offered care in a large obstetric-led unit with links to a cardiac centre and so they considered that the recommendations would reinforce current practice. Furthermore, the number of women affected would be small and the committee did not anticipate a significant resource impact for the NHS. They thought that the recommendation that care for women with WHO 1 or WHO 2 heart disease should be the same as for healthy women could produce some cost savings to the NHS by reducing unnecessary intervention.

Other factors the committee took into account

Despite the lack of the evidence, the committee decided to prioritise other areas addressed by the guideline for future research and therefore made no research recommendations regarding the use of anaesthesia and analgesia for women with heart disease.

Intrapartum care for women with cardiac disease – management of the third stage of labour

Review question

How should the third stage of labour be managed for women with cardiac disease?

Introduction

The aim of this review is to identify if any active management intervention (including use of uterotonics) is more effective than physiological management in women with cardiac conditions for whom the risk of postpartum haemorrhage is of particular concern; this is of particular interest in the case of women whose cardiac condition is related to and affected by the circulating volume of blood. This question is important because there are a variety of options for management of the risk of postpartum haemorrhage, of which uterotonics are the area of biggest clinical disagreement.

Summary of the protocol

See Table 15 for a summary of the population, intervention, comparison and outcome (PICO) characteristics of this review.

Table 15: Summary of the protocol (PICO) table

Population	Women with a cardiac condition in the third stage of labour
Intervention	Active management using: Intervention 1: • Uterotonics such as carboprost (hemabate), syntometrine, syntocinon, misoprostol, ergometrine, or oxytocin (some drugs are given IV or IM) Intervention 2: • Other drugs (for example, tranxamic acid) Intervention 3: • Breast feeding Intervention 4: • Clamping and cutting the umbilical cord Intervention 5: • Controlled cord traction
Comparison	Comparison 1: • Physiological management (such as no cord clamping, waiting for signs of separation, placenta delivered by maternal effort)

	Comparison 2: • Active management options (including regimens) compared against each other
Outcomes	For the woman: • mortality • major morbidity (shock, collapse or other haemodynamic compromise) • women's satisfaction with labour and birth (including psychological wellbeing) • postpartum haemorrhage • admission to intensive treatment unit (ITU)

1 *IM:Intramuscular; IV: Intravenous*

2 For further details see the full review protocol in Appendix A. The search strategies are
3 presented in Appendix B.

Clinical evidence

Included studies

6 One prospective cohort study was included in the review (see 'Summary of clinical studies
7 included in the evidence review').

8 This study compared standard oxytocin infusion (10 units of oxytocin diluted in 500 ml of
9 normal saline and infused at 36 ml/hour) with a bolus dose of oxytocin (2 international units
10 of oxytocin over 10 minutes immediately after birth) in addition to standard oxytocin infusion
11 alone (Cauldwell 2016).

12 Evidence from the studies included in the review is summarised below (see 'Quality
13 assessment of clinical studies included in the evidence review').

14 Data was reported on the important outcome, postpartum haemorrhage of the woman. There
15 was no data available for the following outcomes for the woman, mortality (critical outcome),
16 major morbidity such as shock, collapse or other haemodynamic compromise (critical
17 outcome), women's satisfaction with labour and birth (important outcome) and admission to
18 intensive treatment unit (outcome of limited importance).

19 There was no evidence available for other interventions, uterotonics such as carboprost
20 (hemabate), syntometrine, syntocinon, misoprostol or ergometrine, other drugs (for example,
21 tranxamic acid), breast feeding, clamping and cutting the umbilical cord and controlled cord
22 traction.

23 Similarly, there was no evidence available for the following comparison, physiological
24 management.

25 See also the study selection flow chart in Appendix C.

Excluded studies

27 Studies not included in this review with reasons for their exclusions are provided in Appendix
28 D.

Summary of clinical studies included in the evidence review

Table 16 provides a brief summary of included studies.

Table 16: Summary of included studies

Study	Population	Intervention/Comparison	Outcomes
Cauldwell 2016 Prospective observational cohort study UK	N=59 women with pre-existing congenital or acquired cardiac conditions were included. NYHA > 1: 1.7% Mode of birth - SVB: 25.4% Assisted birth: 33.9% Emergency CS: 22% Elective CS: 24%	• Standard oxytocin infusion*+ bolus oxytocin 2 IU over 10 minutes after birth (n=30) • Standard oxytocin infusion* alone (n=29)	For the woman: • Estimated blood loss at birth • Phenylephrine required • Blood transfusion required • Additional uterotonic agents (Misoprostol or Hemabate) received

** 10 units of oxytocin dissolved in 500 ml of normal saline and infused at 36 ml/hour for 4 hours (12mU/min)*
N: total number of participants in each study
intervention: women in bolus treatment group or intervention group; CS: caesarean section; comparison: women in standard oxytocin alone group; IU: international units; NYHA: New York Heart Association, std: women in standard treatment group or control group, SVB: spontaneous vaginal birth

See also the study evidence tables in Appendix E. No meta-analysis was undertaken for this review (and so there are no forest plots in Appendix F).

Quality assessment of clinical studies included in the evidence review

The clinical evidence profile for this review question is presented in Appendix G.

Economic evidence

Included studies

No economic evidence was identified for this review.

See the study selection flow chart in Supplement 2 (Health economics).

Excluded studies

No full-text copies of articles were requested for this review and so there is no excluded studies list (see Supplement 2 (Health economics)).

Summary of studies included in the economic evidence review

No economic evidence was identified for this review (and so there are no economic evidence tables in Supplement 2 (Health economics)).

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation (see Supplement 2 (Health economics)).

Evidence statements

Bolus oxytocin plus standard oxytocin infusion versus standard oxytocin infusion alone

Outcomes for the woman

Postpartum haemorrhage: estimated blood loss at birth

Very low quality evidence from one prospective cohort study of women with cardiac diseases (N=59) suggested that there was a clinically important benefit of bolus oxytocin injection in addition to standard oxytocin infusion in reducing estimated blood loss at delivery when compared with standard oxytocin infusion alone.

Postpartum haemorrhage: phenylephrine required

Very low quality evidence from one prospective cohort study of women with cardiac diseases (N=59) suggested that there was no clinically important difference in the number of women requiring phenylephrine with bolus oxytocin injection in addition to standard oxytocin infusion when compared with standard oxytocin infusion alone.

Postpartum haemorrhage: blood transfusion required

Very low quality evidence from one prospective cohort study of women with cardiac diseases (N=59) suggested that there was no clinically important difference in the number of women requiring blood transfusion with bolus oxytocin injection in addition to standard oxytocin infusion when compared with standard oxytocin infusion alone.

Postpartum haemorrhage: additional uterotonic agents received

Very low quality evidence from one prospective cohort study of women with cardiac diseases (N=59) suggested that there may be a clinically important beneficial effect of bolus oxytocin injection in addition to standard oxytocin infusion in reducing the number of women requiring additional uterotonic agents when compared with standard oxytocin infusion alone, but there is uncertainty around the estimate.

Recommendations

C40. During pregnancy, prepare an individualised plan for managing the third stage of labour for women with heart disease, involving a multidisciplinary team (outlined in recommendation B1). Consider including a cardiologist with expertise in managing heart disease in pregnant women.

C41. Treat women with WHO 1 heart disease as low risk and consider the full range of management options for healthy women in the third stage of labour described in the NICE guideline on intrapartum care for healthy women and babies.

C42. Consider active management of the third stage of labour for women with WHO 2 heart disease, in line with the NICE guideline on intrapartum care for healthy women and babies.

C43. Consider management of the third stage of labour for women with WHO 3 or WHO 4 heart disease according to Table 17.

Table 17: Management of the third stage of labour for women with WHO 3 or WHO 4 heart disease

Condition	First-line uterotonic	Second-line uterotonics	Drugs to avoid due to potential harm
Significant aortopathy Marfan syndrome and aortic dilatation >40 mm Bicuspid aortopathy and aortic dilatation >45 mm Previous aortic dissection Turner syndrome and aortic size index >25 cm/m^2 All women with Loeys Dietz syndrome[j]	Oxytocin	Misoprostol Carboprost	Ergometrine (due to risk of hypertension-induced aortic dissection or rupture)
Limited or fixed low cardiac output, or preload-dependent circulation Severe systemic ventricular dysfunction (ejection fraction <30%) Severe valvar stenosis Hypertrophic cardiomyopathy with diastolic dysfunction or significant outflow tract obstruction Fontan circulation Cyanotic heart disease	Oxytocin	Misoprostol Carboprost	Long-acting oxytocin analogues and ergometrine (due to risk of hypertension-induced heart failure)

j The committee adapted the modified WHO classification of risk outlined in Thorne et al. 2006, based on their clinical experience to clarify the intrapartum risk associated with heart disease, including the addition of Loeys Dietz syndrome.

Pulmonary arterial hypertension	Oxytocin	Misoprostol	Ergometrine, carboprost and long-acting oxytocin analogues (due to risk of worsening pulmonary hypertension)
Coronary artery disease	Oxytocin	Misoprostol	Ergometrine (due to risk of coronary ischaemia)

C44. For women with a preload-dependent circulation, aim to avoid sudden haemodynamic change when administering oxytocin, for example, by giving a slow infusion rather than bolus.

Research recommendations

What is the optimum uterotonic regime for the prevention of postpartum haemorrhage (PPH) in women with cardiac disease?

Rationale and impact

Why the committee made the recommendations

The committee agreed that heart disease covers a spectrum of pathologies which have different risks associated with management of the third stage of labour. The only evidence was limited, came from a single study and was not helpful in determining management options for women with various heart conditions. Therefore the committee made recommendations based on their knowledge and experience. A management plan developed with multidisciplinary expertise is needed for each woman. Women with less severe heart conditions have similar risks to normal healthy women in the third stage of labour and can be managed accordingly. As the physiological management of the third stage is associated with a higher risk of postpartum haemorrhage, women with WHO 2 heart disease should have the third stage actively managed. Active management is also needed for all women with more severe disease. Oxytocin is the uterotonic of first choice. Second-line options depend on the specific condition. Women with preload dependent circulation are particularly vulnerable to falls in blood pressure and there is some evidence to suggest that oxytocin should be given as an infusion rather than bolus to avoid sudden drops in blood pressure.

Ergometrine and oxytocin, two of the most commonly administered uterotonic agents, are known to have significant cardiovascular side effects and may be contraindicated in some women with heart disease. However, management of the third stage of labour should not put women with heart disease at increased risk of postpartum haemorrhage as some of these women will tolerate even minor haemorrhage very poorly. The women at potential risk of

adverse effects from oxytocin are also those who are at greatest risk if they have a postpartum haemorrhage. The committee took all these factors into account when developing recommendations.

Impact of the recommendations on practice

The recommendations largely reflect current practice. The committee agreed there should be little change, with the exception of reducing the use of long-acting forms of oxytocin.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

Outcomes for the woman were prioritised for this review.

Mortality and major morbidity such as shock, collapse or other haemodynamic compromise for the woman were agreed as outcomes critical to decision making. In the third stage of labour the placenta is delivered and mismanagement could lead to uncontrolled postpartum haemorrhage, haemodynamic compromise and even death. However, postpartum haemorrhage was considered to be an important outcome because it was an intermediate outcome. Women's satisfaction of labour and birth (including psychological wellbeing) was also considered to be an important outcome to highlight that care should centre on the woman.

The quality of the evidence

There was only 1 included study and its limitations led the committee to conclude that it could not help inform recommendations. Firstly women with all types of cardiac conditions (mostly congenital heart conditions) whether trivial or serious were analysed together within treatment groups. Secondly the committee noted there would be great variation in the dose of oxytocin, but doses seemed significantly lower than those currently used by clinicians caring for this such women. Thirdly the outcomes reported were proxy measures for postpartum haemorrhage. The apparent incidence of postpartum haemorrhage based on these measures was remarkably high and the committee hypothesised that this was the result of the inadequately low doses of oxytocin that were given.

Benefits and harms

The committee suggested that all women with cardiac conditions should have an individualised plan for managing the third stage of labour after multidisplinary discussion including a cardiologist with expertise in managing cardiac conditions during pregnancy. The committee recognised that early input from the cardiologist would be critical for optimal management of the third stage of labour for women who are at risk of cardiovascular compromise because of a cardiac condition.

The committee noted that 'healthy' women would be advised to have active management of the third stage of labour because this is associated with a lower risk of a postpartum haemorrhage and need for a blood transfusion. However, women would be supported in a request for physiological management if that was their preference. The NICE guideline on intrapartum care for healthy women and babies (CG190) does not specify cardiac conditions

in the list of risk factors for postpartum haemorrhage and for which active management should be offered.

The committee recognised that the WHO heart disease categorisation primarily related to pregnancy and did not correlate directly to risk of poor outcome in the third stage labour. They considered whether all women with heart conditions would need active management of the third stage of labour and concluded that women with WHO 1 heart conditions would be no more vulnerable to the cardiovascular consequences of postpartum haemorrhage than would healthy women and so for them the management of the third stage should follow the NICE guideline on intrapartum care for healthy women and babies (CG190).

The NICE guideline on intrapartum care for healthy women and babies (CG190) provides estimates for the risk of haemorrhage of more than 1 litre and of a blood transfusion that are higher with physiological compared to active management. This was aligned with the committee's clinical experience and they concluded that given the additional bleeding risk with physiological management, women with WHO 2 heart conditions should be offered routine active management. However, as there was no evidence to support this recommendation and it was based on the committee's clinical knowledge and experience, a 'weak' recommendation was made to consider rather than offer active management of the third stage of labour.

The committee also discussed different uterotonic drugs used to prevent postpartum haemorrhage from uterine atony and their use in women with cardiac conditions of WHO 3 or 4. The committee agreed that the following 4 categories of heart conditions should be considered when assessing the optimal regimen for active management of the third stage of labour for women with heart disease of WHO 3 or 4.

- Women with significant aortopathy have fragile aortas and are at risk of aortic dissection or aortic rupture if a uterotonic regimen that causes hypertension is used.
- Women who are at increased risk of cardiovascular decompensation if they have a postpartum haemorrhage include those with a fixed low cardiac output or limited ability to increase their cardiac output, and those with a preload-dependent circulation. This same group of women is also at risk of decompensation if the uterotonic regimen used causes rapid vasodilation and tachycardia. Thus, a cardiostable regimen should be used. Moreover, women who take anticoagulants because of their heart condition (for example, women who have a mechanical valve), or who have cyanotic heart disease are at increased risk of having a postpartum haemorrhage. Early recourse to an oxytocin infusion, and regular senior clinical review are required in such circumstances. The committee also discussed that there is no evidence to support the use of tranexamic acid as prophylaxis against postpartum haemorrhage (although it is beginning to be more widely used in this way) in the healthy obstetric population. The committee concluded that tranexamic acid should not be offered to women at risk of thrombotic complications, as prophylaxis against postpartum haemorrhage.
- Women with pulmonary arterial hypertension are at risk of cardiopulmonary compromise if a uterotonic regimen that causes bronchoconstriction is used.
- Women with coronary artery disease are at risk of cardiovascular compromise if a uterotonic regimen that causes coronary ischaemia is used.

The committee also shared their knowledge and experience on the use of different uterotonic regimens in details as follows:

- Oxytocin is a neuropeptide hormone that causes dose-related systemic hypotension due to vasodilation. In healthy women this triggers compensatory tachycardia and an increase in cardiac output. Oxytocin can also cause chest pain, probably through coronary spasm. In cardiac disease an infusion is recommended rather than repeated boluses. If a bolus is used the maximum dose should be 5 units and it should be given slowly, for example, in 20 ml over 10 minutes or 3 units given no faster than 15 seconds. Carbetocin is a long-acting analogue of oxytocin and has a similar cardiovascular profile. Its use with cardiac conditions has not been reported. Thus, the committee discussed whether it should be avoided in preload-dependent circulation because of its long duration of action.
- Carboprost, prostaglandin PGF2-a, increases pulmonary vascular resistance, causes bronchoconstriction and can cause pulmonary oedema. Its use in significant cardiac disease is not recommended and it should be avoided in people with asthma, elevated pulmonary arterial pressure, single ventricle and shunt lesions.
- Misoprostol is a synthetic analogue of prostaglandin E1 administered orally, rectally or vaginally. Although, it appears to be less vasoactive than other uterotonics, there have been reports of angina, myocardial infarction and stroke when it is used for termination of pregnancy (although the doses used for termination of pregnancy are much higher than would be used to manage postpartum haemorrhage). It is less effective than oxytocin in preventing postpartum haemorrhage, but may be a useful adjunct to promote uterine contractions when oxytocin cannot be used or when bleeding continues despite oxytocin use. Its use in the third stage of labour in women with cardiac disease has not been reported.
- Ergometrine causes systemic and pulmonary vasoconstriction, and bronchoconstriction. Its use has been associated with coronary artery spasm and pulmonary oedema and it is contraindicated in hypertensive disorders, coronary artery disease and any fragile aorta.

The clinical dilemma of the management of the third stage of labour is that treatment will be a compromise between maintaining blood pressure and avoiding postpartum haemorrhage. Uterotonic agents used to prevent postpartum haemorrhage are vasoactive and have potential to cause adverse cardiovascular effects during active management of the third stage of labour. However, some women with heart disease are particularly vulnerable to postpartum haemorrhage, and the haemodynamic consequences of postpartum haemorrhage, so the risk of using uterotonic agents should be weighed against the risk of bleeding. A rapid drop in blood pressure is more likely to occur when oxytocin is administered as a bolus, in comparison to slower administration as an infusion, but a bolus only needs to be avoided in some women.

Cost effectiveness and resource use

The clinical evidence was limited and the committee made a qualitative assessment of cost effectiveness.

For women with WHO 1 heart disease they recommended that the third stage of labour be managed as described in the NICE guideline on intrapartum care for healthy women and babies (CG190).

Women with WHO 2 heart disease have a higher risk of postpartum haemorrhage and therefore the committee reasoned that active management of the third stage of labour in line with the NICE guideline on intrapartum care for healthy women and babies (CG190) would be cost effective.

The committee noted that in some women there is a compromise between maintaining blood pressure while avoiding postpartum haemorrhage. They reasoned that this clinically complex situation would make the inclusion of a cardiologist with expertise in managing heart disease during pregnancy as a member of the MDT cost effective.

The committee considered that the recommendations largely reflected current practice, although they thought the recommendations could lead to a reduction in the use of long-acting forms of oxytocin. Given the relatively small numbers of women with WHO 3 and WHO 4 in labour the committee did not anticipate that the recommendations would have a significant impact on NHS resources.

Other factors the committee took into account

No clinical studies have determined the most appropriate management regimen to prevent postpartum haemorrhage for women with different categories of cardiac disease. Thus, the committee made a research recommendation to identify the optimal uterotonic regimen for prevention of postpartum haemorrhage in women with cardiac disease. See Appendix L for further details.

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1 Appendices

A Appendix A – Review protocols

B Intrapartum care for women with cardiac disease – stratification of risk

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – stratification of risk	
Review question in the scope	What history, clinical examination and investigation is most useful in antenatal planning for birth in women with congenital cardiac disease?	
Review question for the guideline	What history, clinical examination and investigation is most useful to stratify the intrapartum risk for women with cardiac disease?	
Objective	The aim of this review is to examine cardiac disease symptoms, clinical observations and risk stratification tools for evidence of their value in identifying poor outcomes during intrapartum care and birth.	
Population and directness	Women with a cardiac condition in the intrapartum period	
Intervention	Recorded assessment of 1 or more of the following risk factors by at least a consultant cardiologist (ideally a consultant cardiologist experienced in cardiac disease in pregnancy) Clinical history 1. Family history 2. Smoker 3. Obstetric history Symptoms 1. Breathlessness and severity, orthopnoea, paroxysmal nocturnal dyspnoea 2. Palpitations 3. Syncope 4. Chest pain Clinical observations 1. Pulse 2. Blood pressure 3. Jugular venous pressure 4. Heart sounds 5. Chest auscultation 6. Pitting oedema	

Item	Details	Working notes
	Pre-pregnancy or antenatal cardiac function testing 1. Echocardiogram 2. Electrocardiogram (ECG) and ambulatory ECG 3. Cardiopulmonary exercise testing (CPEX) 4. Exercise testing 5. Chest X-ray 6. Magnetic Resonance Imaging (MRI) 7. Biomarkers – Brain Naturetic Peptide (BNP) Cardiac risk assessment protocols, tools or scoring systems for use at the onset of labour	
Comparison	Each other (different risk factors)	
Outcomes	Critical outcomes: • for the woman: ○ mortality ○ severe morbidity (ITU with organ support and organ transplant, or need for mechanical support) • for the baby: ○ mortality ○ severe morbidity (admission to a neonatal unit or encephalopathy) Important outcomes: • for the woman: ○ mode of birth ○ women's satisfaction with labour and birth (including psychological wellbeing) For studies evaluating cardiac risk assessment protocols, tools or scoring systems: • diagnostic accuracy of risk assessment protocols, tools or scoring systems to identify critical outcomes for the woman ○ if reported dichotomously, sensitivity, specificity, positive and negative likelihood ratios ○ if reported continuously, area under the receiver operating characteristic (ROC) curve	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • for condition–specific information, women with different cardiac conditions will be analysed separately	

Item	Details	Working notes
	Results will be stratified by: • severity of disease (as defined within studies) In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • severity of disease (as defined within studies) • receipt of antenatal care • term and preterm labour or birth Potential confounders: • maternal age • parity • co-morbidity	
Language	English	

Study design	• Published full-text papers only
	• Systematic reviews
	• RCTs
	
	• Only if RCTs unavailable or there is limited data to inform decision making:
	  ○ prospective or retrospective comparative observational studies (including cohort and case-control studies)
	  ○ cross-sectional studies
	• Prospective study designs will be prioritised over retrospective study designs
	• Conference abstracts will not be considered	

Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies Search not date-limited but studies published prior to 1970 were excluded by the reviewer(s) because they would not reflect modern obstetric practice.	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, Cochrane RoB tool for RCTs and QUADAS-2 for diagnostic test accuracy studies) and the quality of the evidence for each	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health

Item	Details	Working notes
	outcome (that is, across studies) will be assessed using GRADE (or an adapted version of GRADE in the case of diagnostic evidence) • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	

Item	Details	Working notes
Key papers	Sara Thorne, Anne MacGregor, and Catherine Nelson-Piercy. Risks of contraception and pregnancy in heart disease. Heart. 2006 Oct; 92(10): 1520–1525. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1861048/ ESC Guidelines on the management of cardiovascular diseases during pregnancy. European Heart Journal (2011) 32, 3147–3197. http://eurheartj.oxfordjournals.org/content/32/24/3147 The MBRRACE-UK 2015 report states the following: -Among the 49 women who died from a cardiac condition in 2011-13, 12 (25%) were classified as Sudden Adult Death Syndrome (SADS), 10 (20%) had an aortic dissection, 10 (20%) had an acute coronary syndrome, 6 women (12%) died from a cardiomyopathy and 11 (22%) had other cardiac conditions. A detailed assessment of the care of the women who died from cardiac disease will be included in the 2016 report. -2009-13 - Medical conditions account for the majority of the remaining 49% of late deaths of which cardiac conditions represent one in eight; cardiac deaths will be reviewed in detail in the 2016 report.	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease	
Review question in the scope	What is the appropriate management of anticoagulation for women with valvular disease in pregnancy and labour?	
Review question for the guideline	What is the appropriate management of anticoagulation for women with valvular disease in planning for childbirth?	
Objective	The aim of this review is to determine appropriate intrapartum anticoagulant management for women with bioprosthetic or mechanical valves.	

Item	Details	Working notes
Population and directness	Women with congenital or acquired valvular heart disease and with bioprosthetic (group 1) or mechanical (group 2) heart valves who are pregnant and beyond 24 weeks of gestation, including those in the intrapartum period	
Intervention	**Group 1 –bioprosthetic valves:** • aspirin (and other antiplatelet agents; clopidogrel, ticagrelor or dipyridamole) • low-molecular-weight heparin (LMWH; dalteparin, enoxaparin, or tinzaparin) **Group 2 – mechanical valves:** ○ aspirin (and other antiplatelet agents; clopidogrel, ticagrelor or dipyridamole) ○ oral anticoagulants (warfarin, acenocoumarol, phenindione) ○ low-molecular-weight heparins (dalteparin, enoxaparin, or tinzaparin) ○ new anticoagulants (direct factor Xa inhibitors: rivaroxaban, apixaban; direct thrombin inhibitors: dabigatran) ○ unfractionated heparin • different treatment regimens according to stage of pregnancy and consisting of combinations of the above drugs, some also including vitamin K antagonist • suspension of anticoagulation during the intrapartum period • bridging anticoagulation postpartum	
Comparison	**Group 1 – bioprosthetic valves:** • no anticoagulation **Group 2 – mechanical valves:** • low-molecular-weight heparin (dalteparin, enoxaparin, or tinzaparin) • warfarin	
Outcomes	**For both types of prosthetic valve:** Critical outcomes: • for the woman: ○ mortality ○ major morbidity (any thromboembolic events - pulmonary embolism, valve thrombosis, stroke or intracranial haemorrhage), obstetric haemorrhage (antenatal or postpartum), cardiovascular compromise (as defined by study), new maternal arrhythmia, infective endocarditis, myocardial infarction) • for the baby: ○ mortality (intrauterine death or neonatal death)	

Item	Details	Working notes
	○ major neonatal morbidity (preterm birth, fetal anticoagulation, fetal haemorrhage, intracerebral or intracranial bleeding) Important outcomes: • for the woman: ○ admission to a high dependency unit (HDU) or intensive treatment unit (ITU) ○ women's satisfaction with labour and birth (including psychological wellbeing) ○ epidural haematoma ○ unplanned general anaesthesia • for the baby: ○ admission to a neonatal unit Outcomes of limited importance: • for the woman: ○ duration of hospital stay	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	Given the small volume of evidence available for inclusion overall, the committee agreed to consider more than the nominal maximum of 7 outcomes for this question
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • type of valve • position of valve (mitral, aortic, pulmonary, or tricuspid) • size of valve in relation to woman (patient-prosthesis mismatch, for example valve replacement before adulthood) • associated atrial fibrillation • according to age at insertion and length of time since insertion • anticoagulation regimen in different stages of pregnancy (LMWH or warfarin) • level of anticoagulation (for example, measured as anti-10a levels)	

Item	Details	Working notes
	In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • according to age at insertion of valve and length of time since insertion • stages of pregnancy • risk of thromboembolism (for example, low/high/very high) • the type and/or position of the valve • associated atrial fibrillation • receipt of antenatal care Potential confounders • maternal age • smoking history • history of thromboembolism • history of cardiovascular events/complications • history of valve thrombosis • other previous cardiac intervention • pregnancy duration • type of the valve • position of the valve	
Language	English	

Item	Details	Working notes
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: • prospective or retrospective comparative cohort studies • case series studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies	

Item	Details	Working notes
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of

Item	Details	Working notes
		the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	MBRRACE-UK 2016 Surveillance data on maternal deaths from 2012–14. Confidential Enquiry reports on deaths and severe morbidity from cardiac causes, deaths from pre-eclampsia and eclampsia and related causes, deaths in early pregnancy, and messages for critical care. SIGN guideline on prevention and management of venous thromboembolism (2015) recommend that “in women with mechanical heart valves, the risks and benefits of vitamin K antagonists and heparin should be assessed on an individual basis” (http://www.sign.ac.uk/pdf/sign122.pdf) ESC Guidelines on the management of cardiovascular diseases during pregnancy, 2011 (http://www.ncbi.nlm.nih.gov/pubmed/21873418) American College of Chest Physicians Guidelines on the Use of Antithrombotic Therapies in Pregnant Women With Mechanical Valves, 2012 (http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3278054/) AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, 2014 (http://circ.ahajournals.org/content/early/2014/02/27/CIR.0000000000000029.full.pdf) Royal Berkshire NHS Foundation Trust. Cardiac Disease in Pregnancy Guideline (GL802) (http://www.royalberkshire.nhs.uk/Downloads/GPs/GP%20protocols%20and%20guidelines/Maternity%20Guidelines%20and%2	

Item	Details	Working notes
	0Policies/Medical%20conditions%20and%20complications/Cardiac%20disease%20in%20pregnancy_V5.1_GL802.pdf)	
Key papers	Iung B & Vahanian A. Epidemiology of acquired valvular heart disease. Can J Cardiol. 2014 Sep;30(9):962-70. (http://www.ncbi.nlm.nih.gov/pubmed/24986049 Nanna M & Stergiopoulos K. Pregnancy complicated by valvular heart disease: an update. J Am Heart Assoc. 2014 Jun 5;3(3):e000712 (http://www.ncbi.nlm.nih.gov/pubmed/24904015) Sadler L et al. Pregnancy outcomes and cardiac complications in women with mechanical, bioprosthetic and homograft valves. BJOG. 2000 Feb;107(2):245-53 (http://www.ncbi.nlm.nih.gov/pubmed/10688509) Lawley et al. Prosthetic heart valves in pregnancy, outcomes for women and their babies: a systematic review and meta-analysis. BJOG. 2015, 11:1446-55	

1 *AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of*
2 *Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of*
3 *Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA:*
4 *Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE:*
5 *National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD:*
6 *standard deviation; ROBIS: Risk of Bias in Systematic Reviews*

Intrapartum care for women with cardiac disease – mode of birth

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – mode of birth	
Review question in the scope	Which women with cardiac disease should be offered elective caesarean section to improve outcomes for reasons specific to cardiac disease?	
Review question for the guideline	Which women with cardiac disease should be offered elective caesarean section or assisted second stage for reasons specific to cardiac disease?	
Objective	The aim of this review is to examine outcomes for the woman and baby following elective caesarean section for reasons related to a cardiac condition compared with outcomes following a planned vaginal birth.	
Population and directness	Women with a cardiac condition in the intrapartum period The WHO classification of maternal risk of pregnancy associated with specific cardiac conditions is described in Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart.	

Item	Details	Working notes
	2006 Oct;92(10):1520-5. Loeys Dietz syndrome was added to the list by the committee. **Conditions in which pregnancy risk is classified as WHO 1** • Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, or anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated **Conditions in which pregnancy risk is classified as WHO 2 or 3** **WHO 2 (if otherwise well and uncomplicated)** • Unoperated atrial or small ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias **WHO 2–3 (depending on the individual)** • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Moderate mitral or aortic regurgitant valvular lesions with normal left ventricular function • Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation **WHO 3** • Mechanical valve • Severe mitral or aortic regurgitant valvular lesions with normal left ventricular function • Systemic right ventricle • Fontan circulation • Coronary disease • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve • Loeys Dietz syndrome	

Item	Details	Working notes
	Conditions in which pregnancy risk is classified as WHO 4 (pregnancy contraindicated) • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation Studies with indirect populations will not be considered	
Intervention	Elective caesarean section	
Comparison	Vaginal birth	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ major morbidity
	• for the baby:
	  ○ mortality
	  ○ major morbidity
	
	Important outcomes:
	• for the woman:
	  ○ women's satisfaction with labour and birth (including psychological wellbeing)
	  ○ emergency caesarean section	

Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • severe left-sided stenotic lesions – aortic stenosis and mitral stenosis • cardiomyopathy/systolic ventricular dysfunction • aortopathies – Marfan and Loeys-Dietz syndromes • pulmonary hypertension • coronary disease	

Item	Details	Working notes
	Stratification by • severity of disease (as defined within studies) In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • conditions that make caesarean section higher risk: for example, maternal obesity, previous abdominal surgery with bowel adhesions, or abdominal fistulae from disease, colostomies, bleeding disorders, muscular dystrophies, conditions that make anaesthesia difficult (general or regional)) • assisted second stage of labour (no pushing) • for preterm babies, the use of steroids • for preterm babies, the use of magnesium • receipt of antenatal care	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies Search not date-limited but studies published prior to 1980 were excluded by the reviewer(s) due to large changes in cardiac care around this time (e.g. use of thrombolytic agents)	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health

Item	Details	Working notes
	outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	
Key papers		.

Item	Details	Working notes

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LVEF: Left ventricular ejection fraction; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NYHA: New York Heart Association; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews; WHO: World Health Organization

Intrapartum care for women with cardiac disease – fluid management

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – fluid management	
Review question in the scope	Which cardiac conditions need additional fluid-balance monitoring or management during and birth: • input–output chart of fluid balance with a urinary catheter or urometer • invasive monitoring using an arterial line and central venous pressure • cardiac output monitoring • fluid restriction?	
Review question for the guideline	Which women with cardiac conditions need additional haemodynamic monitoring or management during childbirth: • input–output chart of fluid balance with a urinary catheter or urometer • invasive monitoring using an arterial line and central venous pressure • cardiac monitoring • fluid restriction?	
Objective	The aim of this review is to determine which women with cardiac disease who are in the peripartum period require more specialist haemodynamic monitoring to avoid issues with circulating blood volume.	
Population and directness	Women with a cardiac condition in the intrapartum period The WHO classification of maternal risk of pregnancy associated with specific cardiac conditions is described in Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart. 2006 Oct;92(10):1520-5. Loeys Dietz syndrome was added to the list by the committee. **Conditions in which pregnancy risk is classified as WHO 1** • Uncomplicated, small or mild - pulmonary stenosis	

Item	Details	Working notes
	- patent ductus arteriosus - mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, or anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated **Conditions in which pregnancy risk is classified as WHO 2 or 3** **WHO 2 (if otherwise well and uncomplicated)** • Unoperated atrial or small ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias **WHO 2–3 (depending on the individual)** • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Moderate mitral or aortic regurgitant valvular lesions with normal left ventricular function • Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation **WHO 3** • Mechanical valve • Severe mitral or aortic regurgitant valvular lesions with normal left ventricular function • Systemic right ventricle • Fontan circulation • Coronary disease • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve • Loeys Dietz syndrome **Conditions in which pregnancy risk is classified as WHO 4 (pregnancy contraindicated)** • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function	

Item	Details	Working notes
	• Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation Studies with indirect populations will not be considered	
Intervention	Fluid monitoring using one or more of: • input–output chart of fluid balance with a urinary catheter or urometer (hourly monitoring) • invasive monitoring using an arterial line and/or central venous pressure • cardiac monitoring (ECG, pulmonary artery thermodilution via a pulmonary artery floatation catheter (PAFC), lithium dilution cardiac output (LiDCO), pulse contour analysis systems (PiCCO and FloTrac), oesophageal Doppler and other ultrasound Doppler techniques (USCOM), thoracic bioreactance based techniques (NICOM), trans-thoracic and trans-oesophageal echo) Note: fluid restriction was excluded as the focus of the question was on monitoring, not management	
Comparison	• No haemodynamic monitoring (for milder groups, WHO 1 and 2) • Invasive versus non-invasive monitoring (ECG, input–output, oxygen saturation, NIBP (non-invasive blood pressure; for more severe groups, WHO 3 and 4)	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ major morbidity (pulmonary oedema, renal impairment, acute kidney injury, infection, complications of central venous cannulation (haematoma, pneumothorax, or air embolus), or inotropic and mechanical heart support)
	• for the baby:
	  ○ mortality
	  ○ major morbidity (respiratory distress, or encephalopathy)
	
	Important outcomes:
	• for the woman:
	  ○ unexpected admission to intensive treatment unit (ITU)	

Item	Details	Working notes
	○ women's satisfaction with labour and birth (including psychological wellbeing) Outcomes of limited importance: • for the woman: ○ emergency caesarean section	
Importance of outcomes	Preliminary classification of the outcomes for decision making: ○ critical (up to 3 outcomes) ○ important but not critical (up to 3 outcomes) ○ of limted importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • severe left-sided stenotic lesions – aortic stenosis and mitral stenosis • cardiomyopathy with systolic ventricular dysfunction • cardiomyopathy with diastolic ventricular dysfunction, for example, hypertrophic cardiomyopathy • aortopathies, for example Marfan, Ehlers Danlos type 4 and Loeys-Dietz syndromes • pulmonary arterial hypertension • coronary disease • planned mode of birth • actual mode of birth Stratification by: • severity of disease (as defined within studies) In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • conditions that make caesarean section higher risk including maternal obesity, previous abdominal surgery with bowel adhesions, or abdominal fistulae from disease, colostomies, bleeding disorders, muscular dystrophies, conditions that make anaesthesia difficult (general or regional) • women with no antenatal care • preterm labour	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making with minimum sample size of studies of 15 women in each group:	

Item	Details	Working notes
	○ prospective or retrospective comparative cohort studies ○ case series studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies. Search not date-limited but studies published prior to 1980 were excluded by the reviewer(s) due to large changes in cardiac care around this time (e.g. use of thrombolytic agents)	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality

Item	Details	Working notes
		assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	
Key papers		

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; ECG: Electrocardiogram; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LVEF: Left ventricular ejection fraction; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NYHA: New York Heart Association; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews; WHO: World Health Organization

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – diagnosis and management of cardiomyopathy	
Review question in the scope	What is the most appropriate method of diagnosis for women with suspected cardiomyopathy in labour?	
Review question for the guideline	What is the most appropriate method of diagnosis for women with suspected cardiomyopathy in labour?	
Objective	The aim of this review is to identify whether biomarker or clinical indications of cardiomyopathy are predictive of the condition to the extent that they necessitate urgent – rather than routine – referral to a cardiologist.	

Item	Details	Working notes
Population and directness	Any of: • pregnant women with suspected cardiomyopathy • women in labour with suspected cardiomyopathy • women in the postpartum period with suspected or confirmed cardiomyopathy up to 6 months postpartum	
Index test/ prognostic test	Biomarkers/enzymes • Brain naturetic peptide (BNP) Clinical history or observation • orthopnoea • breathlessness at rest • pulmonary oedema • tachycardia • hypotension • systemic oedema	
Reference standard/target condition	Peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation (by a cardiologist) Maternal mortality due to peripartum cardiomyopathy	
Outcomes	For diagnostic comparisons: • sensitivity, specificity, positive and negative likelihood ratios For prognostic comparisons: • measures of association (risk ratios, odds ratios or hazard ratios) between prognostic factors and peripartum cardiomyopathy defined as above or related maternal mortality	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • peripartum cardiomyopathy • previously diagnosed cardiomyopathy • receipt of antenatal care Stratification by • severity of disease (as defined within studies)	
Language	English	
Study design	• Published full-text papers only	

Item	Details	Working notes
	• Systematic reviews • Prospective or retrospective comparative observational studies (including cohort and case-control studies) • Cross-sectional studies • Case series studies • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using quality checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR for systematic reviews, QUADAS2 for diagnostic test accuracy studies or QUIPs for prognostic studies) and the quality of the evidence for each outcome (that is, across studies) will be assessed using an adapted version of GRADE for diagnostic test accuracy outcomes only Synthesis of data: • meta-analysis of diagnostic test accuracy evidence will be conducted where appropriate • for risk ratios, default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes, except for recovery of ventricular fraction where a change of ≥10 percentage points in left ventricular fraction will be used as an MID	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the

Item	Details	Working notes
		outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	Eur Heart J. 2008 Jan;29(2):270-6. – for definition of cardiomyopathies	
Key papers	None identified by the committee	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – diagnosis and management of cardiomyopathy	
Review question in the scope	What is the optimal management for women with suspected cardiomyopathy in labour?	
Review question for the guideline	What is the optimal management for women with peripartum cardiomyopathy in labour?	
Objective	The aim of this review is to compare standard management of cardiomyopathy to standard management plus either bromocriptine or cabergoline; these are the pharmaceutical interventions around which there is most important clinical disagreement	

Item	Details	Working notes
Population and directness	Pregnant women who develop symptoms of cardiac failure (secondary to cardiomyopathy) before, during or up to 48 hours after labour	
Intervention	Bromocriptine in addition to standard care Cabergoline in addition to standard care	
Comparison	Standard care	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ recovery of ventricular function measured by left ventricular ejection fraction (at 6 weeks to 1 year)
	• for the baby:
	  ○ mortality
	
	Important outcomes:
	• for the woman:
	  ○ major morbidity
	  ○ women's satisfaction with labour and birth (including psychological wellbeing)
	• for the baby:
	  ○ major morbidity
	
	Outcomes of limited importance:
	• for the woman:
	  ○ women's health related quality of life	

Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	
Setting	All settings	

Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately:
	• receipt of antenatal care
	
	Stratification by:
	• severity of disease
	  ○ milder degrees of breathlessness (in which case the woman may need only oxygen and diuretics as first-line management), cardiogenic shock (requiring admission to coronary care or cardiac ICU, transplant, inotropes and mechanical assist devices (intra-aortic balloon pumps, left ventricular assist devices)
	  ○ left ventricular ejection fraction (under 40% severe, 40-50% mild, Group 1 above would be under 25%)	

Item	Details	Working notes
	Potential confounders: • none specified	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies. Search not date-limited but studies published prior to 1990 were excluded by the reviewer(s) due to market approval for cabergoline.	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes, except for recovery of ventricular fraction where a change of ≥10 percentage points in left ventricular fraction was used as an MID • for continuous data, change scores will be used in preference to final scores for data from non-RCT	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study

Item	Details	Working notes
	studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	Eur Heart J. 2008 Jan;29(2):270-6. – for definition of cardiomyopathies	
Key papers	None identified by the committee	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews

Intrapartum care for women with cardiac disease – anaesthesia

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – anaesthesia and analgesia	
Review question in the scope	Is regional or general anaesthesia safer for women with cardiac disease who need anaesthesia for caesarean section?	

Item	Details	Working notes
Review question for the guideline	Is regional or general anaesthesia safer for women with cardiac disease for peripartum surgical procedures including caesarean section?	
Objective	The aim of this review is to examine outcomes for the woman and baby comparing regional with general anaesthesia. This is important because women with cardiac disease may not be able to tolerate acute changes in heart rate and blood pressure which can occur with use of both regional and general anaesthesia	
Population and directness	Women with a cardiac condition in the intrapartum period The WHO classification of maternal risk of pregnancy associated with specific cardiac conditions is described in Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart. 2006 Oct;92(10):1520-5. Loeys Dietz syndrome was added to the list by the committee **Conditions in which pregnancy risk is classified as WHO 1** • Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, or anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated **Conditions in which pregnancy risk is classified as WHO 2 or 3** **WHO 2 (if otherwise well and uncomplicated)** • Unoperated atrial or small ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias **WHO 2–3 (depending on the individual)** • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered as WHO 1 or 4 • Marfan syndrome without aortic dilatation • Loeys Dietz syndrome • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation **WHO 3**	

Item	Details	Working notes
	• Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve **Conditions in which pregnancy risk is classified as WHO 4 (pregnancy contraindicated)** • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation Studies with indirect populations will not be considered	
Intervention	General anaesthesia	
Comparison	Regional anaesthesia (spinal, epidural, or CSE)	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ major morbidity (including perioperative cardiovascular collapse, stroke, hypotension, cardiac arrest, hypertension, intracranial haemorrhage, or myocardial infarction)
	  ○ women's satisfaction with labour and birth (including psychological wellbeing)
	
	Important outcomes:
	• for the woman:
	  ○ need for a high dependency unit (HDU) or intensive treatment unit (ITU)
	  ○ re-admission to hospital within 6 weeks of birth
	• for the baby:
	  ○ mortality
	  ○ major neonatal morbidity (including ischaemic encephalopathy)
	  ○ unexpected admission to a neonatal unit
	
	Outcomes of limited importance:	

Item	Details	Working notes
	• for the woman: ○ duration of hospital stay	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited importance (1 outcome)	Given the small volume of evidence available for inclusion overall, the committee agreed to consider more than the nominal maximum of 7 outcomes for this question
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • severe left sided stenotic lesions – aortic stenosis and mitral stenosis • cardiomyopathy/systolic ventricular dysfunction • aortopathies – Marfan and Loeys-Dietz, Ehlers-Danlos syndromes • pulmonary hypertension • coronary disease • receipt of antenatal care Stratification by • severity of disease (as defined within studies) Potential confounders: • hyper/hypotension	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used.	

Item	Details	Working notes
	See Appendix B for full strategies. Search not date-limited but studies published prior to 1980 were excluded by the reviewer(s) as prior to this time regional anaesthesia was not considered routinely.	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and

Item	Details	Working notes
		data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	
Key papers		

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LVEF: Left ventricular ejection fraction: MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NYHA: New York Heart Association; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews; WHO: World Health Organization

Intrapartum care for women with cardiac disease – analgesia

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – anaesthesia and analgesia	
Review question in the scope	What is the effectiveness and safety of regional analgesia compared with systemic narcotic analgesia for women with cardiac disease who are in labour?	
Review question for the guideline	What are the risks and benefits of central neuraxial analgesia compared with systemic analgesia, inhaled analgesia or no analgesia for women with cardiac disease who are in labour?	
Objective	The aim of this review is to compare different analgesic techniques and their effects on outcomes for women and babies This is important because painful contractions at any time during labour and pushing during the second stage of labour result in additional demands on the woman's cardiovascular system that can be ameliorated by providing effective analgesia	

Item	Details	Working notes
Population and directness	Women with a cardiac condition in the intrapartum period The WHO classification of maternal risk of pregnancy associated with specific cardiac conditions is described in Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart. 2006 Oct;92(10):1520-5. Loeys Dietz syndrome was added to the list by the committee. **Conditions in which pregnancy risk is classified as WHO 1** • Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, or anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated **Conditions in which pregnancy risk is classified as WHO 2 or 3** **WHO 2 (if otherwise well and uncomplicated)** • Unoperated atrial or small ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias **WHO 2–3 (depending on the individual)** • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Native or tissue valvular heart disease not considered as WHO 1 or 4 • Marfan syndrome without aortic dilatation • Loeys Dietz syndrome • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation **WHO 3** • Mechanical valve • Systemic right ventricle • Fontan circulation • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease	

Item	Details	Working notes
	• Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve **Conditions in which pregnancy risk is classified as WHO 4 (pregnancy contraindicated)** • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation Studies with indirect populations will not be considered	
Intervention	Systemic analgesia (using the opioids pethidine, morphine, diamorphine or remifentanil; or ketamine) Inhaled analgesia (nitrous oxide, or sevoflurane) Non-pharmacological analgesia (TENS, acupuncture, water papules, birthing pools, reflexology, aromatherapy, hypnobirthing, or homeopathy)	
Comparison	Central/regional neuraxial analgesia (spinal, epidural, or combined spinal epidural)	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ major morbidity (respiratory arrest, pulmonary oedema, or haematoma)
	  ○ adequacy of analgesia (woman's perception of pain (pain scores), need for a top up or second technique)
	
	Important outcomes:
	• for the woman:
	  ○ blood pressure (hypertension or hypotension)
	• for the baby:
	  ○ neonatal mortality
	  ○ fetal morbidity (respiratory depression and fetal distress (heart rate changes or abnormalities))
	
	Outcomes of limited importance:
	• for the woman:
	  ○ mode of birth	

Item	Details	Working notes
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of milited importance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	Groups that will be reviewed and analysed separately: • planned mode of birth • actual mode of birth Subgroups • women with no antenatal care • preterm labour Subgroup analysis by • severe left-sided stenotic lesions – aortic stenosis and mitral stenosis • cardiomyopathy with systolic ventricular dysfunction • cardiomyopathy with diastolic ventricular dysfunction, for example, hypertrophic cardiomyopathy • aortopathies, for example Marfan, Ehlers Danlos type 4 and Loeys-Dietz syndromes • pulmonary arterial hypertension • coronary disease In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • conditions that make caesarean section higher risk including maternal obesity, previous abdominal surgery with bowel adhesions, or abdominal fistulae from disease, colostomies, bleeding disorders, muscular dystrophies, conditions that make anaesthesia difficult (general or regional)) • severity of disease (as defined within studies) Potential confounders • none specified	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making: ○ prospective or retrospective comparative cohort studies	

Item	Details	Working notes
	• Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies. Search not date-limited but studies published prior to 1985 were excluded by the reviewer(s) as prior to this time anaesthetic practice was substantially different to current practice.	
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of

Item	Details	Working notes
		weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	
Key papers		

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LVEF: Left ventricular ejection fraction: MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NYHA: New York Heart Association; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews; WHO: World Health Organization

Intrapartum care for women with cardiac disease – management of the third stage of labour

Item	Details	Working notes
Area in the scope	Women at high risk of adverse outcomes for themselves and/or their baby because of existing maternal medical conditions – intrapartum care for women with cardiac disease – management of the third stage of labour	
Review question in the scope	How should the third stage of labour be managed for women with cardiac disease?	
Review question for the guideline	How should the third stage of labour be managed for women with cardiac disease?	
Objective	The aim of this review is to identify if any active management intervention (including use of uterotonics) is more effective than physiological management in women with cardiac conditions for whom the risk of postpartum haemorrhage is of particular concern; this is of particular interest in the case of women whose cardiac condition is related to and affected by the circulating volume of blood. This question is important	

Item	Details	Working notes
	because there are a variety of options for management of the risk of postpartum haemorrhage, of which uterotonics are the area of biggest clinical disagreement.	
Population and directness	Women with a cardiac condition in the third stage of labour The WHO classification of maternal risk of pregnancy associated with specific cardiac conditions is described in Thorne S, MacGregor A, Nelson-Piercy C. Risks of contraception and pregnancy in heart disease. Heart. 2006 Oct;92(10):1520-5. Loeys Dietz syndrome was added to the list by the committee. **Conditions in which pregnancy risk is classified as WHO 1** • Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse • Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, or anomalous pulmonary venous drainage) • Atrial or ventricular ectopic beats, isolated **Conditions in which pregnancy risk is classified as WHO 2 or 3** **WHO 2 (if otherwise well and uncomplicated)** • Unoperated atrial or small ventricular septal defect • Repaired tetralogy of Fallot • Most arrhythmias **WHO 2–3 (depending on the individual)** • Mild left ventricular impairment • Hypertrophic cardiomyopathy • Moderate mitral or aortic regurgitant valvular lesions with normal left ventricular function • Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve • Repaired coarctation **WHO 3** • Mechanical valve • Severe mitral or aortic regurgitant valvular lesions with normal left ventricular function • Systemic right ventricle	

Item	Details	Working notes
	• Fontan circulation • Coronary disease • Cyanotic heart disease (unrepaired) • Other complex congenital heart disease • Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve • Loeys Dietz syndrome **Conditions in which pregnancy risk is classified as WHO 4 (pregnancy contraindicated)** • Pulmonary arterial hypertension of any cause • Severe systemic ventricular dysfunction (LVEF <30%, NYHA III–IV) • Previous peripartum cardiomyopathy with any residual impairment of left ventricular function • Severe mitral stenosis, severe symptomatic aortic stenosis • Marfan syndrome with aorta dilated >45 mm • Aortic dilatation >50 mm in aortic disease associated with bicuspid aortic valve • Native severe coarctation Studies with indirect populations will not be considered	
Intervention	Active management using: • uterotonics such as carboprost (hemabate), syntometrine, syntocinon, misoprostol, ergometrine, or oxytocin (some drugs are given as IV or IM) • other drugs (for example, tranexamic acid) • breastfeeding • clamping and cutting the umbilical cord • controlled cord traction	
Comparison	Physiological management (such as no cord clamping, waiting for signs of separation, placenta delivered by maternal effort) Active management options (including regimens) compared against each other	

Outcomes	Critical outcomes:
	• for the woman:
	  ○ mortality
	  ○ major morbidity (shock, collapse or other haemodynamic compromise)
	
	Important outcomes:	

Item	Details	Working notes
	• for the woman: ○ women's satisfaction with labour and birth (including psychological wellbeing) ○ postpartum haemorrhage Outcomes of limited importance: • for the woman: ○ admission to intensive treatment unit (ITU)	
Importance of outcomes	Preliminary classification of the outcomes for decision making: • critical (up to 3 outcomes) • important but not critical (up to 3 outcomes) • of limited im[ortance (1 outcome)	
Setting	All settings	
Stratified, subgroup and adjusted analyses	In the presence of heterogeneity, the following subgroups will be considered for sensitivity analysis: • type of cardiac condition such as mitral stenosis, Marfan's syndrome and pulmonary hypertension, cardiomyopathy, aortic stenosis, or ischaemic heart disease • maternal age • obesity	
Language	English	
Study design	• Published full-text papers only • Systematic reviews • RCTs • Only if RCTs unavailable or there is limited data to inform decision making with minimum sample size of studies of 15 women in each group: ○ prospective or retrospective comparative cohort studies ○ case series studies • Prospective study designs will be prioritised over retrospective study designs • Conference abstracts will not be considered	
Search strategy	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA and Embase. Limits (e.g. date, study design): All study designs. Apply standard animal/non-English language filters. No date limit. Supplementary search techniques: No supplementary search techniques were used. See Appendix B for full strategies. Search not date-limited but studies published prior to 1995 were excluded by the reviewer(s) due to introduction of syntometrine/syntocinon at this time.	

Item	Details	Working notes
Review strategy	Appraisal of methodological quality: • the methodological quality of each study will be assessed using checklists recommended in the NICE guidelines manual 2014 (for example, AMSTAR or ROBIS for systematic reviews, and Cochrane RoB tool for RCTs) and the quality of the evidence for each outcome (that is, across studies) will be assessed using GRADE • if studies report only p-values, this information will be recorded in GRADE tables without an assessment of imprecision Synthesis of data: • meta-analysis will be conducted where appropriate • default MIDs will be used; 0.8 and 1.25 for dichotomous outcomes; 0.5 times the SD of the measurement in the control arm (or median score across control arms if multiple studies are included) for continuous outcomes • for continuous data, change scores will be used in preference to final scores for data from non-RCT studies; final and change scores will not be pooled; if any study reports both, the method used in the majority of studies will be adopted	Review questions selected as high priorities for health economic analysis (and those selected as medium priorities and where health economic analysis could influence recommendations) will be subject to dual weeding and study selection; any discrepancies will be resolved through discussion between the first and second reviewers or by reference to a third person. This review question was not prioritised for health economic analysis and so no formal dual weeding, study selection (inclusion/exclusion) or data extraction into evidence tables will be undertaken. However, internal (NGA) quality assurance processes will include consideration of the outcomes of weeding, study selection and data extraction and the committee will review the results of study selection and data extraction
Equalities	Equalities considerations will be considered systematically in relation to the available evidence and draft recommendations. The guideline scope includes women with cognitive or physical disability as populations for whom there may be equalities issues. Women who have received no antenatal care will be considered as a subgroup for all systematic reviews performed within the medical conditions work stream	

Item	Details	Working notes
	and a specific question has been included in the obstetric complications work stream for this population	
Notes/additional information	None	
Key papers	RCOG: Cardiac Disease and Pregnancy, Good Practice no 13, June 2011 Management of cardiac disease in pregnancy by C Burt and J Durbridge (2009)	

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CDSR: Cochrane Database of Systematic Reviews; CENTRAL: Cochrane Central Register of Controlled Trials; DARE: Database of Abstracts of Reviews of Effects; GRADE: Grading of Recommendations Assessment, Development and Evaluation; HTA: Health Technology Assessment; LVEF: Left ventricular ejection fraction: MID: minimally important difference; NGA: National Guideline Alliance; NICE: National Institute for Health and Care Excellence; NYHA: New York Heart Association; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation; ROBIS: Risk of Bias in Systematic Reviews; WHO: World Health Organization

Appendix B – Literature search strategies

Intrapartum care for women with cardiac disease – stratification of risk

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.

#	Searches
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.

#	Searches
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	MEDICAL HISTORY TAKING/
84	(history adj3 (take or taking)).ti,ab.
85	(history adj3 clinical).ti,ab.
86	(history adj3 (family or families or parent$)).ti,ab.
87	*SMOKING/
88	(Smoke$ or smoking).ti.
89	(Smoke$ or smoking).ab. /freq=2
90	(history adj3 obstetric$).ti,ab.
91	or/83-90
92	"SIGNS AND SYMPTOMS"/
93	exp DYSPNEA/
94	Breathless$.ti,ab.
95	(Short$ adj2 breath$).ti,ab.
96	Dyspnea?.ti,ab.
97	Orthopnoea?.ti,ab.
98	Palpitat$.ti,ab.
99	exp SYNCOPE/
100	Syncop$.ti,ab.

#	Searches
101	Fainting.ti,ab.
102	Drop attack?.ti,ab.
103	exp CHEST PAIN/
104	(Chest? adj3 pain$).ti,ab.
105	angina pectoris.ti,ab.
106	stenocardia?.ti,ab.
107	((unstable or stable or preinfarction) adj3 angina).ti,ab.
108	or/92-107
109	PHYSICAL EXAMINATION/
110	(clinical$ adj3 (examin$ or investigat$ or observ$)).ti,ab.
111	PULSE/
112	Pulse?.ti.
113	Pulse?.ab. /freq=2
114	*BLOOD PRESSURE/
115	((Blood or systolic or diastolic) adj3 pressure?).ti.
116	((Blood or systolic or diastolic) adj3 pressure?).ab. /freq=2
117	JUGULAR VEINS/ and VENOUS PRESSURE/
118	JUGULAR VEINS/ and pressure?.ti,ab.
119	(Jugular adj3 (vein? or venous) adj3 pressure?).ti,ab.
120	HEART SOUNDS/
121	((Heart or cardiac) adj3 sound?).ti,ab.
122	RESPIRATORY SOUNDS/
123	((respirator$ or breath$ or lung) adj3 sound?).ti,ab.
124	(crackle? or rale? or rhonch$ or stridor? or wheez$).ti,ab.
125	HEART MURMURS/
126	((Heart or cardiac) adj3 murmur?).ti,ab.
127	HEART AUSCULTATION/
128	((heart? or cardiac or Chest?) adj3 auscultation?).ti,ab.
129	EDEMA, CARDIAC/
130	((Pitting or cardiac) adj3 (oedema? or edema?)).ti,ab.
131	(function$ adj3 test$).ti,ab.
132	or/109-131
133	exp *ECHOCARDIOGRAPHY/
134	echocardiograph$.ti.
135	echocardiograph$.ab. /freq=2
136	ECHO.ti,ab.
137	exp *ELECTROCARDIOGRAPHY/
138	electrocardiograph$.ti.
139	electrocardiograph$.ab. /freq=2
140	polarcardiograph$.ti,ab.

#	Searches
141	Vectorcardiograph$.ti,ab.
142	ECG.ti.
143	ECG.ab. /freq=2
144	EKG.ti,ab.
145	EXERCISE TEST/
146	(Exercise adj3 test$).ti,ab.
147	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).ti,ab.
148	CPEX.ti,ab.
149	X-RAYS/
150	(X-ray? or xray?).ti,ab.
151	*MAGNETIC RESONANCE IMAGING/
152	magnetic resonance imag$.ti,ab.
153	MRI.ti,ab.
154	*BIOMARKERS/
155	Biomarker?.ti,ab.
156	NATRIURETIC PEPTIDE, BRAIN/
157	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
158	BNP.ti,ab.
159	or/133-158
160	RISK/
161	RISK ASSESSMENT/
162	RISK FACTORS/ and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).ti,ab.
163	risk?.ti.
164	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).ti,ab.
165	risk factor?.ti,ab.
166	or/160-165
167	82 and 91 and 166
168	82 and 108 and 166
169	82 and 132 and 166
170	82 and 159 and 166
171	sudden cardiac death?.ti,ab.
172	SCD.ti,ab.
173	sudden arrhythmic death? syndrome.ti,ab.
174	SADS.ti,ab.
175	or/171-174
176	9 and 166 and 175
177	UK Obstetric Surveillance System.ti,ab.
178	UKOSS.ti,ab.

#	Searches
179	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
180	MBRRACE.ti,ab.
181	Scottish confidential audit of severe maternal morbidity.ti,ab.
182	SCASMM.ti,ab.
183	"Confidential Enquiry into Maternal and Child Health".ti,ab.
184	CEMACH.ti,ab.
185	or/177-184
186	82 and 185
187	(cardiac$ adj5 risk$ adj3 scor$).ti,ab.
188	modified World Health Organization.ti,ab.
189	modified WHO.ti,ab.
190	Zwangerschap bij Aangeboren Hartafwijking$.ti,ab.
191	ZAHARA.ti,ab.
192	(CARdiac disease in PREGnancy adj5 scor$).ti,ab.
193	CARPREG.ti,ab.
194	or/187-193
195	9 and 194
196	167 or 168 or 169 or 170 or 176 or 186 or 195
197	limit 196 to english language
198	LETTER/
199	EDITORIAL/
200	NEWS/
201	exp HISTORICAL ARTICLE/
202	ANECDOTES AS TOPIC/
203	COMMENT/
204	CASE REPORT/
205	(letter or comment*).ti.
206	or/198-205
207	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
208	206 not 207
209	ANIMALS/ not HUMANS/
210	exp ANIMALS, LABORATORY/
211	exp ANIMAL EXPERIMENTATION/
212	exp MODELS, ANIMAL/
213	exp RODENTIA/
214	(rat or rats or mouse or mice).ti.
215	or/208-214
216	197 not 215

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab,kw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab,kw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab,kw.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
32	Brugada Syndrome.ti,ab,kw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab,kw.
35	Long QT Syndrome.ti,ab,kw.
36	Parasystole.ti,ab,kw.
37	Pre-Excitation Syndrome?.ti,ab,kw.
38	Tachycardia?.ti,ab,kw.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.

#	Searches
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab,kw.
51	Loeys-Dietz Syndrome.ti,ab,kw.
52	Leriche Syndrome.ti,ab,kw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab,kw.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78

#	Searches
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	MEDICAL HISTORY TAKING/
84	(history adj3 (take or taking)).ti,ab.
85	(history adj3 clinical).ti,ab.
86	(history adj3 (family or families or parent$)).ti,ab.
87	*SMOKING/
88	(Smoke$ or smoking).ti.
89	(Smoke$ or smoking).ab. /freq=2
90	(history adj3 obstetric$).ti,ab.
91	or/83-90
92	"SIGNS AND SYMPTOMS"/
93	exp DYSPNEA/
94	Breathless$.ti,ab,kw.
95	(Short$ adj2 breath$).ti,ab.
96	Dyspnea?.ti,ab,kw.
97	Orthopnoea?.ti,ab,kw.
98	Palpitat$.ti,ab,kw.
99	exp SYNCOPE/
100	Syncop$.ti,ab,kw.
101	Fainting.ti,ab,kw.
102	Drop attack?.ti,ab,kw.
103	exp CHEST PAIN/
104	(Chest? adj3 pain$).ti,ab.
105	angina pectoris.ti,ab,kw.
106	stenocardia?.ti,ab,kw.
107	((unstable or stable or preinfarction) adj3 angina).ti,ab.
108	or/92-107
109	PHYSICAL EXAMINATION/
110	(clinical$ adj3 (examin$ or investigat$ or observ$)).ti,ab.
111	PULSE/
112	Pulse?.ti.
113	Pulse?.ab. /freq=2
114	*BLOOD PRESSURE/
115	((Blood or systolic or diastolic) adj3 pressure?).ti.
116	((Blood or systolic or diastolic) adj3 pressure?).ab. /freq=2
117	JUGULAR VEINS/ and VENOUS PRESSURE/
118	JUGULAR VEINS/ and pressure?.ti,ab.
119	(Jugular adj3 (vein? or venous) adj3 pressure?).ti,ab.

#	Searches
120	HEART SOUNDS/
121	((Heart or cardiac) adj3 sound?).ti,ab.
122	RESPIRATORY SOUNDS/
123	((respirator$ or breath$ or lung) adj3 sound?).ti,ab.
124	(crackle? or rale? or rhonch$ or stridor? or wheez$).ti,ab.
125	HEART MURMURS/
126	((Heart or cardiac) adj3 murmur?).ti,ab.
127	HEART AUSCULTATION/
128	((heart? or cardiac or Chest?) adj3 auscultation?).ti,ab.
129	EDEMA, CARDIAC/
130	((Pitting or cardiac) adj3 (oedema? or edema?)).ti,ab.
131	(function$ adj3 test$).ti,ab.
132	or/109-131
133	exp *ECHOCARDIOGRAPHY/
134	echocardiograph$.ti.
135	echocardiograph$.ab. /freq=2
136	ECHO.ti,ab.
137	exp *ELECTROCARDIOGRAPHY/
138	electrocardiograph$.ti.
139	electrocardiograph$.ab. /freq=2
140	polarcardiograph$.ti,ab,kw.
141	Vectorcardiograph$.ti,ab,kw.
142	ECG.ti.
143	ECG.ab. /freq=2
144	EKG.ti,ab.
145	EXERCISE TEST/
146	(Exercise adj3 test$).ti,ab.
147	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).ti,ab.
148	CPEX.ti,ab.
149	X-RAYS/
150	(X-ray? or xray?).ti,ab,kw.
151	*MAGNETIC RESONANCE IMAGING/
152	magnetic resonance imag$.ti,ab,kw.
153	MRI.ti,ab.
154	*BIOMARKERS/
155	Biomarker?.ti,ab,kw.
156	NATRIURETIC PEPTIDE, BRAIN/
157	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
158	BNP.ti,ab.
159	or/133-158

#	Searches
160	RISK/
161	RISK ASSESSMENT/
162	RISK FACTORS/ and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).ti,ab.
163	risk?.ti.
164	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).ti,ab.
165	risk factor?.ti,ab.
166	or/160-165
167	82 and 91 and 166
168	82 and 108 and 166
169	82 and 132 and 166
170	82 and 159 and 166
171	sudden cardiac death?.ti,ab,kw.
172	SCD.ti,ab.
173	sudden arrhythmic death? syndrome.ti,ab,kw.
174	SADS.ti,ab.
175	or/171-174
176	9 and 166 and 175
177	UK Obstetric Surveillance System.ti,ab.
178	UKOSS.ti,ab.
179	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
180	MBRRACE.ti,ab.
181	Scottish confidential audit of severe maternal morbidity.ti,ab.
182	SCASMM.ti,ab.
183	"Confidential Enquiry into Maternal and Child Health".ti,ab.
184	CEMACH.ti,ab.
185	or/177-184
186	82 and 185
187	(cardiac$ adj5 risk$ adj3 scor$).ti,ab.
188	modified World Health Organization.ti,ab.
189	modified WHO.ti,ab.
190	mWHO.ti,ab.
191	Zwangerschap bij Aangeboren Hartafwijking$.ti,ab.
192	ZAHARA.ti,ab.
193	(CARdiac disease in PREGnancy adj5 scor$).ti,ab.
194	CARPREG.ti,ab.
195	or/187-194
196	9 and 195
197	167 or 168 or 169 or 170 or 176 or 186 or 196

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.

#	Searches
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).ti,ab.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).ti,ab.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78

#	Searches
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	MEDICAL HISTORY TAKING.kw.
84	(history adj3 (take or taking)).ti,ab.
85	(history adj3 clinical).ti,ab.
86	(history adj3 (family or families or parent$)).ti,ab.
87	SMOKING.kw.
88	(Smoke$ or smoking).ti.
89	(Smoke$ or smoking).ab. /freq=2
90	(history adj3 obstetric$).ti,ab.
91	or/83-90
92	"SIGNS AND SYMPTOMS".kw.
93	DYSPNEA.kw.
94	Breathless$.ti,ab.
95	(Short$ adj2 breath$).ti,ab.
96	Dyspnea?.ti,ab.
97	Orthopnoea?.ti,ab.
98	Palpitat$.ti,ab.
99	SYNCOPE.kw.
100	Syncop$.ti,ab.
101	Fainting.ti,ab.
102	Drop attack?.ti,ab.
103	CHEST PAIN.kw.
104	(Chest? adj3 pain$).ti,ab.
105	angina pectoris.ti,ab.
106	stenocardia?.ti,ab.
107	((unstable or stable or preinfarction) adj3 angina).ti,ab.
108	or/92-107
109	PHYSICAL EXAMINATION.kw.
110	(clinical$ adj3 (examin$ or investigat$ or observ$)).ti,ab.
111	PULSE.kw.
112	Pulse?.ti.
113	Pulse?.ab. /freq=2
114	BLOOD PRESSURE.kw.
115	((Blood or systolic or diastolic) adj3 pressure?).ti.
116	((Blood or systolic or diastolic) adj3 pressure?).ab. /freq=2
117	(JUGULAR VEINS and VENOUS PRESSURE).kw.
118	JUGULAR VEINS.kw. and pressure?.ti,ab.
119	(Jugular adj3 (vein? or venous) adj3 pressure?).ti,ab.

#	Searches
120	HEART SOUNDS.kw.
121	((Heart or cardiac) adj3 sound?).ti,ab.
122	RESPIRATORY SOUNDS.kw.
123	((respirator$ or breath$ or lung) adj3 sound?).ti,ab.
124	(crackle? or rale? or rhonch$ or stridor? or wheez$).ti,ab.
125	HEART MURMURS.kw.
126	((Heart or cardiac) adj3 murmur?).ti,ab.
127	HEART AUSCULTATION.kw.
128	((heart? or cardiac or Chest?) adj3 auscultation?).ti,ab.
129	EDEMA, CARDIAC.kw.
130	((Pitting or cardiac) adj3 (oedema? or edema?)).ti,ab.
131	(function$ adj3 test$).ti,ab.
132	or/109-131
133	ECHOCARDIOGRAPHY.kw.
134	echocardiograph$.ti.
135	echocardiograph$.ab. /freq=2
136	ECHO.ti,ab.
137	ELECTROCARDIOGRAPHY.kw.
138	electrocardiograph$.ti.
139	electrocardiograph$.ab. /freq=2
140	polarcardiograph$.ti,ab.
141	Vectorcardiograph$.ti,ab.
142	ECG.ti.
143	ECG.ab. /freq=2
144	EKG.ti,ab.
145	EXERCISE TEST.kw.
146	(Exercise adj3 test$).ti,ab.
147	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).ti,ab.
148	CPEX.ti,ab.
149	X-RAYS.kw.
150	(X-ray? or xray?).ti,ab.
151	MAGNETIC RESONANCE IMAGING.kw.
152	magnetic resonance imag$.ti,ab.
153	MRI.ti,ab.
154	BIOMARKERS.kw.
155	Biomarker?.ti,ab.
156	NATRIURETIC PEPTIDE, BRAIN.kw.
157	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
158	BNP.ti,ab.
159	or/133-158

#	Searches
160	RISK.kw.
161	RISK ASSESSMENT.kw.
162	RISK FACTORS.kw. and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).ti,ab.
163	risk?.ti.
164	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).ti,ab.
165	risk factor?.ti,ab.
166	or/160-165
167	82 and 91 and 166
168	82 and 108 and 166
169	82 and 132 and 166
170	82 and 159 and 166
171	sudden cardiac death?.ti,ab.
172	SCD.ti,ab.
173	sudden arrhythmic death? syndrome.ti,ab.
174	SADS.ti,ab.
175	or/171-174
176	9 and 166 and 175
177	UK Obstetric Surveillance System.ti,ab.
178	UKOSS.ti,ab.
179	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
180	MBRRACE.ti,ab.
181	Scottish confidential audit of severe maternal morbidity.ti,ab.
182	SCASMM.ti,ab.
183	"Confidential Enquiry into Maternal and Child Health".ti,ab.
184	CEMACH.ti,ab.
185	or/177-184
186	82 and 185
187	(cardiac$ adj5 risk$ adj3 scor$).ti,ab.
188	modified World Health Organization.ti,ab.
189	modified WHO.ti,ab.
190	mWHO.ti,ab.
191	Zwangerschap bij Aangeboren Hartafwijking$.ti,ab.
192	ZAHARA.ti,ab.
193	(CARdiac disease in PREGnancy adj5 scor$).ti,ab.
194	CARPREG.ti,ab.
195	or/187-194
196	9 and 195
197	167 or 168 or 169 or 170 or 176 or 186 or 196

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).tw,tx.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).tw,tx.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
16	click murmur syndrome?.tw,tx.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
21	(persist$ adj2 ostium primum).tw,tx.
22	anomal$ pulmonary venous drain$.tw,tx.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
25	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).tw,tx.
30	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
31	(Bradycardia? or bradyarrhythmia?).tw,tx.
32	Brugada Syndrome.tw,tx.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
34	Heart Block.tw,tx.
35	Long QT Syndrome.tw,tx.
36	Parasystole.tw,tx.
37	Pre-Excitation Syndrome?.tw,tx.
38	Tachycardia?.tw,tx.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.

#	Searches
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).tw,tx.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).tw,tx.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
50	Aortitis.tw,tx.
51	Loeys-Dietz Syndrome.tw,tx.
52	Leriche Syndrome.tw,tx.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.tw,tx.
65	(complex$ adj10 congenital$ heart disease?).tw,tx.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).tw,tx.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).tw,tx.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).tw,tx.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).tw,tx.
79	or/10-78

#	Searches
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	MEDICAL HISTORY TAKING.kw.
84	(history adj3 (take or taking)).tw,tx.
85	(history adj3 clinical).tw,tx.
86	(history adj3 (family or families or parent$)).tw,tx.
87	SMOKING.kw.
88	(Smoke$ or smoking).tw.
89	(Smoke$ or smoking).tx.
90	(history adj3 obstetric$).tw,tx.
91	or/83-90
92	"SIGNS AND SYMPTOMS".kw.
93	DYSPNEA.kw.
94	Breathless$.tw,tx.
95	(Short$ adj2 breath$).tw,tx.
96	Dyspnea?.tw,tx.
97	Orthopnoea?.tw,tx.
98	Palpitat$.tw,tx.
99	SYNCOPE.kw.
100	Syncop$.tw,tx.
101	Fainting.tw,tx.
102	Drop attack?.tw,tx.
103	CHEST PAIN.kw.
104	(Chest? adj3 pain$).tw,tx.
105	angina pectoris.tw,tx.
106	stenocardia?.tw,tx.
107	((unstable or stable or preinfarction) adj3 angina).tw,tx.
108	or/92-107
109	PHYSICAL EXAMINATION.kw.
110	(clinical$ adj3 (examin$ or investigat$ or observ$)).tw,tx.
111	PULSE.kw.
112	Pulse?.tw.
113	Pulse?.tx.
114	BLOOD PRESSURE.kw.
115	((Blood or systolic or diastolic) adj3 pressure?).tw.
116	((Blood or systolic or diastolic) adj3 pressure?).tx.
117	(JUGULAR VEINS and VENOUS PRESSURE).kw.
118	JUGULAR VEINS.kw. and pressure?.tw,tx.
119	(Jugular adj3 (vein? or venous) adj3 pressure?).tw,tx.

#	Searches
120	HEART SOUNDS.kw.
121	((Heart or cardiac) adj3 sound?).tw,tx.
122	RESPIRATORY SOUNDS.kw.
123	((respirator$ or breath$ or lung) adj3 sound?).tw,tx.
124	(crackle? or rale? or rhonch$ or stridor? or wheez$).tw,tx.
125	HEART MURMURS.kw.
126	((Heart or cardiac) adj3 murmur?).tw,tx.
127	HEART AUSCULTATION.kw.
128	((heart? or cardiac or Chest?) adj3 auscultation?).tw,tx.
129	EDEMA, CARDIAC.kw.
130	((Pitting or cardiac) adj3 (oedema? or edema?)).tw,tx.
131	(function$ adj3 test$).tw,tx.
132	or/109-131
133	ECHOCARDIOGRAPHY.kw.
134	echocardiograph$.tw.
135	echocardiograph$.tx.
136	ECHO.tw,tx.
137	ELECTROCARDIOGRAPHY.kw.
138	electrocardiograph$.tw.
139	electrocardiograph$.tx.
140	polarcardiograph$.tw,tx.
141	Vectorcardiograph$.tw,tx.
142	ECG.tw.
143	ECG.tx.
144	EKG.tw,tx.
145	EXERCISE TEST.kw.
146	(Exercise adj3 test$).tw,tx.
147	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).tw,tx.
148	CPEX.tw,tx.
149	X-RAYS.kw.
150	(X-ray? or xray?).tw,tx.
151	MAGNETIC RESONANCE IMAGING.kw.
152	magnetic resonance imag$.tw,tx.
153	MRI.tw,tx.
154	BIOMARKERS.kw.
155	Biomarker?.tw,tx.
156	NATRIURETIC PEPTIDE, BRAIN.kw.
157	((B-type or type-b or brain) adj3 natriuretic peptide?).tw,tx.
158	BNP.tw,tx.
159	or/133-158

#	Searches
160	RISK.kw.
161	RISK ASSESSMENT.kw.
162	RISK FACTORS.kw. and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).tw,tx.
163	risk?.tw,tx.
164	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).tw,tx.
165	risk factor?.tw,tx.
166	or/160-165
167	82 and 91 and 166
168	82 and 108 and 166
169	82 and 132 and 166
170	82 and 159 and 166
171	sudden cardiac death?.tx,tx.
172	SCD.tx,tx.
173	sudden arrhythmic death? syndrome.tw,tx.
174	SADS.tw,tx.
175	or/171-174
176	9 and 166 and 175
177	UK Obstetric Surveillance System.tw,tx.
178	UKOSS.tw,tx.
179	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw,tx.
180	MBRRACE.tw,tx.
181	Scottish confidential audit of severe maternal morbidity.tw,tx.
182	SCASMM.tw,tx.
183	"Confidential Enquiry into Maternal and Child Health".tw,tx.
184	CEMACH.tw,tx.
185	or/177-184
186	82 and 185
187	167 or 168 or 169 or 170 or 176 or 186

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.

#	Searches
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).tw.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).tw.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).tw.
16	click murmur syndrome?.tw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
21	(persist$ adj2 ostium primum).tw.
22	anomal$ pulmonary venous drain$.tw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
25	((Atrial or ventricular) adj2 extrasystole?).tw.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
28	exp *ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).tw.
30	(Atrial adj2 (Fibrillation or Flutter)).tw.
31	(Bradycardia? or bradyarrhythmia?).tw.
32	Brugada Syndrome.tw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
34	Heart Block.tw.
35	Long QT Syndrome.tw.
36	Parasystole.tw.
37	Pre-Excitation Syndrome?.tw.
38	Tachycardia?.tw.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).tw.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).tw.

#	Searches
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
50	Aortitis.tw.
51	Loeys-Dietz Syndrome.tw.
52	Leriche Syndrome.tw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).tw.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).tw.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.tw.
65	(complex$ adj10 congenital$ heart disease?).tw.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).tw.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).tw.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).tw.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).tw.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	MEDICAL HISTORY TAKING/
84	(history adj3 (take or taking)).tw.
85	(history adj3 clinical).tw.
86	(history adj3 (family or families or parent$)).tw.
87	SMOKING/

#	Searches
88	(Smoke$ or smoking).tw.
89	(history adj3 obstetric$).tw.
90	or/83-89
91	"SIGNS AND SYMPTOMS"/
92	exp DYSPNEA/
93	Breathless$.tw.
94	(Short$ adj2 breath$).tw.
95	Dyspnea?.tw.
96	Orthopnoea?.tw.
97	Palpitat$.tw.
98	exp SYNCOPE/
99	Syncop$.tw.
100	Fainting.tw.
101	Drop attack?.tw.
102	exp CHEST PAIN/
103	(Chest? adj3 pain$).tw.
104	angina pectoris.tw.
105	stenocardia?.tw.
106	((unstable or stable or preinfarction) adj3 angina).tw.
107	or/91-106
108	PHYSICAL EXAMINATION/
109	(clinical$ adj3 (examin$ or investigat$ or observ$)).tw.
110	PULSE/
111	Pulse?.tw.
112	BLOOD PRESSURE/
113	((Blood or systolic or diastolic) adj3 pressure?).tw.
114	JUGULAR VEINS/ and VENOUS PRESSURE/
115	JUGULAR VEINS/ and pressure?.tw.
116	(Jugular adj3 (vein? or venous) adj3 pressure?).tw.
117	HEART SOUNDS/
118	((Heart or cardiac) adj3 sound?).tw.
119	RESPIRATORY SOUNDS/
120	((respirator$ or breath$ or lung) adj3 sound?).tw.
121	(crackle? or rale? or rhonch$ or stridor? or wheez$).tw.
122	HEART MURMURS/
123	((Heart or cardiac) adj3 murmur?).tw.
124	HEART AUSCULTATION/
125	((heart? or cardiac or Chest?) adj3 auscultation?).tw.
126	EDEMA, CARDIAC/
127	((Pitting or cardiac) adj3 (oedema? or edema?)).tw.

#	Searches
128	(function$ adj3 test$).tw.
129	or/108-128
130	exp ECHOCARDIOGRAPHY/
131	echocardiograph$.tw.
132	ECHO.tw.
133	exp ELECTROCARDIOGRAPHY/
134	electrocardiograph$.tw.
135	polarcardiograph$.tw.
136	Vectorcardiograph$.tw.
137	ECG.tw.
138	EKG.tw.
139	EXERCISE TEST/
140	(Exercise adj3 test$).tw.
141	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).tw.
142	CPEX.tw.
143	X-RAYS/
144	(X-ray? or xray?).tw.
145	MAGNETIC RESONANCE IMAGING/
146	magnetic resonance imag$.tw.
147	MRI.tw.
148	BIOMARKERS/
149	Biomarker?.tw.
150	NATRIURETIC PEPTIDE, BRAIN/
151	((B-type or type-b or brain) adj3 natriuretic peptide?).tw.
152	BNP.tw.
153	or/130-152
154	RISK/
155	RISK ASSESSMENT/
156	RISK FACTORS/ and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).tw.
157	risk?.tw.
158	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).tw.
159	risk factor?.tw.
160	or/154-159
161	82 and 90 and 160
162	82 and 107 and 160
163	82 and 129 and 160
164	82 and 153 and 160
165	sudden cardiac death?.tw.
166	SCD.tw.

#	Searches
167	sudden arrhythmic death? syndrome.tw.
168	SADS.tw.
169	or/165-168
170	9 and 160 and 169
171	UK Obstetric Surveillance System.tw.
172	UKOSS.tw.
173	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
174	MBRRACE.tw.
175	Scottish confidential audit of severe maternal morbidity.tw.
176	SCASMM.tw.
177	"Confidential Enquiry into Maternal and Child Health".tw.
178	CEMACH.tw.
179	or/171-178
180	82 and 179
181	(cardiac$ adj5 risk$ adj3 scor$).tw.
182	modified World Health Organization.tw.
183	modified WHO.tw.
184	mWHO.tw.
185	Zwangerschap bij Aangeboren Hartafwijking$.tw.
186	ZAHARA.tw.
187	(CARdiac disease in PREGnancy adj5 scor$).tw.
188	CARPREG.tw.
189	or/181-188
190	9 and 189
191	161 or 162 or 163 or 164 or 170 or 180 or 190

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	PULMONARY VALVE STENOSIS/
12	(pulmonary adj2 stenos$).ti,ab.

#	Searches
13	PATENT DUCTUS ARTERIOSUS/
14	(Paten$ adj2 ductus arteriosus).ti,ab.
15	MITRAL VALVE PROLAPSE/
16	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
17	click murmur syndrome?.ti,ab.
18	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
19	HEART SEPTUM DEFECT/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	EXTRASYSTOLE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	FALLOT TETRALOGY/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *HEART ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp *HYPERTROPHIC CARDIOMYOPATHY/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE REGURGITATION/
43	MITRAL VALVE REGURGITATION/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp *AORTA DISEASE/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.

#	Searches
53	AORTA COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	exp *HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	GREAT VESSELS TRANSPOSITION/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp *CORONARY ARTERY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	CYANOTIC HEART DISEASE/
64	Cyanotic heart disease?.ti,ab.
65	*CONGENITAL HEART DISEASE/
66	(complex$ adj10 congenital$ heart disease?).ti,ab.
67	*PULMONARY HYPERTENSION/
68	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
69	exp *HEART VENTRICLE FAILURE/
70	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
71	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
72	exp CARDIOMYOPATHY/ and TIME FACTOR/
73	(previous$ adj5 cardiomyopath$).ti,ab.
74	MITRAL VALVE STENOSIS/
75	(mitral adj2 stenos?s).ti,ab.
76	AORTA VALVE STENOSIS/
77	(aort$ adj2 stenos?s).ti,ab.
78	AORTA COARCTATION/
79	(Coarctation? adj3 aort$).ti,ab.
80	or/11-79
81	10 and 80
82	exp ANAMNESIS/
83	(history adj3 (take or taking)).ti,ab.
84	(history adj3 clinical).ti,ab.
85	(history adj3 (family or families or parent$)).ti,ab.
86	*SMOKING/
87	(Smoke$ or smoking).ti.
88	(Smoke$ or smoking).ab. /freq=2
89	(history adj3 obstetric$).ti,ab.
90	or/82-89
91	*PHYSICAL DISEASE BY BODY FUNCTION/
92	DYSPNEA/

#	Searches
93	Breathless$.ti,ab.
94	(Short$ adj2 breath$).ti,ab.
95	Dyspnea?.ti,ab.
96	Orthopnoea?.ti,ab.
97	Palpitat$.ti,ab.
98	FAINTNESS/
99	Syncop$.ti,ab.
100	Fainting.ti,ab.
101	Drop attack?.ti,ab.
102	THORAX PAIN/
103	(Chest? adj3 pain$).ti,ab.
104	ANGINA PECTORIS/
105	angina pectoris.ti,ab.
106	stenocardia?.ti,ab.
107	((unstable or stable or preinfarction) adj3 angina).ti,ab.
108	or/91-107
109	*PHYSICAL EXAMINATION/
110	(clinical$ adj3 (examin$ or investigat$ or observ$)).ti,ab.
111	PULSE RATE/
112	Pulse?.ti.
113	Pulse?.ab. /freq=2
114	*BLOOD PRESSURE/
115	((Blood or systolic or diastolic) adj3 pressure?).ti.
116	((Blood or systolic or diastolic) adj3 pressure?).ab. /freq=2
117	CENTRAL VENOUS PRESSURE/
118	(Jugular adj3 (vein? or venous) adj3 pressure?).ti,ab.
119	HEART SOUND/
120	((Heart or cardiac) adj3 sound?).ti,ab.
121	exp ABNORMAL RESPIRATORY SOUND/
122	((respirator$ or breath$ or lung) adj3 sound?).ti,ab.
123	(crackle? or rale? or rhonch$ or stridor? or wheez$).ti,ab.
124	exp HEART MURMUR/
125	((Heart or cardiac) adj3 murmur?).ti,ab.
126	HEART AUSCULTATION/
127	((heart? or cardiac or Chest?) adj3 auscultation?).ti,ab.
128	HEART EDEMA/
129	((Pitting or cardiac) adj3 (oedema? or edema?)).ti,ab.
130	(function$ adj3 test$).ti,ab.
131	or/109-130
132	exp *ECHOCARDIOGRAPHY/

#	Searches
133	echocardiograph$.ti.
134	echocardiograph$.ab. /freq=2
135	ECHO.ti,ab.
136	exp *ELECTROCARDIOGRAPHY/
137	electrocardiograph$.ti.
138	electrocardiograph$.ab. /freq=2
139	polarcardiograph$.ti,ab.
140	Vectorcardiograph$.ti,ab.
141	ECG.ti.
142	ECG.ab. /freq=2
143	EKG.ti,ab.
144	exp EXERCISE TEST/
145	(Exercise adj3 test$).ti,ab.
146	(Test$ adj3 (arm? or bicycle? or step? or stress or treadmill? or cardiopulmonary)).ti,ab.
147	CPEX.ti,ab.
148	*X-RAY/
149	(X-ray? or xray?).ti,ab.
150	exp *NUCLEAR MAGNETIC RESONANCE IMAGING/
151	magnetic resonance imag$.ti,ab.
152	MRI.ti,ab.
153	*BIOLOGICAL MARKER/
154	Biomarker?.ti,ab.
155	*BRAIN NATRIURETIC PEPTIDE/
156	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
157	BNP.ti,ab.
158	or/132-157
159	*RISK/
160	*RISK ASSESSMENT/
161	*RISK FACTOR/ and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).ti,ab.
162	risk?.ti.
163	(risk? adj10 (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$)).ti,ab.
164	risk factor?.ti,ab.
165	or/159-164
166	81 and 90 and 165
167	81 and 108 and 165
168	81 and 131 and 165
169	81 and 158 and 165

#	Searches
170	exp *CARDIOVASCULAR RISK/ and (assess$ or stratif$ or protocol? or tool? or score? or scoring or system? or strateg$ or screen$ or manag$ or prognos$ or identif$ or quantif$).ti,ab.
171	10 and 170
172	sudden cardiac death?.ti,ab.
173	SCD.ti,ab.
174	sudden arrhythmic death? syndrome.ti,ab.
175	SADS.ti,ab.
176	or/172-175
177	10 and 165 and 176
178	UK Obstetric Surveillance System.ti,ab.
179	UKOSS.ti,ab.
180	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
181	MBRRACE.ti,ab.
182	Scottish confidential audit of severe maternal morbidity.ti,ab.
183	SCASMM.ti,ab.
184	"Confidential Enquiry into Maternal and Child Health".ti,ab.
185	CEMACH.ti,ab.
186	or/178-185
187	81 and 186
188	(cardiac$ adj5 risk$ adj3 scor$).ti,ab.
189	modified World Health Organization.ti,ab.
190	modified WHO.ti,ab.
191	mWHO.ti,ab.
192	Zwangerschap bij Aangeboren Hartafwijking$.ti,ab.
193	ZAHARA.ti,ab.
194	(CARdiac disease in PREGnancy adj5 scor$).ti,ab.
195	CARPREG.ti,ab.
196	or/188-195
197	10 and 196
198	166 or 167 or 168 or 169 or 171 or 177 or 187 or 197
199	limit 198 to english language
200	letter.pt. or LETTER/
201	note.pt.
202	editorial.pt.
203	CASE REPORT/ or CASE STUDY/
204	(letter or comment*).ti.
205	or/200-204
206	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
207	205 not 206

#	Searches
208	ANIMAL/ not HUMAN/
209	NONHUMAN/
210	exp ANIMAL EXPERIMENT/
211	exp EXPERIMENTAL ANIMAL/
212	ANIMAL MODEL/
213	exp RODENT/
214	(rat or rats or mouse or mice).ti.
215	or/207-214
216	199 not 215

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	HEART VALVE PROSTHESIS/
11	BIOPROSTHESIS/
12	HEART VALVE PROSTHESIS IMPLANTATION/
13	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).ti,ab.
14	or/10-13
15	exp ANTICOAGULANTS/
16	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
17	exp PLATELET AGGREGATION INHIBITORS/
18	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).ti,ab.
19	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).ti,ab.

#	Searches
20	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil or clopidogrel or ticagrelor).mp.
21	VITAMIN K/
22	VITAMIN K 1/
23	VITAMIN K 2/
24	VITAMIN K 3/
25	VITAMIN K DEFICIENCY/
26	vitamin k$.mp.
27	or/15-26
28	UK Obstetric Surveillance System.ti,ab.
29	UKOSS.ti,ab.
30	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
31	MBRRACE.ti,ab.
32	Scottish confidential audit of severe maternal morbidity.ti,ab.
33	SCASMM.ti,ab.
34	"Confidential Enquiry into Maternal and Child Health".ti,ab.
35	CEMACH.ti,ab.
36	or/28-35
37	9 and 14 and 27
38	14 and 36
39	27 and 36
40	or/37-39
41	limit 40 to english language
42	LETTER/
43	EDITORIAL/
44	NEWS/
45	exp HISTORICAL ARTICLE/
46	ANECDOTES AS TOPIC/
47	COMMENT/
48	CASE REPORT/
49	(letter or comment*).ti.
50	or/42-49
51	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
52	50 not 51
53	ANIMALS/ not HUMANS/
54	exp ANIMALS, LABORATORY/
55	exp ANIMAL EXPERIMENTATION/
56	exp MODELS, ANIMAL/
57	exp RODENTIA/

#	Searches
58	(rat or rats or mouse or mice).ti.
59	or/52-58
60	41 not 59

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	HEART VALVE PROSTHESIS/
11	BIOPROSTHESIS/
12	HEART VALVE PROSTHESIS IMPLANTATION/
13	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).ti,ab.
14	or/10-13
15	exp ANTICOAGULANTS/
16	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
17	exp PLATELET AGGREGATION INHIBITORS/
18	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).ti,ab.
19	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).ti,ab.
20	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil or clopidogrel or ticagrelor).mp.
21	VITAMIN K/
22	VITAMIN K 1/
23	VITAMIN K 2/
24	VITAMIN K 3/
25	VITAMIN K DEFICIENCY/
26	vitamin k$.mp.
27	or/15-26
28	UK Obstetric Surveillance System.ti,ab.
29	UKOSS.ti,ab.

#	Searches
30	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
31	MBRRACE.ti,ab.
32	Scottish confidential audit of severe maternal morbidity.ti,ab.
33	SCASMM.ti,ab.
34	"Confidential Enquiry into Maternal and Child Health".ti,ab.
35	CEMACH.ti,ab.
36	or/28-35
37	9 and 14 and 27
38	14 and 36
39	27 and 36
40	or/37-39

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	HEART VALVE PROSTHESIS.kw.
11	BIOPROSTHESIS.kw.
12	HEART VALVE PROSTHESIS IMPLANTATION.kw.
13	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).ti,ab.
14	or/10-13
15	ANTICOAGULANTS.kw.
16	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
17	PLATELET AGGREGATION INHIBITORS.kw.
18	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).ti,ab.
19	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).ti,ab.
20	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil or clopidogrel or ticagrelor).mp.

#	Searches
21	VITAMIN K.kw.
22	VITAMIN K 1.kw.
23	VITAMIN K 2.kw.
24	VITAMIN K 3.kw.
25	VITAMIN K DEFICIENCY.kw.
26	vitamin k$.mp.
27	or/15-26
28	UK Obstetric Surveillance System.ti,ab.
29	UKOSS.ti,ab.
30	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
31	MBRRACE.ti,ab.
32	Scottish confidential audit of severe maternal morbidity.ti,ab.
33	SCASMM.ti,ab.
34	"Confidential Enquiry into Maternal and Child Health".ti,ab.
35	CEMACH.ti,ab.
36	or/28-35
37	9 and 14 and 27
38	14 and 36
39	27 and 36
40	or/37-39

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	HEART VALVE PROSTHESIS.kw.
11	BIOPROSTHESIS.kw.
12	HEART VALVE PROSTHESIS IMPLANTATION.kw.
13	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).tw,tx.
14	or/10-13
15	ANTICOAGULANTS.kw.
16	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or

#	Searches
	Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
17	PLATELET AGGREGATION INHIBITORS.kw.
18	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).tw,tx.
19	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).tw,tx.
20	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil).mp.
21	VITAMIN K.kw.
22	VITAMIN K 1.kw.
23	VITAMIN K 2.kw.
24	VITAMIN K 3.kw.
25	VITAMIN K DEFICIENCY.kw.
26	vitamin k$.mp.
27	or/15-26
28	UK Obstetric Surveillance System.tw,tx.
29	UKOSS.tw,tx.
30	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw,tx.
31	MBRRACE.tw,tx.
32	Scottish confidential audit of severe maternal morbidity.tw,tx.
33	SCASMM.tw,tx.
34	"Confidential Enquiry into Maternal and Child Health".tw,tx.
35	CEMACH.tw,tx.
36	or/28-35
37	9 and 14 and 27
38	14 and 36
39	27 and 36
40	or/37-39

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.

#	Searches
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	HEART VALVE PROSTHESIS/
11	BIOPROSTHESIS/
12	HEART VALVE PROSTHESIS IMPLANTATION/
13	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).tw.
14	or/10-13
15	exp ANTICOAGULANTS/
16	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
17	exp PLATELET AGGREGATION INHIBITORS/
18	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).tw.
19	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).tw.
20	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil or clopidogrel or ticagrelor).mp.
21	VITAMIN K/
22	VITAMIN K 1/
23	VITAMIN K 2/
24	VITAMIN K 3/
25	VITAMIN K DEFICIENCY/
26	vitamin k$.mp.
27	or/15-26
28	UK Obstetric Surveillance System.tw.
29	UKOSS.tw.
30	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
31	MBRRACE.tw.
32	Scottish confidential audit of severe maternal morbidity.tw.
33	SCASMM.tw.
34	"Confidential Enquiry into Maternal and Child Health".tw.
35	CEMACH.tw.
36	or/28-35
37	9 and 14 and 27
38	14 and 36
39	27 and 36
40	or/37-39

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	exp HEART VALVE PROSTHESIS/
12	BIOPROSTHESIS/
13	exp HEART VALVE REPLACEMENT/
14	(valve? adj5 (prosthe$ or bioprosthe$ or mechanic$)).ti,ab.
15	or/11-14
16	exp ANTICOAGULANT AGENT/
17	(Anticoagula$ or Anti-coagula$ or 4-Hydroxycoumarin or Acenocoumarol or Ancrod or Blood Coagulation Factor Inhibitor? or Citric Acid or Dalteparin or Dermatan Sulfate or Dextran? or Dicumarol or Edetic Acid or Enoxaparin or Ethyl Biscoumacetate or Fibrin Fibrinogen Degradation Product? or Gabexate or Heparin$ or Nadroparin or Pentosan Sulfuric Polyester or Phenindione or Phenprocoumon or Protein C or Protein S or Warfarin or beta 2-Glycoprotein or Antithrombin? or Dabigatran or Hirudin? or Factor Xa Inhibitor? or Rivaroxaban or tinzaparin or apixaban).mp.
18	exp ANTITHROMBOCYTIC AGENT/
19	((antiplatelet? or anti-platelet?) adj3 (agent? or drug?)).ti,ab.
20	(platelet adj3 (antagonist? or antiaggregant? or anti-aggregant? or inhibitor?)).ti,ab.
21	(Alprostadil or Aspirin or Dipyridamole or Disintegrin? or Epoprostenol or Iloprost or Ketanserin or Milrinone or Pentoxifylline or Prasugrel Hydrochloride or S-Nitrosoglutathione or S-Nitrosothiol? or Ticlopidine or Trapidil or clopidogrel or ticagrelor).mp.
22	VITAMIN K GROUP/
23	VITAMIN K DEFICIENCY/
24	vitamin k$.mp.
25	or/16-24
26	UK Obstetric Surveillance System.ti,ab.
27	UKOSS.ti,ab.
28	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
29	MBRRACE.ti,ab.
30	Scottish confidential audit of severe maternal morbidity.ti,ab.
31	SCASMM.ti,ab.
32	"Confidential Enquiry into Maternal and Child Health".ti,ab.
33	CEMACH.ti,ab.

#	Searches
34	or/26-33
35	10 and 15 and 25
36	15 and 34
37	25 and 34
38	or/35-37
39	limit 38 to english language
40	letter.pt. or LETTER/
41	note.pt.
42	editorial.pt.
43	CASE REPORT/ or CASE STUDY/
44	(letter or comment*).ti.
45	or/40-44
46	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
47	45 not 46
48	ANIMAL/ not HUMAN/
49	NONHUMAN/
50	exp ANIMAL EXPERIMENT/
51	exp EXPERIMENTAL ANIMAL/
52	ANIMAL MODEL/
53	exp RODENT/
54	(rat or rats or mouse or mice).ti.
55	or/47-54
56	39 not 55
57	(2016$ or 2017$).dd,yr.
58	56 and 57

Intrapartum care for women with cardiac disease – mode of birth

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/

#	Searches
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.

#	Searches
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(exp CESAREAN SECTION/ or SURGICAL PROCEDURES, ELECTIVE/) and (PERINATAL CARE/ or PRENATAL CARE/ or PATIENT CARE PLANNING/ or ADVANCE CARE PLANNING/)
84	exp CESAREAN SECTION/ and (plan$ or elect$ or non emergency).ti,ab.
85	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
86	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
87	or/83-86

#	Searches
88	82 and 87
89	exp CESAREAN SECTION/
90	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
91	or/89-90
92	LABOR, INDUCED/
93	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).ti,ab.
94	exp EXTRACTION, OBSTETRICAL/
95	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).ti,ab.
96	(vacuum$ adj3 extract$).ti,ab.
97	ventouse?.ti,ab.
98	OBSTETRICAL FORCEPS/
99	forcep?.ti,ab.
100	or/92-99
101	82 and 91 and 100
102	NATURAL CHILDBIRTH/
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).ti,ab.
104	(spontaneous$ adj3 (birth$ or born or deliver$)).ti,ab.
105	or/102-104
106	82 and 91 and 105
107	VAGINAL BIRTH AFTER CESAREAN/
108	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).ti,ab.
109	or/107-108
110	82 and 91 and 109
111	LABOR STAGE, SECOND/ and assist$.ti,ab.
112	((second stage? or 2nd stage?) adj10 assist$).ti,ab.
113	or/111-112
114	82 and 91 and 113
115	*DELIVERY, OBSTETRIC/mt [Methods]
116	(mode? adj2 (birth$ or born or deliver$)).ti,ab.
117	or/115-116
118	82 and 117
119	88 or 101 or 106 or 110 or 114 or 118
120	limit 119 to english language
121	LETTER/
122	EDITORIAL/
123	NEWS/
124	exp HISTORICAL ARTICLE/
125	ANECDOTES AS TOPIC/
126	COMMENT/
127	CASE REPORT/

#	Searches
128	(letter or comment*).ti.
129	or/121-128
130	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
131	129 not 130
132	ANIMALS/ not HUMANS/
133	exp ANIMALS, LABORATORY/
134	exp ANIMAL EXPERIMENTATION/
135	exp MODELS, ANIMAL/
136	exp RODENTIA/
137	(rat or rats or mouse or mice).ti.
138	or/131-137
139	120 not 138

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab,kw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab,kw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.

#	Searches
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab,kw.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
32	Brugada Syndrome.ti,ab,kw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab,kw.
35	Long QT Syndrome.ti,ab,kw.
36	Parasystole.ti,ab,kw.
37	Pre-Excitation Syndrome?.ti,ab,kw.
38	Tachycardia?.ti,ab,kw.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab,kw.
51	Loeys-Dietz Syndrome.ti,ab,kw.
52	Leriche Syndrome.ti,ab,kw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab,kw.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.

#	Searches
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(exp CESAREAN SECTION/ or SURGICAL PROCEDURES, ELECTIVE/) and (PERINATAL CARE/ or PRENATAL CARE/ or PATIENT CARE PLANNING/ or ADVANCE CARE PLANNING/)
84	exp CESAREAN SECTION/ and (plan$ or elect$ or non emergency).ti,ab.
85	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
86	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
87	or/83-86
88	82 and 87
89	exp CESAREAN SECTION/
90	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab,kw.
91	or/89-90
92	LABOR, INDUCED/
93	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).ti,ab.
94	exp EXTRACTION, OBSTETRICAL/
95	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).ti,ab.
96	(vacuum$ adj3 extract$).ti,ab.
97	ventouse?.ti,ab,kw.
98	OBSTETRICAL FORCEPS/
99	forcep?.ti,ab.
100	or/92-99
101	82 and 91 and 100
102	NATURAL CHILDBIRTH/
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).ti,ab.

#	Searches
104	(spontaneous$ adj3 (birth$ or born or deliver$)).ti,ab.
105	or/102-104
106	82 and 91 and 105
107	VAGINAL BIRTH AFTER CESAREAN/
108	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).ti,ab.
109	or/107-108
110	82 and 91 and 109
111	LABOR STAGE, SECOND/ and assist$.ti,ab.
112	((second stage? or 2nd stage?) adj10 assist$).ti,ab.
113	or/111-112
114	82 and 91 and 113
115	*DELIVERY, OBSTETRIC/mt [Methods]
116	(mode? adj2 (birth$ or born or deliver$)).ti,ab.
117	or/115-116
118	82 and 117
119	88 or 101 or 106 or 110 or 114 or 118

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.

#	Searches
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).ti,ab.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	CORONARY DISEASE.kw.

#	Searches
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).ti,ab.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	((CESAREAN SECTION or SURGICAL PROCEDURES, ELECTIVE) and (PERINATAL CARE or PRENATAL CARE or PATIENT CARE PLANNING or ADVANCE CARE PLANNING)).kw.
84	CESAREAN SECTION.kw. and (plan$ or elect$ or non emergency).ti,ab.
85	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
86	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
87	or/83-86
88	82 and 87
89	CESAREAN SECTION.kw.
90	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
91	or/89-90
92	LABOR, INDUCED.kw.
93	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).ti,ab.
94	EXTRACTION, OBSTETRICAL.kw.
95	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).ti,ab.
96	(vacuum$ adj3 extract$).ti,ab.
97	ventouse?.ti,ab.
98	OBSTETRICAL FORCEPS.kw.

#	Searches
99	forcep?.ti,ab.
100	or/92-99
101	82 and 91 and 100
102	NATURAL CHILDBIRTH.kw.
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).ti,ab.
104	(spontaneous$ adj3 (birth$ or born or deliver$)).ti,ab.
105	or/102-104
106	82 and 91 and 105
107	VAGINAL BIRTH AFTER CESAREAN.kw.
108	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).ti,ab.
109	or/107-108
110	82 and 91 and 109
111	LABOR STAGE, SECOND.kw. and assist$.ti,ab.
112	((second stage? or 2nd stage?) adj10 assist$).ti,ab.
113	or/111-112
114	82 and 91 and 113
115	(mode? adj2 (birth$ or born or deliver$)).ti,ab.
116	82 and 115
117	88 or 101 or 106 or 110 or 114 or 116

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).tw,tx.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).tw,tx.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
16	click murmur syndrome?.tw,tx.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.

#	Searches
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
21	(persist$ adj2 ostium primum).tw,tx.
22	anomal$ pulmonary venous drain$.tw,tx.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
25	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).tw,tx.
30	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
31	(Bradycardia? or bradyarrhythmia?).tw,tx.
32	Brugada Syndrome.tw,tx.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
34	Heart Block.tw,tx.
35	Long QT Syndrome.tw,tx.
36	Parasystole.tw,tx.
37	Pre-Excitation Syndrome?.tw,tx.
38	Tachycardia?.tw,tx.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).tw,tx.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).tw,tx.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
50	Aortitis.tw,tx.
51	Loeys-Dietz Syndrome.tw,tx.
52	Leriche Syndrome.tw,tx.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
59	FONTAN PROCEDURE.kw.

#	Searches
60	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.tw,tx.
65	(complex$ adj10 congenital$ heart disease?).tw,tx.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).tw,tx.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).tw,tx.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).tw,tx.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).tw,tx.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	((CESAREAN SECTION or SURGICAL PROCEDURES, ELECTIVE) and (PERINATAL CARE or PRENATAL CARE or PATIENT CARE PLANNING or ADVANCE CARE PLANNING)).kw.
84	CESAREAN SECTION.kw. and (plan$ or elect$ or non emergency).tw,tx.
85	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw,tx.
86	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw,tx.
87	or/83-86
88	82 and 87
89	CESAREAN SECTION.kw.
90	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).tw,tx.
91	or/89-90
92	LABOR, INDUCED.kw.
93	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).tw,tx.
94	EXTRACTION, OBSTETRICAL.kw.
95	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).tw,tx.
96	(vacuum$ adj3 extract$).tw,tx.

#	Searches
97	ventouse?.tw,tx.
98	OBSTETRICAL FORCEPS.kw.
99	forcep?.tw,tx.
100	or/92-99
101	82 and 91 and 100
102	NATURAL CHILDBIRTH.kw.
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).tw,tx.
104	(spontaneous$ adj3 (birth$ or born or deliver$)).tw,tx.
105	or/102-104
106	82 and 91 and 105
107	VAGINAL BIRTH AFTER CESAREAN.kw.
108	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).tw,tx.
109	or/107-108
110	82 and 91 and 109
111	LABOR STAGE, SECOND.kw. and assist$.tw,tx.
112	((second stage? or 2nd stage?) adj10 assist$).tw,tx.
113	or/111-112
114	82 and 91 and 113
115	(mode? adj2 (birth$ or born or deliver$)).tw,tx.
116	82 and 115
117	88 or 101 or 106 or 110 or 114 or 116

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).tw.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).tw.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).tw.
16	click murmur syndrome?.tw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.

#	Searches
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
21	(persist$ adj2 ostium primum).tw.
22	anomal$ pulmonary venous drain$.tw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
25	((Atrial or ventricular) adj2 extrasystole?).tw.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
28	exp *ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).tw.
30	(Atrial adj2 (Fibrillation or Flutter)).tw.
31	(Bradycardia? or bradyarrhythmia?).tw.
32	Brugada Syndrome.tw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
34	Heart Block.tw.
35	Long QT Syndrome.tw.
36	Parasystole.tw.
37	Pre-Excitation Syndrome?.tw.
38	Tachycardia?.tw.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).tw.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).tw.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
50	Aortitis.tw.
51	Loeys-Dietz Syndrome.tw.
52	Leriche Syndrome.tw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).tw.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
57	"TRANSPOSITION OF GREAT VESSELS"/

#	Searches
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).tw.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.tw.
65	(complex$ adj10 congenital$ heart disease?).tw.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).tw.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).tw.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).tw.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).tw.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(exp CESAREAN SECTION/ or SURGICAL PROCEDURES, ELECTIVE/) and (PERINATAL CARE/ or PRENATAL CARE/ or PATIENT CARE PLANNING/ or ADVANCE CARE PLANNING/)
84	exp CESAREAN SECTION/ and (plan$ or elect$ or non emergency).tw.
85	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
86	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).tw.
87	or/83-86
88	82 and 87
89	exp CESAREAN SECTION/
90	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).tw.
91	or/89-90
92	LABOR, INDUCED/
93	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).tw.
94	exp EXTRACTION, OBSTETRICAL/

#	Searches
95	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).tw.
96	(vacuum$ adj3 extract$).tw.
97	ventouse?.tw.
98	OBSTETRICAL FORCEPS/
99	forcep?.tw.
100	or/92-99
101	82 and 91 and 100
102	NATURAL CHILDBIRTH/
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).tw.
104	(spontaneous$ adj3 (birth$ or born or deliver$)).tw.
105	or/102-104
106	82 and 91 and 105
107	VAGINAL BIRTH AFTER CESAREAN/
108	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).tw.
109	or/107-108
110	82 and 91 and 109
111	LABOR STAGE, SECOND/ and assist$.tw.
112	((second stage? or 2nd stage?) adj10 assist$).tw.
113	or/111-112
114	82 and 91 and 113
115	*DELIVERY, OBSTETRIC/mt [Methods]
116	(mode? adj2 (birth$ or born or deliver$)).tw.
117	or/115-116
118	82 and 117
119	88 or 101 or 106 or 110 or 114 or 118

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	PULMONARY VALVE STENOSIS/
12	(pulmonary adj2 stenos$).ti,ab.
13	PATENT DUCTUS ARTERIOSUS/

#	Searches
14	(Paten$ adj2 ductus arteriosus).ti,ab.
15	MITRAL VALVE PROLAPSE/
16	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
17	click murmur syndrome?.ti,ab.
18	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
19	HEART SEPTUM DEFECT/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	EXTRASYSTOLE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	FALLOT TETRALOGY/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *HEART ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp *HYPERTROPHIC CARDIOMYOPATHY/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE REGURGITATION/
43	MITRAL VALVE REGURGITATION/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp *AORTA DISEASE/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTA COARCTATION/su [Surgery]

#	Searches
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	exp *HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	GREAT VESSELS TRANSPOSITION/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp *CORONARY ARTERY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	CYANOTIC HEART DISEASE/
64	Cyanotic heart disease?.ti,ab.
65	*CONGENITAL HEART DISEASE/
66	(complex$ adj10 congenital$ heart disease?).ti,ab.
67	*PULMONARY HYPERTENSION/
68	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
69	exp *HEART VENTRICLE FAILURE/
70	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
71	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
72	exp CARDIOMYOPATHY/ and TIME FACTOR/
73	(previous$ adj5 cardiomyopath$).ti,ab.
74	MITRAL VALVE STENOSIS/
75	(mitral adj2 stenos?s).ti,ab.
76	AORTA VALVE STENOSIS/
77	(aort$ adj2 stenos?s).ti,ab.
78	AORTA COARCTATION/
79	(Coarctation? adj3 aort$).ti,ab.
80	or/11-79
81	10 and 80
82	(exp CESAREAN SECTION/ or ELECTIVE SURGERY/) and (PERINATAL CARE/ or PRENATAL CARE/ or PATIENT CARE PLANNING/)
83	exp CESAREAN SECTION/ and (plan$ or elect$ or non emergency).ti,ab.
84	(plan$ adj10 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
85	((elect$ or request$ or schedul$ or intend$ or intent$ or demand$ or non emergency) adj3 (c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$))).ti,ab.
86	or/82-85
87	81 and 86
88	exp CESAREAN SECTION/
89	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
90	or/88-89
91	LABOR, INDUCTION/

#	Searches
92	(induc$ adj3 (labo?r$ or birth$ or born or deliver$ or obstetric$)).ti,ab.
93	VACUUM EXTRACTION/
94	((extract$ or vacuum$) adj3 (birth$ or born or deliver$ or obstetric$)).ti,ab.
95	(vacuum$ adj3 extract$).ti,ab.
96	ventouse?.ti,ab.
97	FORCEPS DELIVERY/
98	OBSTETRIC FORCEPS/
99	forcep?.ti,ab.
100	or/91-99
101	81 and 90 and 100
102	NATURAL CHILDBIRTH/
103	((natural$ or unassisted or un-assisted) adj3 (birth$ or born or deliver$)).ti,ab.
104	(spontaneous$ adj3 (birth$ or born or deliver$)).ti,ab.
105	or/102-104
106	81 and 90 and 105
107	VAGINAL DELIVERY/
108	VAGINAL BIRTH AFTER CESAREAN/
109	((vagina$ or cephalic$) adj1 (birth$ or born or deliver$)).ti,ab.
110	or/107-109
111	81 and 90 and 110
112	LABOR STAGE 2/ and assist$.ti,ab.
113	((second stage? or 2nd stage?) adj10 assist$).ti,ab.
114	or/112-113
115	81 and 90 and 114
116	(mode? adj2 (birth$ or born or deliver$)).ti,ab.
117	81 and 116
118	87 or 101 or 106 or 111 or 115 or 117
119	limit 118 to english language
120	letter.pt. or LETTER/
121	note.pt.
122	editorial.pt.
123	CASE REPORT/ or CASE STUDY/
124	(letter or comment*).ti.
125	or/120-124
126	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
127	125 not 126
128	ANIMAL/ not HUMAN/
129	NONHUMAN/
130	exp ANIMAL EXPERIMENT/
131	exp EXPERIMENTAL ANIMAL/

#	Searches
132	ANIMAL MODEL/
133	exp RODENT/
134	(rat or rats or mouse or mice).ti.
135	or/127-134
136	119 not 135

Intrapartum care for women with cardiac disease – fluid management

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab.

#	Searches
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.

#	Searches
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	HEMODYNAMICS/ and MONITORING, PHYSIOLOGIC/
84	(h?emodynamic? adj5 monitor$).ti,ab.
85	(input? adj5 output? adj5 (chart? or monitor$)).ti,ab.
86	URINARY CATHETERS/
87	URINARY CATHETERIZATION/
88	((urinary or urethral or ureteral) adj3 catheter$).ti,ab.
89	urometer?.ti,ab.
90	(urine adj3 output?).ti,ab.
91	((invasive$ or non-invasive$) adj5 monitor$).ti,ab.
92	exp VASCULAR ACCESS DEVICES/ and MONITORING, PHYSIOLOGIC/
93	CATHETERS, INDWELLING/ and MONITORING, PHYSIOLOGIC/
94	exp CARDIAC CATHETERIZATION/ and MONITORING, PHYSIOLOGIC/
95	((arterial line? or catheter$) adj5 monitor$).ti,ab.
96	(vascular access adj3 (device? or port)).ti,ab.
97	CENTRAL VENOUS PRESSURE/ and MONITORING, PHYSIOLOGIC/
98	((central adj2 (venous or vein) adj2 pressure?) and monitor$).ti,ab.
99	(CVP and monitor$).ti,ab.
100	CARDIAC OUTPUT/ and MONITORING, PHYSIOLOGIC/
101	(cardiac adj3 output? adj5 monitor$).ti,ab.
102	PULMONARY ARTERY/ and THERMODILUTION/
103	(pulmonary arter$ adj3 thermodilution).ti,ab.
104	pulmonary artery floatation catheter$.ti,ab.
105	PAFC.ti,ab.
106	Lithium dilution cardiac output?.ti,ab.
107	LiDCO.ti,ab.
108	Pulse contour analysis system?.ti,ab.
109	pulse indicator continuous cardiac output.ti,ab.

#	Searches
110	PiCCO.ti,ab.
111	FloTrac.ti,ab.
112	Oesophageal Doppler.ti,ab.
113	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).ti,ab.
114	ultrasonic cardiac output monitor$.ti,ab.
115	USCOM.ti,ab.
116	(Thoracic adj3 bioreactance).ti,ab.
117	NICOM.ti,ab.
118	(Trans thoracic echo$ or Transthoracic echo$).ti,ab.
119	TTE.ti,ab.
120	(trans oesophageal echo$ or transoesophageal echo$).ti,ab.
121	TOE.ti,ab.
122	non-invasive blood pressure.ti,ab.
123	NIBP.ti,ab.
124	oxygen saturation.ti,ab.
125	or/83-124
126	ELECTROCARDIOGRAPHY/
127	electrocardiogra$.ti,ab.
128	ECG.ti,ab.
129	or/126-128
130	HEMODYNAMICS/
131	h?emodynamic?.ti,ab.
132	or/130-131
133	exp BODY FLUIDS/ and MONITORING, PHYSIOLOGIC/
134	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).ti,ab.
135	or/133-134
136	HYPOVOLEMIA/
137	hypovol?emi$.ti,ab.
138	hypervol?emi$.ti,ab.
139	(fluid? adj3 overload$).ti,ab.
140	((abnormal$ or reduc$ or increase$) adj3 blood volume?).ti,ab.
141	or/136-140
142	UK Obstetric Surveillance System.ti,ab.
143	UKOSS.ti,ab.
144	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
145	MBRRACE.ti,ab.
146	Scottish confidential audit of severe maternal morbidity.ti,ab.
147	SCASMM.ti,ab.
148	"Confidential Enquiry into Maternal and Child Health".ti,ab.
149	CEMACH.ti,ab.

#	Searches
150	or/142-149
151	82 and 125
152	82 and 129 and 132
153	82 and 135
154	82 and 141
155	82 and 150
156	or/151-155
157	limit 156 to english language
158	LETTER/
159	EDITORIAL/
160	NEWS/
161	exp HISTORICAL ARTICLE/
162	ANECDOTES AS TOPIC/
163	COMMENT/
164	CASE REPORT/
165	(letter or comment*).ti.
166	or/158-165
167	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
168	166 not 167
169	ANIMALS/ not HUMANS/
170	exp ANIMALS, LABORATORY/
171	exp ANIMAL EXPERIMENTATION/
172	exp MODELS, ANIMAL/
173	exp RODENTIA/
174	(rat or rats or mouse or mice).ti.
175	or/168-174
176	157 not 175

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.

#	Searches
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab,kw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab,kw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab,kw.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
32	Brugada Syndrome.ti,ab,kw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab,kw.
35	Long QT Syndrome.ti,ab,kw.
36	Parasystole.ti,ab,kw.
37	Pre-Excitation Syndrome?.ti,ab,kw.
38	Tachycardia?.ti,ab,kw.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab,kw.
51	Loeys-Dietz Syndrome.ti,ab,kw.

#	Searches
52	Leriche Syndrome.ti,ab,kw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab,kw.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	HEMODYNAMICS/ and MONITORING, PHYSIOLOGIC/
84	(h?emodynamic? adj5 monitor$).ti,ab.
85	(input? adj5 output? adj5 (chart? or monitor$)).ti,ab.
86	URINARY CATHETERS/
87	URINARY CATHETERIZATION/
88	((urinary or urethral or ureteral) adj3 catheter$).ti,ab.
89	urometer?.ti,ab,kw.
90	(urine adj3 output?).ti,ab.
91	((invasive$ or non-invasive$) adj5 monitor$).ti,ab.

#	Searches
92	exp VASCULAR ACCESS DEVICES/ and MONITORING, PHYSIOLOGIC/
93	CATHETERS, INDWELLING/ and MONITORING, PHYSIOLOGIC/
94	exp CARDIAC CATHETERIZATION/ and MONITORING, PHYSIOLOGIC/
95	((arterial line? or catheter$) adj5 monitor$).ti,ab.
96	(vascular access adj3 (device? or port)).ti,ab.
97	CENTRAL VENOUS PRESSURE/ and MONITORING, PHYSIOLOGIC/
98	((central adj2 (venous or vein) adj2 pressure?) and monitor$).ti,ab.
99	(CVP and monitor$).ti,ab.
100	CARDIAC OUTPUT/ and MONITORING, PHYSIOLOGIC/
101	(cardiac adj3 output? adj5 monitor$).ti,ab.
102	PULMONARY ARTERY/ and THERMODILUTION/
103	(pulmonary arter$ adj3 thermodilution).ti,ab.
104	pulmonary artery floatation catheter$.ti,ab,kw.
105	PAFC.ti,ab.
106	Lithium dilution cardiac output?.ti,ab,kw.
107	LiDCO.ti,ab.
108	Pulse contour analysis system?.ti,ab,kw.
109	pulse indicator continuous cardiac output.ti,ab,kw.
110	PiCCO.ti,ab.
111	FloTrac.ti,ab.
112	Oesophageal Doppler.ti,ab,kw.
113	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).ti,ab.
114	ultrasonic cardiac output monitor$.ti,ab,kw.
115	USCOM.ti,ab.
116	(Thoracic adj3 bioreactance).ti,ab.
117	NICOM.ti,ab.
118	(Trans thoracic echo$ or Transthoracic echo$).ti,ab,kw.
119	TTE.ti,ab.
120	(trans oesophageal echo$ or transoesophageal echo$).ti,ab,kw.
121	TOE.ti,ab.
122	non-invasive blood pressure.ti,ab,kw.
123	NIBP.ti,ab.
124	oxygen saturation.ti,ab,kw.
125	or/83-124
126	ELECTROCARDIOGRAPHY/
127	electrocardiogra$.ti,ab,kw.
128	ECG.ti,ab.
129	or/126-128
130	HEMODYNAMICS/
131	h?emodynamic?.ti,ab,kw.

#	Searches
132	or/130-131
133	exp BODY FLUIDS/ and MONITORING, PHYSIOLOGIC/
134	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).ti,ab.
135	or/133-134
136	HYPOVOLEMIA/
137	hypovol?emi$.ti,ab,kw.
138	hypervol?emi$.ti,ab,kw.
139	(fluid? adj3 overload$).ti,ab.
140	((abnormal$ or reduc$ or increase$) adj3 blood volume?).ti,ab.
141	or/136-140
142	UK Obstetric Surveillance System.ti,ab.
143	UKOSS.ti,ab.
144	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
145	MBRRACE.ti,ab.
146	Scottish confidential audit of severe maternal morbidity.ti,ab.
147	SCASMM.ti,ab.
148	"Confidential Enquiry into Maternal and Child Health".ti,ab.
149	CEMACH.ti,ab.
150	or/142-149
151	82 and 125
152	82 and 129 and 132
153	82 and 135
154	82 and 141
155	82 and 150
156	or/151-155

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT.kw.

#	Searches
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).ti,ab.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.

#	Searches
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).ti,ab.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	(HEMODYNAMICS and MONITORING, PHYSIOLOGIC).kw.
84	(h?emodynamic? adj5 monitor$).ti,ab.
85	(input? adj5 output? adj5 (chart? or monitor$)).ti,ab.
86	URINARY CATHETERS.kw.
87	URINARY CATHETERIZATION.kw.
88	((urinary or urethral or ureteral) adj3 catheter$).ti,ab.
89	urometer?.ti,ab.
90	(urine adj3 output?).ti,ab.
91	((invasive$ or non-invasive$) adj5 monitor$).ti,ab.
92	(VASCULAR ACCESS DEVICES and MONITORING, PHYSIOLOGIC).kw.

#	Searches
93	(CATHETERS, INDWELLING and MONITORING, PHYSIOLOGIC).kw.
94	(CARDIAC CATHETERIZATION and MONITORING, PHYSIOLOGIC).kw.
95	((arterial line? or catheter$) adj5 monitor$).ti,ab.
96	(vascular access adj3 (device? or port)).ti,ab.
97	(CENTRAL VENOUS PRESSURE and MONITORING, PHYSIOLOGIC).kw.
98	((central adj2 (venous or vein) adj2 pressure?) and monitor$).ti,ab.
99	(CVP and monitor$).ti,ab.
100	(CARDIAC OUTPUT and MONITORING, PHYSIOLOGIC).kw.
101	(cardiac adj3 output? adj5 monitor$).ti,ab.
102	(PULMONARY ARTERY and THERMODILUTION).kw.
103	(pulmonary arter$ adj3 thermodilution).ti,ab.
104	pulmonary artery floatation catheter$.ti,ab.
105	PAFC.ti,ab.
106	Lithium dilution cardiac output?.ti,ab.
107	LiDCO.ti,ab.
108	Pulse contour analysis system?.ti,ab.
109	pulse indicator continuous cardiac output.ti,ab.
110	PiCCO.ti,ab.
111	FloTrac.ti,ab.
112	Oesophageal Doppler.ti,ab.
113	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).ti,ab.
114	ultrasonic cardiac output monitor$.ti,ab.
115	USCOM.ti,ab.
116	(Thoracic adj3 bioreactance).ti,ab.
117	NICOM.ti,ab.
118	(Trans thoracic echo$ or Transthoracic echo$).ti,ab.
119	TTE.ti,ab.
120	(trans oesophageal echo$ or transoesophageal echo$).ti,ab.
121	TOE.ti,ab.
122	non-invasive blood pressure.ti,ab.
123	NIBP.ti,ab.
124	oxygen saturation.ti,ab.
125	or/83-124
126	ELECTROCARDIOGRAPHY.kw.
127	electrocardiogra$.ti,ab.
128	ECG.ti,ab.
129	or/126-128
130	HEMODYNAMICS.kw.
131	h?emodynamic?.ti,ab.
132	or/130-131

#	Searches
133	(BODY FLUIDS and MONITORING, PHYSIOLOGIC).kw.
134	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).ti,ab.
135	or/133-134
136	HYPOVOLEMIA.kw.
137	hypovol?emi$.ti,ab.
138	hypervol?emi$.ti,ab.
139	(fluid? adj3 overload$).ti,ab.
140	((abnormal$ or reduc$ or increase$) adj3 blood volume?).ti,ab.
141	or/136-140
142	UK Obstetric Surveillance System.ti,ab.
143	UKOSS.ti,ab.
144	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
145	MBRRACE.ti,ab.
146	Scottish confidential audit of severe maternal morbidity.ti,ab.
147	SCASMM.ti,ab.
148	"Confidential Enquiry into Maternal and Child Health".ti,ab.
149	CEMACH.ti,ab.
150	or/142-149
151	82 and 125
152	82 and 129 and 132
153	82 and 135
154	82 and 141
155	82 and 150
156	or/151-155

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).tw,tx.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).tw,tx.

#	Searches
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
16	click murmur syndrome?.tw,tx.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
21	(persist$ adj2 ostium primum).tw,tx.
22	anomal$ pulmonary venous drain$.tw,tx.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
25	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).tw,tx.
30	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
31	(Bradycardia? or bradyarrhythmia?).tw,tx.
32	Brugada Syndrome.tw,tx.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
34	Heart Block.tw,tx.
35	Long QT Syndrome.tw,tx.
36	Parasystole.tw,tx.
37	Pre-Excitation Syndrome?.tw,tx.
38	Tachycardia?.tw,tx.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).tw,tx.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).tw,tx.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
50	Aortitis.tw,tx.
51	Loeys-Dietz Syndrome.tw,tx.
52	Leriche Syndrome.tw,tx.
53	AORTIC COARCTATION.kw.

#	Searches
54	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arteriosclerosis or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.tw,tx.
65	(complex$ adj10 congenital$ heart disease?).tw,tx.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).tw,tx.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).tw,tx.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).tw,tx.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).tw,tx.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	(HEMODYNAMICS and MONITORING, PHYSIOLOGIC).kw.
84	(h?emodynamic? adj5 monitor$).tw,tx.
85	(input? adj5 output? adj5 (chart? or monitor$)).tw,tx.
86	URINARY CATHETERS.kw.
87	URINARY CATHETERIZATION.kw.
88	((urinary or urethral or ureteral) adj3 catheter$).tw,tx.
89	urometer?.tw,tx.
90	(urine adj3 output?).tw,tx.
91	((invasive$ or non-invasive$) adj5 monitor$).tw,tx.
92	(VASCULAR ACCESS DEVICES and MONITORING, PHYSIOLOGIC).kw.
93	(CATHETERS, INDWELLING and MONITORING, PHYSIOLOGIC).kw.

#	Searches
94	(CARDIAC CATHETERIZATION and MONITORING, PHYSIOLOGIC).kw.
95	((arterial line? or catheter$) adj5 monitor$).tw,tx.
96	(vascular access adj3 (device? or port)).tw,tx.
97	(CENTRAL VENOUS PRESSURE and MONITORING, PHYSIOLOGIC).kw.
98	((central adj2 (venous or vein) adj2 pressure?) and monitor$).tw,tx.
99	(CVP and monitor$).tw,tx.
100	(CARDIAC OUTPUT and MONITORING, PHYSIOLOGIC).kw.
101	(cardiac adj3 output? adj5 monitor$).tw,tx.
102	(PULMONARY ARTERY and THERMODILUTION).kw.
103	(pulmonary arter$ adj3 thermodilution).tw,tx.
104	pulmonary artery floatation catheter$.tw,tx.
105	PAFC.tw,tx.
106	Lithium dilution cardiac output?.tw,tx.
107	LiDCO.tw,tx.
108	Pulse contour analysis system?.tw,tx.
109	pulse indicator continuous cardiac output.tw,tx.
110	PiCCO.tw,tx.
111	FloTrac.tw,tx.
112	Oesophageal Doppler.tw,tx.
113	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).tw,tx.
114	ultrasonic cardiac output monitor$.tw,tx.
115	USCOM.tw,tx.
116	(Thoracic adj3 bioreactance).tw,tx.
117	NICOM.tw,tx.
118	(Trans thoracic echo$ or Transthoracic echo$).tw,tx.
119	TTE.tw,tx.
120	(trans oesophageal echo$ or transoesophageal echo$).tw,tx.
121	TOE.tw,tx.
122	non-invasive blood pressure.tw,tx.
123	NIBP.tw,tx.
124	oxygen saturation.tw,tx.
125	or/83-124
126	ELECTROCARDIOGRAPHY.kw.
127	electrocardiogra$.tw,tx.
128	ECG.tw,tx.
129	or/126-128
130	HEMODYNAMICS.kw.
131	h?emodynamic?.tw,tx.
132	or/130-131
133	(BODY FLUIDS and MONITORING, PHYSIOLOGIC).kw.

#	Searches
134	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).tw,tx.
135	or/133-134
136	HYPOVOLEMIA.kw.
137	hypovol?emi$.tw,tx.
138	hypervol?emi$.tw,tx.
139	(fluid? adj3 overload$).tw,tx.
140	((abnormal$ or reduc$ or increase$) adj3 blood volume?).tw,tx.
141	or/136-140
142	UK Obstetric Surveillance System.tw,tx.
143	UKOSS.tw,tx.
144	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw,tx.
145	MBRRACE.tw,tx.
146	Scottish confidential audit of severe maternal morbidity.tw,tx.
147	SCASMM.tw,tx.
148	"Confidential Enquiry into Maternal and Child Health".tw,tx.
149	CEMACH.tw,tx.
150	or/142-149
151	82 and 125
152	82 and 129 and 132
153	82 and 135
154	82 and 141
155	82 and 150
156	or/151-155

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).tw.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).tw.
14	MITRAL VALVE PROLAPSE/

#	Searches
15	(mitral valve? adj2 (prolapse? or floppy)).tw.
16	click murmur syndrome?.tw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
21	(persist$ adj2 ostium primum).tw.
22	anomal$ pulmonary venous drain$.tw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
25	((Atrial or ventricular) adj2 extrasystole?).tw.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
28	exp ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).tw.
30	(Atrial adj2 (Fibrillation or Flutter)).tw.
31	(Bradycardia? or bradyarrhythmia?).tw.
32	Brugada Syndrome.tw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
34	Heart Block.tw.
35	Long QT Syndrome.tw.
36	Parasystole.tw.
37	Pre-Excitation Syndrome?.tw.
38	Tachycardia?.tw.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).tw.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).tw.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
50	Aortitis.tw.
51	Loeys-Dietz Syndrome.tw.
52	Leriche Syndrome.tw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).tw.

#	Searches
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).tw.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.tw.
65	(complex$ adj10 congenital$ heart disease?).tw.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).tw.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).tw.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).tw.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).tw.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	HEMODYNAMICS/ and MONITORING, PHYSIOLOGIC/
84	(h?emodynamic? adj5 monitor$).tw.
85	(input? adj5 output? adj5 (chart? or monitor$)).tw.
86	URINARY CATHETERS/
87	URINARY CATHETERIZATION/
88	((urinary or urethral or ureteral) adj3 catheter$).tw.
89	urometer?.tw.
90	(urine adj3 output?).tw.
91	((invasive$ or non-invasive$) adj5 monitor$).tw.
92	CATHETERS, INDWELLING/ and MONITORING, PHYSIOLOGIC/
93	exp Heart Catheterization/ and MONITORING, PHYSIOLOGIC/
94	((arterial line? or catheter$) adj5 monitor$).tw.

#	Searches
95	(vascular access adj3 (device? or port)).tw.
96	CENTRAL VENOUS PRESSURE/ and MONITORING, PHYSIOLOGIC/
97	((central adj2 (venous or vein) adj2 pressure?) and monitor$).tw.
98	(CVP and monitor$).tw.
99	CARDIAC OUTPUT/ and MONITORING, PHYSIOLOGIC/
100	(cardiac adj3 output? adj5 monitor$).tw.
101	PULMONARY ARTERY/ and THERMODILUTION/
102	(pulmonary arter$ adj3 thermodilution).tw.
103	pulmonary artery floatation catheter$.tw.
104	PAFC.tw.
105	Lithium dilution cardiac output?.tw.
106	LiDCO.tw.
107	Pulse contour analysis system?.tw.
108	pulse indicator continuous cardiac output.tw.
109	PiCCO.tw.
110	FloTrac.tw.
111	Oesophageal Doppler.tw.
112	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).tw.
113	ultrasonic cardiac output monitor$.tw.
114	USCOM.tw.
115	(Thoracic adj3 bioreactance).tw.
116	NICOM.tw.
117	(Trans thoracic echo$ or Transthoracic echo$).tw.
118	TTE.tw.
119	(trans oesophageal echo$ or transoesophageal echo$).tw.
120	TOE.tw.
121	non-invasive blood pressure.tw.
122	NIBP.tw.
123	oxygen saturation.tw.
124	or/83-123
125	ELECTROCARDIOGRAPHY/
126	electrocardiogra$.tw.
127	ECG.tw.
128	or/125-127
129	HEMODYNAMICS/
130	h?emodynamic?.tw.
131	or/129-130
132	exp BODY FLUIDS/ and MONITORING, PHYSIOLOGIC/
133	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).tw.
134	or/132-133

#	Searches
135	HYPOVOLEMIA/
136	hypovol?emi$.tw.
137	hypervol?emi$.tw.
138	(fluid? adj3 overload$).tw.
139	((abnormal$ or reduc$ or increase$) adj3 blood volume?).tw.
140	or/135-139
141	UK Obstetric Surveillance System.tw.
142	UKOSS.tw.
143	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
144	MBRRACE.tw.
145	Scottish confidential audit of severe maternal morbidity.tw.
146	SCASMM.tw.
147	"Confidential Enquiry into Maternal and Child Health".tw.
148	CEMACH.tw.
149	or/141-148
150	82 and 124
151	82 and 128 and 131
152	82 and 134
153	82 and 140
154	82 and 149
155	or/150-154

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	PULMONARY VALVE STENOSIS/
12	(pulmonary adj2 stenos$).ti,ab.
13	PATENT DUCTUS ARTERIOSUS/
14	(Paten$ adj2 ductus arteriosus).ti,ab.
15	MITRAL VALVE PROLAPSE/
16	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.

#	Searches
17	click murmur syndrome?.ti,ab.
18	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
19	HEART SEPTUM DEFECT/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	EXTRASYSTOLE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	FALLOT TETRALOGY/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *HEART ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp *HYPERTROPHIC CARDIOMYOPATHY/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE REGURGITATION/
43	MITRAL VALVE REGURGITATION/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp *AORTA DISEASE/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTA COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	exp *HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.

#	Searches
57	GREAT VESSELS TRANSPOSITION/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp *CORONARY ARTERY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	CYANOTIC HEART DISEASE/
64	Cyanotic heart disease?.ti,ab.
65	*CONGENITAL HEART DISEASE/
66	(complex$ adj10 congenital$ heart disease?).ti,ab.
67	*PULMONARY HYPERTENSION/
68	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
69	exp *HEART VENTRICLE FAILURE/
70	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
71	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
72	exp CARDIOMYOPATHY/ and TIME FACTOR/
73	(previous$ adj5 cardiomyopath$).ti,ab.
74	MITRAL VALVE STENOSIS/
75	(mitral adj2 stenos?s).ti,ab.
76	AORTA VALVE STENOSIS/
77	(aort$ adj2 stenos?s).ti,ab.
78	AORTA COARCTATION/
79	(Coarctation? adj3 aort$).ti,ab.
80	or/11-79
81	10 and 80
82	exp HEMODYNAMICS/ and PHYSIOLOGIC MONITORING/
83	exp HEMODYNAMIC MONITORING/
84	(h?emodynamic? adj5 monitor$).ti,ab.
85	(input? adj5 output? adj5 (chart? or monitor$)).ti,ab.
86	URINARY CATHETER/
87	URETHRAL CATHETER/
88	INDWELLING URINARY CATHETER/
89	BLADDER CATHETERIZATION/
90	URETHRAL CATHETERIZATION/
91	((urinary or urethral or ureteral) adj3 catheter$).ti,ab.
92	urometer?.ti,ab.
93	(urine adj3 output?).ti,ab.
94	((invasive$ or non-invasive$) adj5 monitor$).ti,ab.
95	VASCULAR ACCESS DEVICE/ and PHYSIOLOGIC MONITORING/

#	Searches
96	ARTERIAL LINE.mp. and PHYSIOLOGIC MONITORING/ [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
97	INDWELLING CATHETER/ and PHYSIOLOGIC MONITORING/
98	HEART CATHETERIZATION/ and PHYSIOLOGIC MONITORING/
99	((arterial line? or catheter$) adj5 monitor$).ti,ab.
100	(vascular access adj3 (device? or port)).ti,ab.
101	CENTRAL VENOUS PRESSURE/ and PHYSIOLOGIC MONITORING/
102	((central adj2 (venous or vein) adj2 pressure?) and monitor$).ti,ab.
103	(CVP and monitor$).ti,ab.
104	HEART OUTPUT/ and PHYSIOLOGIC MONITORING/
105	(cardiac adj3 output? adj5 monitor$).ti,ab.
106	PULMONARY ARTERY/ and THERMODILUTION/
107	(pulmonary arter$ adj3 thermodilution).ti,ab.
108	pulmonary artery floatation catheter$.ti,ab.
109	PAFC.ti,ab.
110	Lithium dilution cardiac output?.ti,ab.
111	LiDCO.ti,ab.
112	Pulse contour analysis system?.ti,ab.
113	pulse indicator continuous cardiac output.ti,ab.
114	PiCCO.ti,ab.
115	FloTrac.ti,ab.
116	Oesophageal Doppler.ti,ab.
117	((Doppler or ultrasound or ultrasonic$) adj5 cardiac output?).ti,ab.
118	ultrasonic cardiac output monitor$.ti,ab.
119	USCOM.ti,ab.
120	(Thoracic adj3 bioreactance).ti,ab.
121	NICOM.ti,ab.
122	(Trans thoracic echo$ or Transthoracic echo$).ti,ab.
123	TTE.ti,ab.
124	(trans oesophageal echo$ or transoesophageal echo$).ti,ab.
125	TOE.ti,ab.
126	non-invasive blood pressure.ti,ab.
127	NIBP.ti,ab.
128	oxygen saturation.ti,ab.
129	or/82-128
130	ELECTROCARDIOGRAPHY/
131	electrocardiogra$.ti,ab.
132	ECG.ti,ab.
133	or/130-132
134	exp HEMODYNAMICS/

#	Searches
135	h?emodynamic?.ti,ab.
136	or/134-135
137	ELECTROCARDIOGRAPHY MONITORING/
138	exp BODY FLUID/ and PHYSIOLOGIC MONITORING/
139	((fluid? or water or blood or plasma? or serum? or urine) adj5 monitor$).ti,ab.
140	or/138-139
141	HYPOVOLEMIA/
142	HYPERVOLEMIA/
143	hypovol?emi$.ti,ab.
144	hypervol?emi$.ti,ab.
145	(fluid? adj3 overload$).ti,ab.
146	((abnormal$ or reduc$ or increase$) adj3 blood volume?).ti,ab.
147	or/141-146
148	UK Obstetric Surveillance System.ti,ab.
149	UKOSS.ti,ab.
150	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
151	MBRRACE.ti,ab.
152	Scottish confidential audit of severe maternal morbidity.ti,ab.
153	SCASMM.ti,ab.
154	"Confidential Enquiry into Maternal and Child Health".ti,ab.
155	CEMACH.ti,ab.
156	or/148-155
157	81 and 129
158	81 and 133 and 136
159	81 and 137
160	81 and 140
161	81 and 147
162	81 and 156
163	or/157-162
164	limit 163 to english language
165	letter.pt. or LETTER/
166	note.pt.
167	editorial.pt.
168	CASE REPORT/ or CASE STUDY/
169	(letter or comment*).ti.
170	or/165-169
171	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
172	170 not 171
173	ANIMAL/ not HUMAN/
174	NONHUMAN/

#	Searches
175	exp ANIMAL EXPERIMENT/
176	exp EXPERIMENTAL ANIMAL/
177	ANIMAL MODEL/
178	exp RODENT/
179	(rat or rats or mouse or mice).ti.
180	or/172-179
181	164 not 180

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	POSTPARTUM PERIOD/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	(postpartum or post-partum).ti,ab.
11	puerperium.ti,ab.
12	or/1-11
13	exp CARDIOMYOPATHIES/
14	cardiomyopath$.ti,ab.
15	myocardiopath$.ti,ab.
16	myocardial disease?.ti,ab.
17	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
18	Endocardial Fibroelastos?s.ti,ab.
19	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
20	Endomyocardial Fibros?s.ti,ab.
21	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
22	((antopol or danon) adj2 disease?).ti,ab.
23	(Kearn$ adj3 Syndrome).ti,ab.
24	Myocardial Reperfusion Injur$.ti,ab.
25	Myocarditi$.ti,ab.
26	Carditis.ti,ab.
27	Sarcoglycanopath$.ti,ab.
28	or/13-27
29	12 and 28
30	PPCM.ti,ab.
31	or/29-30
32	BIOMARKERS/
33	Biomarker?.ti,ab.
34	NATRIURETIC PEPTIDE, BRAIN/
35	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.

#	Searches
36	BNP.ti,ab.
37	exp ENZYMES/
38	(enzyme? or biocatalyst?).ti,ab.
39	or/32-38
40	MEDICAL HISTORY TAKING/
41	(histor$ adj3 (take or taking)).ti,ab.
42	(histor$ adj3 clinical).ti,ab.
43	PHYSICAL EXAMINATION/
44	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).ti,ab.
45	exp DYSPNEA/
46	Breathless$.ti,ab.
47	(Short$ adj2 breath$).ti,ab.
48	Dyspnea?.ti,ab.
49	Orthopnoea?.ti,ab.
50	PULMONARY EDEMA/
51	pulmonary edema?.ti,ab.
52	wet lung?.ti,ab.
53	exp TACHYCARDIA/
54	(tachycardi$ or tachyarrhythmi$).ti,ab.
55	Palpitat$.ti,ab.
56	exp CHEST PAIN/
57	(Chest? adj3 pain$).ti,ab.
58	angina pectoris.ti,ab.
59	stenocardia?.ti,ab.
60	((unstable or stable or preinfarction) adj3 angina).ti,ab.
61	or/40-60
62	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).ti,ab.
63	exp DIAGNOSIS/
64	diagnos$.ti,ab.
65	or/63-64
66	exp *CARDIOMYOPATHIES/di [Diagnosis]
67	31 and 39 and 65
68	31 and 61 and 65
69	12 and 62 and 65
70	12 and 66
71	or/67-70
72	limit 71 to english language
73	LETTER/
74	EDITORIAL/
75	NEWS/
76	exp HISTORICAL ARTICLE/
77	ANECDOTES AS TOPIC/
78	COMMENT/
79	CASE REPORT/
80	(letter or comment*).ti.
81	or/73-80

#	Searches
82	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
83	81 not 82
84	ANIMALS/ not HUMANS/
85	exp ANIMALS, LABORATORY/
86	exp ANIMAL EXPERIMENTATION/
87	exp MODELS, ANIMAL/
88	exp RODENTIA/
89	(rat or rats or mouse or mice).ti.
90	or/83-89
91	72 not 90

1

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	POSTPARTUM PERIOD/
7	pregnan$.ti,ab,kw.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
9	((during or giving or give) adj3 birth?).ti,ab.
10	(postpartum or post-partum).ti,ab,kw.
11	puerperium.ti,ab,kw.
12	or/1-11
13	exp CARDIOMYOPATHIES/
14	cardiomyopath$.ti,ab,kw.
15	myocardiopath$.ti,ab,kw.
16	myocardial disease?.ti,ab,kw.
17	Arrhythmogenic Right Ventricular Dysplasia.ti,ab,kw.
18	Endocardial Fibroelastos?s.ti,ab,kw.
19	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
20	Endomyocardial Fibros?s.ti,ab,kw.
21	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
22	((antopol or danon) adj2 disease?).ti,ab.
23	(Kearn$ adj3 Syndrome).ti,ab.
24	Myocardial Reperfusion Injur$.ti,ab,kw.
25	Myocarditi$.ti,ab,kw.
26	Carditis.ti,ab,kw.
27	Sarcoglycanopath$.ti,ab,kw.
28	or/13-27

#	Searches
29	12 and 28
30	PPCM.ti,ab.
31	or/29-30
32	BIOMARKERS/
33	Biomarker?.ti,ab,kw.
34	NATRIURETIC PEPTIDE, BRAIN/
35	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
36	BNP.ti,ab.
37	exp ENZYMES/
38	(enzyme? or biocatalyst?).ti,ab.
39	or/32-38
40	MEDICAL HISTORY TAKING/
41	(histor$ adj3 (take or taking)).ti,ab.
42	(histor$ adj3 clinical).ti,ab.
43	PHYSICAL EXAMINATION/
44	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).ti,ab.
45	exp DYSPNEA/
46	Breathless$.ti,ab,kw.
47	(Short$ adj2 breath$).ti,ab.
48	Dyspnea?.ti,ab,kw.
49	Orthopnoea?.ti,ab,kw.
50	PULMONARY EDEMA/
51	pulmonary edema?.ti,ab,kw.
52	wet lung?.ti,ab.
53	exp TACHYCARDIA/
54	(tachycardi$ or tachyarrhythmi$).ti,ab,kw.
55	Palpitat$.ti,ab.
56	exp CHEST PAIN/
57	(Chest? adj3 pain$).ti,ab.
58	angina pectoris.ti,ab,kw.
59	stenocardia?.ti,ab,kw.
60	((unstable or stable or preinfarction) adj3 angina).ti,ab.
61	or/40-60
62	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).ti,ab.
63	exp DIAGNOSIS/
64	diagnos$.ti,ab,kw.
65	or/63-64

#	Searches
66	exp *CARDIOMYOPATHIES/di [Diagnosis]
67	31 and 39 and 65
68	31 and 61 and 65
69	12 and 62 and 65
70	12 and 66
71	or/67-70

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	POSTPARTUM PERIOD.kw.
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	(postpartum or post-partum).ti,ab.
11	puerperium.ti,ab.
12	or/1-11
13	CARDIOMYOPATHIES.kw.
14	cardiomyopath$.ti,ab.
15	myocardiopath$.ti,ab.
16	myocardial disease?.ti,ab.
17	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
18	Endocardial Fibroelastos?s.ti,ab.
19	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
20	Endomyocardial Fibros?s.ti,ab.
21	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
22	((antopol or danon) adj2 disease?).ti,ab.
23	(Kearn$ adj3 Syndrome).ti,ab.
24	Myocardial Reperfusion Injur$.ti,ab.
25	Myocarditi$.ti,ab.
26	Carditis.ti,ab.
27	Sarcoglycanopath$.ti,ab.
28	or/13-27
29	12 and 28
30	PPCM.ti,ab.
31	or/29-30
32	BIOMARKERS.kw.

#	Searches
33	Biomarker?.ti,ab.
34	NATRIURETIC PEPTIDE, BRAIN.kw.
35	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
36	BNP.ti,ab.
37	ENZYMES.kw.
38	(enzyme? or biocatalyst?).ti,ab.
39	or/32-38
40	MEDICAL HISTORY TAKING.kw.
41	(histor$ adj3 (take or taking)).ti,ab.
42	(histor$ adj3 clinical).ti,ab.
43	PHYSICAL EXAMINATION.kw.
44	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).ti,ab.
45	DYSPNEA.kw.
46	Breathless$.ti,ab.
47	(Short$ adj2 breath$).ti,ab.
48	Dyspnea?.ti,ab.
49	Orthopnoea?.ti,ab.
50	PULMONARY EDEMA.kw.
51	pulmonary edema?.ti,ab.
52	wet lung?.ti,ab.
53	TACHYCARDIA.kw.
54	(tachycardi$ or tachyarrhythmi$).ti,ab.
55	Palpitat$.ti,ab.
56	CHEST PAIN.kw.
57	(Chest? adj3 pain$).ti,ab.
58	angina pectoris.ti,ab.
59	stenocardia?.ti,ab.
60	((unstable or stable or preinfarction) adj3 angina).ti,ab.
61	or/40-60
62	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).ti,ab.
63	DIAGNOSIS.kw.
64	diagnos$.ti,ab.
65	or/63-64
66	31 and 39 and 65
67	31 and 61 and 65
68	12 and 62 and 65
69	or/66-68

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	POSTPARTUM PERIOD.kw.
7	pregnan$.tw,tx.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
9	((during or giving or give) adj3 birth?).tw,tx.
10	(postpartum or post-partum).tw,tx.
11	puerperium.tw,tx.
12	or/1-11
13	CARDIOMYOPATHIES.kw.
14	cardiomyopath$.tw,tx.
15	myocardiopath$.tw,tx.
16	myocardial disease?.tw,tx.
17	Arrhythmogenic Right Ventricular Dysplasia.tw,tx.
18	Endocardial Fibroelastos?s.tw,tx.
19	(Isolated Noncompaction adj3 Ventricular Myocardium).tw,tx.
20	Endomyocardial Fibros?s.tw,tx.
21	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).tw,tx.
22	((antopol or danon) adj2 disease?).tw,tx.
23	(Kearn$ adj3 Syndrome).tw,tx.
24	Myocardial Reperfusion Injur$.tw,tx.
25	Myocarditi$.tw,tx.
26	Carditis.tw,tx.
27	Sarcoglycanopath$.tw,tx.
28	or/13-27
29	12 and 28
30	PPCM.tw,tx.
31	or/29-30
32	BIOMARKERS.kw.
33	Biomarker?.tw,tx.
34	NATRIURETIC PEPTIDE, BRAIN.kw.
35	((B-type or type-b or brain) adj3 natriuretic peptide?).tw,tx.
36	BNP.tw,tx.
37	ENZYMES.kw.
38	(enzyme? or biocatalyst?).tw,tx.
39	or/32-38
40	MEDICAL HISTORY TAKING.kw.
41	(histor$ adj3 (take or taking)).tw,tx.
42	(histor$ adj3 clinical).tw,tx.
43	PHYSICAL EXAMINATION.kw.
44	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).tw,tx.
45	DYSPNEA.kw.
46	Breathless$.tw,tx.
47	(Short$ adj2 breath$).tw,tx.
48	Dyspnea?.tw,tx.
49	Orthopnoea?.tw,tx.
50	PULMONARY EDEMA.kw.

#	Searches
51	pulmonary edema?.tw,tx.
52	wet lung?.tw,tx.
53	TACHYCARDIA.kw.
54	(tachycardi$ or tachyarrhythmi$).tw,tx.
55	Palpitat$.tw,tx.
56	CHEST PAIN.kw.
57	(Chest? adj3 pain$).tw,tx.
58	angina pectoris.tw,tx.
59	stenocardia?.tw,tx.
60	((unstable or stable or preinfarction) adj3 angina).tw,tx.
61	or/40-60
62	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).tw,tx.
63	DIAGNOSIS.kw.
64	diagnos$.tw,tx.
65	or/63-64
66	31 and 39 and 65
67	31 and 61 and 65
68	12 and 62 and 65
69	or/66-68

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	POSTPARTUM PERIOD/
7	pregnan$.tw.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
9	((during or giving or give) adj3 birth?).tw.
10	(postpartum or post-partum).tw.
11	puerperium.tw.
12	or/1-11
13	exp CARDIOMYOPATHIES/
14	cardiomyopath$.tw.
15	myocardiopath$.tw.
16	myocardial disease?.tw.
17	Arrhythmogenic Right Ventricular Dysplasia.tw.
18	Endocardial Fibroelastos?s.tw.
19	(Isolated Noncompaction adj3 Ventricular Myocardium).tw.
20	Endomyocardial Fibros?s.tw.
21	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).tw.
22	((antopol or danon) adj2 disease?).tw.
23	(Kearn$ adj3 Syndrome).tw.
24	Myocardial Reperfusion Injur$.tw.

#	Searches
25	Myocarditi$.tw.
26	Carditis.tw.
27	Sarcoglycanopath$.tw.
28	or/13-27
29	12 and 28
30	PPCM.tw.
31	or/29-30
32	BIOMARKERS/
33	Biomarker?.tw.
34	NATRIURETIC PEPTIDE, BRAIN/
35	((B-type or type-b or brain) adj3 natriuretic peptide?).tw.
36	BNP.tw.
37	exp ENZYMES/
38	(enzyme? or biocatalyst?).tw.
39	or/32-38
40	MEDICAL HISTORY TAKING/
41	(histor$ adj3 (take or taking)).tw.
42	(histor$ adj3 clinical).tw.
43	PHYSICAL EXAMINATION/
44	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).tw.
45	exp DYSPNEA/
46	Breathless$.tw.
47	(Short$ adj2 breath$).tw.
48	Dyspnea?.tw.
49	Orthopnoea?.tw.
50	PULMONARY EDEMA/
51	pulmonary edema?.tw.
52	wet lung?.tw.
53	exp TACHYCARDIA/
54	(tachycardi$ or tachyarrhythmi$).tw.
55	Palpitat$.tw.
56	exp CHEST PAIN/
57	(Chest? adj3 pain$).tw.
58	angina pectoris.tw.
59	stenocardia?.tw.
60	((unstable or stable or preinfarction) adj3 angina).tw.
61	or/40-60
62	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).tw.
63	exp DIAGNOSIS/
64	diagnos$.tw.
65	or/63-64
66	exp *CARDIOMYOPATHIES/di [Diagnosis]
67	31 and 39 and 65
68	31 and 61 and 65
69	12 and 62 and 65
70	12 and 66

#	Searches
71	or/67-70

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*PUERPERIUM/
7	*INTRAPARTUM CARE/
8	pregnan$.ti,ab.
9	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
10	((during or giving or give) adj3 birth?).ti,ab.
11	(postpartum or post-partum).ti,ab.
12	puerperium.ti,ab.
13	or/1-12
14	exp CARDIOMYOPATHY/
15	cardiomyopath$.ti,ab.
16	myocardiopath$.ti,ab.
17	myocardial disease?.ti,ab.
18	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
19	Endocardial Fibroelastos?s.ti,ab.
20	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
21	Endomyocardial Fibros?s.ti,ab.
22	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
23	((antopol or danon) adj2 disease?).ti,ab.
24	(Kearn$ adj3 Syndrome).ti,ab.
25	Myocardial Reperfusion Injur$.ti,ab.
26	Myocarditi$.ti,ab.
27	Carditis.ti,ab.
28	Sarcoglycanopath$.ti,ab.
29	or/14-28
30	13 and 29
31	PPCM.ti,ab.
32	or/30-31
33	BIOLOGICAL MARKER/
34	Biomarker?.ti,ab.
35	BRAIN NATRIURETIC PEPTIDE/
36	((B-type or type-b or brain) adj3 natriuretic peptide?).ti,ab.
37	BNP.ti,ab.
38	exp ENZYME/
39	(enzyme? or biocatalyst?).ti,ab.
40	or/33-39
41	exp ANAMNESIS/
42	(histor$ adj3 (take or taking)).ti,ab.
43	(histor$ adj3 clinical).ti,ab.
44	*PHYSICAL EXAMINATION/
45	((clinical$ or physical$) adj5 (examin$ or investigat$ or observ$)).ti,ab.
46	exp DYSPNEA/

#	Searches
47	Breathless$.ti,ab.
48	(Short$ adj2 breath$).ti,ab.
49	Dyspnea?.ti,ab.
50	Orthopnoea?.ti,ab.
51	LUNG EDEMA/
52	pulmonary edema?.ti,ab.
53	wet lung?.ti,ab.
54	exp TACHYCARDIA/
55	(tachycardi$ or tachyarrhythmi$).ti,ab.
56	Palpitat$.ti,ab.
57	THORAX PAIN/
58	(Chest? adj3 pain$).ti,ab.
59	ANGINA PECTORIS/
60	angina pectoris.ti,ab.
61	stenocardia?.ti,ab.
62	((unstable or stable or preinfarction) adj3 angina).ti,ab.
63	or/41-62
64	((cardiomyopath$ or myocardiopath$ or myocardial disease? or PPCM or Arrhythmogenic Right Ventricular Dysplasia or Endocardial Fibroelastos?s or (Isolated Noncompaction adj3 Ventricular Myocardium) or Endomyocardial Fibros?s or (Glycogen Storage Disease adj3 (Type IIb or type 2b)) or ((antopol or danon) adj2 disease?) or (Kearn$ adj3 Syndrome) or Myocardial Reperfusion Injur$ or Myocarditi$ or Carditis or Sarcoglycanopath$) adj5 (examin$ or investigat$ or observ$ or sign? or symptom$)).ti,ab.
65	DIAGNOSIS/ or DIAGNOSTIC ACCURACY/ or DIAGNOSTIC ERROR/ or DIFFERENTIAL DIAGNOSIS/ or EARLY DIAGNOSIS/
66	diagnos$.ti,ab.
67	or/65-66
68	exp *CARDIOMYOPATHY/di [Diagnosis]
69	32 and 40 and 67
70	32 and 63 and 67
71	13 and 64 and 67
72	13 and 68
73	or/69-72
74	limit 73 to english language
75	letter.pt. or LETTER/
76	note.pt.
77	editorial.pt.
78	CASE REPORT/ or CASE STUDY/
79	(letter or comment*).ti.
80	or/75-79
81	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
82	80 not 81
83	ANIMAL/ not HUMAN/
84	NONHUMAN/
85	exp ANIMAL EXPERIMENT/
86	exp EXPERIMENTAL ANIMAL/
87	ANIMAL MODEL/
88	exp RODENT/
89	(rat or rats or mouse or mice).ti.
90	or/82-89
91	74 not 90

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	exp CARDIOMYOPATHIES/
11	cardiomyopath$.ti,ab.
12	myocardiopath$.ti,ab.
13	myocardial disease?.ti,ab.
14	PPCM.ti,ab.
15	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
16	Endocardial Fibroelastos?s.ti,ab.
17	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
18	Endomyocardial Fibros?s.ti,ab.
19	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
20	((antopol or danon) adj2 disease?).ti,ab.
21	(Kearn$ adj3 Syndrome).ti,ab.
22	Myocardial Reperfusion Injur$.ti,ab.
23	Myocarditi$.ti,ab.
24	Carditis.ti,ab.
25	Sarcoglycanopath$.ti,ab.
26	or/10-25
27	DISEASE MANAGEMENT/
28	manag$.ti,ab.
29	or/27-28
30	BROMOCRIPTINE/
31	Bromocriptine.mp.
32	ERGOLINES/
33	Cabergoline.mp.
34	or/30-33
35	9 and 26 and 29
36	9 and 26 and 34

#	Searches
37	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
38	34 and 37
39	35 or 36 or 38
40	limit 39 to english language
41	LETTER/
42	EDITORIAL/
43	NEWS/
44	exp HISTORICAL ARTICLE/
45	ANECDOTES AS TOPIC/
46	COMMENT/
47	CASE REPORT/
48	(letter or comment*).ti.
49	or/41-48
50	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
51	49 not 50
52	ANIMALS/ not HUMANS/
53	exp ANIMALS, LABORATORY/
54	exp ANIMAL EXPERIMENTATION/
55	exp MODELS, ANIMAL/
56	exp RODENTIA/
57	(rat or rats or mouse or mice).ti.
58	or/51-57
59	40 not 58

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	exp CARDIOMYOPATHIES/
11	cardiomyopath$.ti,ab,kw.
12	myocardiopath$.ti,ab,kw.
13	myocardial disease?.ti,ab,kw.
14	PPCM.ti,ab.
15	Arrhythmogenic Right Ventricular Dysplasia.ti,ab,kw.

#	Searches
16	Endocardial Fibroelastos?s.ti,ab,kw.
17	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
18	Endomyocardial Fibros?s.ti,ab,kw.
19	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
20	((antopol or danon) adj2 disease?).ti,ab.
21	(Kearn$ adj3 Syndrome).ti,ab.
22	Myocardial Reperfusion Injur$.ti,ab,kw.
23	Myocarditi$.ti,ab,kw.
24	Carditis.ti,ab,kw.
25	Sarcoglycanopath$.ti,ab,kw.
26	or/10-25
27	DISEASE MANAGEMENT/
28	manag$.ti,ab.
29	or/27-28
30	BROMOCRIPTINE/
31	Bromocriptine.mp.
32	ERGOLINES/
33	Cabergoline.mp.
34	or/30-33
35	9 and 26 and 29
36	9 and 26 and 34
37	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
38	34 and 37
39	35 or 36 or 38

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	CARDIOMYOPATHIES.kw.
11	cardiomyopath$.ti,ab.
12	myocardiopath$.ti,ab.
13	myocardial disease?.ti,ab.
14	PPCM.ti,ab.

#	Searches
15	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
16	Endocardial Fibroelastos?s.ti,ab.
17	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
18	Endomyocardial Fibros?s.ti,ab.
19	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
20	((antopol or danon) adj2 disease?).ti,ab.
21	(Kearn$ adj3 Syndrome).ti,ab.
22	Myocardial Reperfusion Injur$.ti,ab.
23	Myocarditi$.ti,ab.
24	Carditis.ti,ab.
25	Sarcoglycanopath$.ti,ab.
26	or/10-25
27	DISEASE MANAGEMENT.kw.
28	manag$.ti,ab.
29	or/27-28
30	BROMOCRIPTINE.kw.
31	Bromocriptine.mp.
32	ERGOLINES.kw.
33	Cabergoline.mp.
34	or/30-33
35	9 and 26 and 29
36	9 and 26 and 34
37	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
38	34 and 37
39	35 or 36 or 38

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	CARDIOMYOPATHIES.kw.
11	cardiomyopath$.tw,tx.
12	myocardiopath$.tw,tx.
13	myocardial disease?.tw,tx.

#	Searches
14	PPCM.tw,tx.
15	Arrhythmogenic Right Ventricular Dysplasia.tw,tx.
16	Endocardial Fibroelastos?s.tw,tx.
17	(Isolated Noncompaction adj3 Ventricular Myocardium).tw,tx.
18	Endomyocardial Fibros?s.tw,tx.
19	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).tw,tx.
20	((antopol or danon) adj2 disease?).tw,tx.
21	(Kearn$ adj3 Syndrome).tw,tx.
22	Myocardial Reperfusion Injur$.tw,tx.
23	Myocarditi$.tw,tx.
24	Carditis.tw,tx.
25	Sarcoglycanopath$.tw,tx.
26	or/10-25
27	DISEASE MANAGEMENT.kw.
28	manag$.tw,tx.
29	or/27-28
30	BROMOCRIPTINE.kw.
31	Bromocriptine.tw,tx.
32	ERGOLINES.kw.
33	Cabergoline.tw,tx.
34	or/30-33
35	9 and 26 and 29
36	9 and 26 and 34
37	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
38	34 and 37
39	35 or 36 or 38

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	exp CARDIOMYOPATHIES/
11	cardiomyopath$.tw.
12	myocardiopath$.tw.

#	Searches
13	myocardial disease?.tw.
14	PPCM.tw.
15	Arrhythmogenic Right Ventricular Dysplasia.tw.
16	Endocardial Fibroelastos?s.tw.
17	(Isolated Noncompaction adj3 Ventricular Myocardium).tw.
18	Endomyocardial Fibros?s.tw.
19	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).tw.
20	((antopol or danon) adj2 disease?).tw.
21	(Kearn$ adj3 Syndrome).tw.
22	Myocardial Reperfusion Injur$.tw.
23	Myocarditi$.tw.
24	Carditis.tw.
25	Sarcoglycanopath$.tw.
26	or/10-25
27	DISEASE MANAGEMENT/
28	manag$.tw.
29	or/27-28
30	BROMOCRIPTINE/
31	Bromocriptine.mp.
32	ERGOLINES/
33	Cabergoline.mp.
34	or/30-33
35	9 and 26 and 29
36	9 and 26 and 34
37	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
38	34 and 37
39	35 or 36 or 38

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	exp CARDIOMYOPATHY/

#	Searches
12	cardiomyopath$.ti,ab.
13	myocardiopath$.ti,ab.
14	myocardial disease?.ti,ab.
15	PPCM.ti,ab.
16	Arrhythmogenic Right Ventricular Dysplasia.ti,ab.
17	Endocardial Fibroelastos?s.ti,ab.
18	(Isolated Noncompaction adj3 Ventricular Myocardium).ti,ab.
19	Endomyocardial Fibros?s.ti,ab.
20	(Glycogen Storage Disease adj3 (Type IIb or type 2b)).ti,ab.
21	((antopol or danon) adj2 disease?).ti,ab.
22	(Kearn$ adj3 Syndrome).ti,ab.
23	Myocardial Reperfusion Injur$.ti,ab.
24	Myocarditi$.ti,ab.
25	Carditis.ti,ab.
26	Sarcoglycanopath$.ti,ab.
27	or/11-26
28	DISEASE MANAGEMENT/
29	manag$.ti,ab.
30	or/28-29
31	BROMOCRIPTINE/
32	Bromocriptine.mp.
33	CABERGOLINE/
34	Cabergoline.mp.
35	or/31-34
36	10 and 27 and 30
37	10 and 27 and 35
38	PERIPARTUM CARDIOMYOPATHY/dm [Disease Management]
39	PERIPARTUM CARDIOMYOPATHY/dt [Drug Therapy]
40	or/36-39
41	limit 40 to english language
42	letter.pt. or LETTER/
43	note.pt.
44	editorial.pt.
45	CASE REPORT/ or CASE STUDY/
46	(letter or comment*).ti.
47	or/42-46
48	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
49	47 not 48
50	ANIMAL/ not HUMAN/
51	NONHUMAN/

#	Searches
52	exp ANIMAL EXPERIMENT/
53	exp EXPERIMENTAL ANIMAL/
54	ANIMAL MODEL/
55	exp RODENT/
56	(rat or rats or mouse or mice).ti.
57	or/49-56
58	41 not 57

Intrapartum care for women with cardiac disease – anaesthesia

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.

#	Searches
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.

#	Searches
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	exp ANESTHESIA, CONDUCTION/
84	((nerve or ganglion or plexus) adj3 block$).ti,ab.
85	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).ti,ab.
86	epidural$.ti,ab.
87	CSE.ti,ab.
88	((nerve or ganglion or plexus or neuraxial$) adj5 block$).ti,ab.
89	(neuraxial$ adj5 an?esthe$).ti,ab.
90	or/83-89
91	exp ANESTHESIA, GENERAL/
92	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).ti,ab.
93	or/91-92
94	RISK/
95	RISK ASSESSMENT/
96	risk?.ti,ab.
97	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
98	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
99	harm$.ti,ab.
100	THERAPEUTIC USES/
101	(therapeutic$ adj3 (effect? or use?)).ti,ab.
102	benefi$.ti,ab.
103	effective$.ti,ab.
104	efficacy.ti,ab.
105	or/94-104
106	COMPARATIVE EFFECTIVENESS RESEARCH/
107	Comparative Study.pt.

#	Searches
108	(compar$ adj3 (study or studies or research$)).ti,ab.
109	or/106-108
110	ANESTHESIA, OBSTETRICAL/ae [Adverse Effects]
111	exp ANESTHESIA, CONDUCTION/ae [Adverse Effects]
112	exp ANESTHESIA, CONDUCTION/tu [Therapeutic Use]
113	exp ANESTHESIA, GENERAL/ae [Adverse Effects]
114	or/110-113
115	ANESTHESIA, OBSTETRICAL/mt [Methods]
116	(an?esthe$ adj5 manag$).ti.
117	UK Obstetric Surveillance System.ti,ab.
118	UKOSS.ti,ab.
119	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
120	MBRRACE.ti,ab.
121	Scottish confidential audit of severe maternal morbidity.ti,ab.
122	SCASMM.ti,ab.
123	"Confidential Enquiry into Maternal and Child Health".ti,ab.
124	CEMACH.ti,ab.
125	or/117-124
126	82 and 90 and 93
127	82 and (90 or 93) and 105
128	82 and (90 or 93) and 109
129	82 and 114
130	82 and 115
131	82 and 116
132	82 and 125
133	or/126-132
134	limit 133 to english language
135	LETTER/
136	EDITORIAL/
137	NEWS/
138	exp HISTORICAL ARTICLE/
139	ANECDOTES AS TOPIC/
140	COMMENT/
141	CASE REPORT/
142	(letter or comment*).ti.
143	or/135-142
144	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
145	143 not 144
146	ANIMALS/ not HUMANS/
147	exp ANIMALS, LABORATORY/

#	Searches
148	exp ANIMAL EXPERIMENTATION/
149	exp MODELS, ANIMAL/
150	exp RODENTIA/
151	(rat or rats or mouse or mice).ti.
152	or/145-151
153	134 not 152

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab,kw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab,kw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab,kw.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.

#	Searches
32	Brugada Syndrome.ti,ab,kw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab,kw.
35	Long QT Syndrome.ti,ab,kw.
36	Parasystole.ti,ab,kw.
37	Pre-Excitation Syndrome?.ti,ab,kw.
38	Tachycardia?.ti,ab,kw.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab,kw.
51	Loeys-Dietz Syndrome.ti,ab,kw.
52	Leriche Syndrome.ti,ab,kw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab,kw.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/

#	Searches
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	exp ANESTHESIA, CONDUCTION/
84	((nerve or ganglion or plexus) adj3 block$).ti,ab.
85	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).ti,ab.
86	epidural$.ti,ab,kw.
87	CSE.ti,ab.
88	((nerve or ganglion or plexus or neuraxial$) adj5 block$).ti,ab.
89	(neuraxial$ adj5 an?esthe$).ti,ab.
90	or/83-89
91	exp ANESTHESIA, GENERAL/
92	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).ti,ab.
93	or/91-92
94	RISK/
95	RISK ASSESSMENT/
96	risk?.ti,ab.
97	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
98	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
99	harm$.ti,ab.
100	THERAPEUTIC USES/
101	(therapeutic$ adj3 (effect? or use?)).ti,ab.
102	benefi$.ti,ab.
103	effective$.ti,ab.
104	efficacy.ti,ab.
105	or/94-104
106	COMPARATIVE EFFECTIVENESS RESEARCH/
107	Comparative Study.pt.
108	(compar$ adj3 (study or studies or research$)).ti,ab.
109	or/106-108
110	ANESTHESIA, OBSTETRICAL/ae [Adverse Effects]
111	exp ANESTHESIA, CONDUCTION/ae [Adverse Effects]

#	Searches
112	exp ANESTHESIA, CONDUCTION/tu [Therapeutic Use]
113	exp ANESTHESIA, GENERAL/ae [Adverse Effects]
114	or/110-113
115	ANESTHESIA, OBSTETRICAL/mt [Methods]
116	(an?esthe$ adj5 manag$).ti.
117	UK Obstetric Surveillance System.ti,ab.
118	UKOSS.ti,ab.
119	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
120	MBRRACE.ti,ab.
121	Scottish confidential audit of severe maternal morbidity.ti,ab.
122	SCASMM.ti,ab.
123	"Confidential Enquiry into Maternal and Child Health".ti,ab.
124	CEMACH.ti,ab.
125	or/117-124
126	82 and 90 and 93
127	82 and (90 or 93) and 105
128	82 and (90 or 93) and 109
129	82 and 114
130	82 and 115
131	82 and 116
132	82 and 125
133	or/126-132

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.

#	Searches
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).ti,ab.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS.kw.

#	Searches
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).ti,ab.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	ANESTHESIA, CONDUCTION.kw.
84	((nerve or ganglion or plexus) adj3 block$).ti,ab.
85	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).ti,ab.
86	epidural$.ti,ab.
87	CSE.ti,ab.
88	((nerve or ganglion or plexus or neuraxial$) adj5 block$).ti,ab.
89	(neuraxial$ adj5 an?esthe$).ti,ab.
90	or/83-89
91	ANESTHESIA, GENERAL.kw.
92	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).ti,ab.
93	or/91-92
94	RISK.kw.

#	Searches
95	RISK ASSESSMENT.kw.
96	risk?.ti,ab.
97	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS".kw.
98	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
99	harm$.ti,ab.
100	THERAPEUTIC USES.kw.
101	(therapeutic$ adj3 (effect? or use?)).ti,ab.
102	benefi$.ti,ab.
103	effective$.ti,ab.
104	efficacy.ti,ab.
105	or/94-104
106	COMPARATIVE EFFECTIVENESS RESEARCH.kw.
107	Comparative Study.pt.
108	(compar$ adj3 (study or studies or research$)).ti,ab.
109	or/106-108
110	(an?esthe$ adj5 manag$).ti.
111	UK Obstetric Surveillance System.ti,ab.
112	UKOSS.ti,ab.
113	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
114	MBRRACE.ti,ab.
115	Scottish confidential audit of severe maternal morbidity.ti,ab.
116	SCASMM.ti,ab.
117	"Confidential Enquiry into Maternal and Child Health".ti,ab.
118	CEMACH.ti,ab.
119	or/111-118
120	82 and 90 and 93
121	82 and (90 or 93) and 105
122	82 and (90 or 93) and 109
123	82 and 110
124	82 and 119
125	or/120-124

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.

#	Searches
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).tw,tx.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).tw,tx.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
16	click murmur syndrome?.tw,tx.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
21	(persist$ adj2 ostium primum).tw,tx.
22	anomal$ pulmonary venous drain$.tw,tx.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
25	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).tw,tx.
30	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
31	(Bradycardia? or bradyarrhythmia?).tw,tx.
32	Brugada Syndrome.tw,tx.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
34	Heart Block.tw,tx.
35	Long QT Syndrome.tw,tx.
36	Parasystole.tw,tx.
37	Pre-Excitation Syndrome?.tw,tx.
38	Tachycardia?.tw,tx.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).tw,tx.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
46	MARFAN SYNDROME.kw.

#	Searches
47	(Marfan$ adj2 syndrome).tw,tx.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
50	Aortitis.tw,tx.
51	Loeys-Dietz Syndrome.tw,tx.
52	Leriche Syndrome.tw,tx.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.tw,tx.
65	(complex$ adj10 congenital$ heart disease?).tw,tx.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).tw,tx.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).tw,tx.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).tw,tx.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).tw,tx.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	ANESTHESIA, CONDUCTION.kw.
84	((nerve or ganglion or plexus) adj3 block$).tw,tx.
85	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).tw,tx.
86	epidural$.tw,tx.

#	Searches
87	CSE.tw,tx.
88	((nerve or ganglion or plexus or neuraxial$) adj5 block$).tw,tx.
89	(neuraxial$ adj5 an?esthe$).tw,tx.
90	or/83-89
91	ANESTHESIA, GENERAL.kw.
92	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).tw,tx.
93	or/91-92
94	RISK.kw.
95	RISK ASSESSMENT.kw.
96	risk?.tw,tx.
97	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS".kw.
98	(adverse$ adj3 (effect? or event? or reaction?)).tw,tx.
99	harm$.tw,tx.
100	THERAPEUTIC USES.kw.
101	(therapeutic$ adj3 (effect? or use?)).tw,tx.
102	benefi$.tw,tx.
103	effective$.tw,tx.
104	efficacy.tw,tx.
105	or/94-104
106	COMPARATIVE EFFECTIVENESS RESEARCH.kw.
107	Comparative Study.pt.
108	(compar$ adj3 (study or studies or research$)).tw,tx.
109	or/106-108
110	(an?esthe$ adj5 manag$).ti.
111	UK Obstetric Surveillance System.tw,tx.
112	UKOSS.tw,tx.
113	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw,tx.
114	MBRRACE.tw,tx.
115	Scottish confidential audit of severe maternal morbidity.tw,tx.
116	SCASMM.tw,tx.
117	"Confidential Enquiry into Maternal and Child Health".tw,tx.
118	CEMACH.tw,tx.
119	or/111-118
120	82 and 90 and 93
121	82 and (90 or 93) and 105
122	82 and (90 or 93) and 109
123	82 and 110
124	82 and 119
125	or/120-124

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).tw.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).tw.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).tw.
16	click murmur syndrome?.tw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
21	(persist$ adj2 ostium primum).tw.
22	anomal$ pulmonary venous drain$.tw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
25	((Atrial or ventricular) adj2 extrasystole?).tw.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
28	exp ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).tw.
30	(Atrial adj2 (Fibrillation or Flutter)).tw.
31	(Bradycardia? or bradyarrhythmia?).tw.
32	Brugada Syndrome.tw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
34	Heart Block.tw.
35	Long QT Syndrome.tw.
36	Parasystole.tw.
37	Pre-Excitation Syndrome?.tw.
38	Tachycardia?.tw.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw.

#	Searches
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).tw.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).tw.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
50	Aortitis.tw.
51	Loeys-Dietz Syndrome.tw.
52	Leriche Syndrome.tw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).tw.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).tw.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.tw.
65	(complex$ adj10 congenital$ heart disease?).tw.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).tw.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).tw.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).tw.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).tw.
79	or/10-78

#	Searches
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	exp ANESTHESIA, CONDUCTION/
84	((nerve or ganglion or plexus) adj3 block$).tw.
85	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).tw.
86	epidural$.tw.
87	CSE.tw.
88	((nerve or ganglion or plexus or neuraxial$) adj5 block$).tw.
89	(neuraxial$ adj5 an?esthe$).tw.
90	or/83-89
91	exp ANESTHESIA, GENERAL/
92	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).tw.
93	or/91-92
94	RISK/
95	RISK ASSESSMENT/
96	risk?.tw.
97	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
98	(adverse$ adj3 (effect? or event? or reaction?)).tw.
99	harm$.tw.
100	THERAPEUTIC USES/
101	(therapeutic$ adj3 (effect? or use?)).tw.
102	benefi$.tw.
103	effective$.tw.
104	efficacy.tw.
105	or/94-104
106	COMPARATIVE EFFECTIVENESS RESEARCH/
107	Comparative Study.pt.
108	(compar$ adj3 (study or studies or research$)).tw.
109	or/106-108
110	ANESTHESIA, OBSTETRICAL/ae [Adverse Effects]
111	exp ANESTHESIA, CONDUCTION/ae [Adverse Effects]
112	exp ANESTHESIA, CONDUCTION/tu [Therapeutic Use]
113	exp ANESTHESIA, GENERAL/ae [Adverse Effects]
114	or/110-113
115	ANESTHESIA, OBSTETRICAL/mt [Methods]
116	(an?esthe$ adj5 manag$).ti.
117	UK Obstetric Surveillance System.tw.
118	UKOSS.tw.

#	Searches
119	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".tw.
120	MBRRACE.tw.
121	Scottish confidential audit of severe maternal morbidity.tw.
122	SCASMM.tw.
123	"Confidential Enquiry into Maternal and Child Health".tw.
124	CEMACH.tw.
125	or/117-124
126	82 and 90 and 93
127	82 and (90 or 93) and 105
128	82 and (90 or 93) and 109
129	82 and 114
130	82 and 115
131	82 and 116
132	82 and 125
133	or/126-132

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	PULMONARY VALVE STENOSIS/
12	(pulmonary adj2 stenos$).ti,ab.
13	PATENT DUCTUS ARTERIOSUS/
14	(Paten$ adj2 ductus arteriosus).ti,ab.
15	MITRAL VALVE PROLAPSE/
16	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
17	click murmur syndrome?.ti,ab.
18	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
19	HEART SEPTUM DEFECT/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.

#	Searches
23	EXTRASYSTOLE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	FALLOT TETRALOGY/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *HEART ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp *HYPERTROPHIC CARDIOMYOPATHY/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE REGURGITATION/
43	MITRAL VALVE REGURGITATION/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp *AORTA DISEASE/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTA COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	exp *HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	GREAT VESSELS TRANSPOSITION/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp *CORONARY ARTERY DISEASE/

#	Searches
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	CYANOTIC HEART DISEASE/
64	Cyanotic heart disease?.ti,ab.
65	*CONGENITAL HEART DISEASE/
66	(complex$ adj10 congenital$ heart disease?).ti,ab.
67	*PULMONARY HYPERTENSION/
68	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
69	exp *HEART VENTRICLE FAILURE/
70	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
71	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
72	exp CARDIOMYOPATHY/ and TIME FACTOR/
73	(previous$ adj5 cardiomyopath$).ti,ab.
74	MITRAL VALVE STENOSIS/
75	(mitral adj2 stenos?s).ti,ab.
76	AORTA VALVE STENOSIS/
77	(aort$ adj2 stenos?s).ti,ab.
78	AORTA COARCTATION/
79	(Coarctation? adj3 aort$).ti,ab.
80	or/11-79
81	10 and 80
82	exp EPIDURAL ANESTHESIA/
83	exp LOCAL ANESTHESIA/
84	exp REGIONAL ANESTHESIA/
85	exp SPINAL ANESTHESIA/
86	((nerve or ganglion or plexus) adj3 block$).ti,ab.
87	(an?esthe$ adj5 (conduction or region$ or caudal$ or local$ or spinal$)).ti,ab.
88	epidural$.ti,ab.
89	CSE.ti,ab.
90	((nerve or ganglion or plexus or neuraxial$) adj5 block$).ti,ab.
91	(neuraxial$ adj5 an?esthe$).ti,ab.
92	or/82-91
93	exp GENERAL ANESTHESIA/
94	(an?esthe$ adj5 (general$ or inhal$ or closed circuit or rebreath$ or re-breath$ or rectal$ or balanced)).ti,ab.
95	or/93-94
96	*RISK/
97	*RISK ASSESSMENT/
98	risk?.ti,ab.
99	*SIDE EFFECT/
100	*ADVERSE DRUG REACTION/

#	Searches
101	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
102	harm$.ti,ab.
103	*THERAPY EFFECT/
104	*DRUG EFFICACY/
105	(therapeutic$ adj3 (effect? or use?)).ti,ab.
106	benefi$.ti,ab.
107	effective$.ti,ab.
108	efficacy.ti,ab.
109	or/96-108
110	COMPARATIVE EFFECTIVENESS/
111	COMPARATIVE STUDY/
112	(compar$ adj3 (study or studies or research$)).ti,ab.
113	or/110-112
114	exp EPIDURAL ANESTHESIA/ae [Adverse Drug Reaction]
115	exp LOCAL ANESTHESIA/ae [Adverse Drug Reaction]
116	exp REGIONAL ANESTHESIA/ae [Adverse Drug Reaction]
117	exp REGIONAL ANESTHESIA/dt [Drug Therapy]
118	exp SPINAL ANESTHESIA/ae [Adverse Drug Reaction]
119	exp GENERAL ANESTHESIA/ae [Adverse Drug Reaction]
120	or/114-119
121	(an?esthe$ adj5 manag$).ti.
122	UK Obstetric Surveillance System.ti,ab.
123	UKOSS.ti,ab.
124	"Mothers and babies? reducing risk through audits and confidential enquiries across the UK".ti,ab.
125	MBRRACE.ti,ab.
126	Scottish confidential audit of severe maternal morbidity.ti,ab.
127	SCASMM.ti,ab.
128	"Confidential Enquiry into Maternal and Child Health".ti,ab.
129	CEMACH.ti,ab.
130	or/122-129
131	81 and 92 and 95
132	81 and (92 or 95) and 109
133	81 and (92 or 95) and 113
134	81 and 120
135	81 and 121
136	81 and 130
137	or/131-136
138	limit 137 to english language
139	letter.pt. or LETTER/
140	note.pt.

#	Searches
141	editorial.pt.
142	CASE REPORT/ or CASE STUDY/
143	(letter or comment*).ti.
144	or/139-143
145	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
146	144 not 145
147	ANIMAL/ not HUMAN/
148	NONHUMAN/
149	exp ANIMAL EXPERIMENT/
150	exp EXPERIMENTAL ANIMAL/
151	ANIMAL MODEL/
152	exp RODENT/
153	(rat or rats or mouse or mice).ti.
154	or/146-153
155	138 not 154

Intrapartum care for women with cardiac disease – analgesia

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.

#	Searches
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.

#	Searches
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(systemic$ adj3 analgesi$).ti,ab.
84	exp ANALGESICS, OPIOID/
85	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
86	remifentanil.mp.
87	KETAMINE/
88	ketamine.mp.
89	(inhal$ adj3 analgesi$).ti,ab.
90	exp NITROUS OXIDE/
91	(nitrous oxide or N2O).mp.
92	laughing gas.ti,ab.
93	(gas adj2 air).ti,ab.
94	Entonox.mp.
95	Nitronox.mp.

#	Searches
96	sevoflurane.mp.
97	desflurane.mp.
98	((Non-pharma$ or Nonpharma$) adj3 analgesi$).ti,ab.
99	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/
100	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).ti,ab.
101	TENS.ti,ab.
102	electroanalgesi$.ti,ab.
103	electroacupuncture.ti,ab.
104	ACUPUNCTURE THERAPY/
105	ACUPUNCTURE ANALGESIA/
106	acupuncture.ti,ab.
107	water papule?.ti,ab.
108	BATHS/
109	birthing pool?.ti,ab.
110	MASSAGE/
111	massag$.ti,ab.
112	reflexolog$.ti,ab.
113	AROMATHERAPY/
114	aromatherap$.ti,ab.
115	hypnobirth$.ti,ab.
116	HOMEOPATHY/
117	hom?eopath$.ti,ab.
118	or/83-117
119	ANALGESIA, EPIDURAL/
120	INJECTIONS, EPIDURAL/
121	((Spinal$ or spinous$) adj5 analges$).ti,ab.
122	epidural$.ti,ab.
123	CSE.ti,ab.
124	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
125	(neuraxial$ adj5 analges$).ti,ab.
126	or/119-125
127	RISK/
128	RISK ASSESSMENT/
129	risk?.ti,ab.
130	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
131	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
132	harm$.ti,ab.
133	THERAPEUTIC USES/
134	(therapeutic$ adj3 (effect? or use?)).ti,ab.
135	benefi$.ti,ab.

#	Searches
136	or/127-135
137	exp ANALGESICS, OPIOID/ae [Adverse Effects]
138	exp ANALGESICS, OPIOID/tu [Therapeutic Use]
139	KETAMINE/ae [Adverse Effects]
140	KETAMINE/tu [Therapeutic Use]
141	NITROUS OXIDE/ae [Adverse Effects]
142	NITROUS OXIDE/tu [Therapeutic Use]
143	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/ae [Adverse Effects]
144	ACUPUNCTURE THERAPY/ae [Adverse Effects]
145	ACUPUNCTURE ANALGESIA/ae [Adverse Effects]
146	BATHS/ae [Adverse Effects]
147	MASSAGE/ae [Adverse Effects]
148	MASSAGE/tu [Therapeutic Use]
149	AROMATHERAPY/ae [Adverse Effects]
150	HOMEOPATHY/ae [Adverse Effects]
151	ANALGESIA, EPIDURAL/ae [Adverse Effects]
152	INJECTIONS, EPIDURAL/ae [Adverse Effects]
153	or/137-152
154	PAIN MANAGEMENT/
155	ANALGESIA, PATIENT-CONTROLLED/mt [Methods]
156	ANALGESIA, OBSTETRICAL/mt [Methods]
157	or/154-156
158	82 and 118 and 126
159	82 and (118 or 126) and 136
160	82 and 153
161	82 and 157
162	or/158-161
163	limit 162 to english language
164	LETTER/
165	EDITORIAL/
166	NEWS/
167	exp HISTORICAL ARTICLE/
168	ANECDOTES AS TOPIC/
169	COMMENT/
170	CASE REPORT/
171	(letter or comment*).ti.
172	or/164-171
173	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
174	172 not 173
175	ANIMALS/ not HUMANS/

#	Searches
176	exp ANIMALS, LABORATORY/
177	exp ANIMAL EXPERIMENTATION/
178	exp MODELS, ANIMAL/
179	exp RODENTIA/
180	(rat or rats or mouse or mice).ti.
181	or/174-180
182	163 not 181

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/
6	pregnan$.ti,ab,kw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab,kw.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab,kw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab,kw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *ARRHYTHMIAS, CARDIAC/
29	(arrhythmia? or dysrhythmia?).ti,ab,kw.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.

#	Searches
31	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab,kw.
35	Long QT Syndrome.ti,ab,kw.
36	Parasystole.ti,ab,kw.
37	Pre-Excitation Syndrome?.ti,ab,kw.
38	Tachycardia?.ti,ab,kw.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab,kw.
51	Loeys-Dietz Syndrome.ti,ab,kw.
52	Leriche Syndrome.ti,ab,kw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.ti,ab,kw.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.

#	Searches
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).ti,ab.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(systemic$ adj3 analgesi$).ti,ab.
84	exp ANALGESICS, OPIOID/
85	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
86	remifentanil.mp.
87	KETAMINE/
88	ketamine.mp.
89	(inhal$ adj3 analgesi$).ti,ab.
90	exp NITROUS OXIDE/
91	(nitrous oxide or N2O).mp.
92	laughing gas.ti,ab,kw.
93	(gas adj2 air).ti,ab.
94	Entonox.mp.
95	Nitronox.mp.
96	sevoflurane.mp.
97	desflurane.mp.
98	((Non-pharma$ or Nonpharma$) adj3 analgesi$).ti,ab.
99	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/
100	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).ti,ab.
101	TENS.ti,ab.
102	electroanalgesi$.ti,ab,kw.
103	electroacupuncture.ti,ab,kw.
104	ACUPUNCTURE THERAPY/
105	ACUPUNCTURE ANALGESIA/
106	acupuncture.ti,ab,kw.

#	Searches
107	water papule?.ti,ab,kw.
108	BATHS/
109	birthing pool?.ti,ab,kw.
110	MASSAGE/
111	massag$.ti,ab,kw.
112	reflexolog$.ti,ab,kw.
113	AROMATHERAPY/
114	aromatherap$.ti,ab,kw.
115	hypnobirth$.ti,ab,kw.
116	HOMEOPATHY/
117	hom?eopath$.ti,ab,kw.
118	or/83-117
119	ANALGESIA, EPIDURAL/
120	INJECTIONS, EPIDURAL/
121	((Spinal$ or spinous$) adj5 analges$).ti,ab.
122	epidural$.ti,ab,kw.
123	CSE.ti,ab.
124	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
125	(neuraxial$ adj5 analges$).ti,ab.
126	or/119-125
127	RISK/
128	RISK ASSESSMENT/
129	risk?.ti,ab.
130	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
131	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
132	harm$.ti,ab.
133	THERAPEUTIC USES/
134	(therapeutic$ adj3 (effect? or use?)).ti,ab.
135	benefi$.ti,ab.
136	or/127-135
137	exp ANALGESICS, OPIOID/ae [Adverse Effects]
138	exp ANALGESICS, OPIOID/tu [Therapeutic Use]
139	KETAMINE/ae [Adverse Effects]
140	KETAMINE/tu [Therapeutic Use]
141	NITROUS OXIDE/ae [Adverse Effects]
142	NITROUS OXIDE/tu [Therapeutic Use]
143	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/ae [Adverse Effects]
144	ACUPUNCTURE THERAPY/ae [Adverse Effects]
145	ACUPUNCTURE ANALGESIA/ae [Adverse Effects]
146	BATHS/ae [Adverse Effects]

#	Searches
147	MASSAGE/ae [Adverse Effects]
148	MASSAGE/tu [Therapeutic Use]
149	AROMATHERAPY/ae [Adverse Effects]
150	HOMEOPATHY/ae [Adverse Effects]
151	ANALGESIA, EPIDURAL/ae [Adverse Effects]
152	INJECTIONS, EPIDURAL/ae [Adverse Effects]
153	or/137-152
154	PAIN MANAGEMENT/
155	ANALGESIA, PATIENT-CONTROLLED/mt [Methods]
156	ANALGESIA, OBSTETRICAL/mt [Methods]
157	or/154-156
158	82 and 118 and 126
159	82 and (118 or 126) and 136
160	82 and 153
161	82 and 157
162	or/158-161

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.ti,ab.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
8	((during or giving or give) adj3 birth?).ti,ab.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).ti,ab.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).ti,ab.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
16	click murmur syndrome?.ti,ab.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.

#	Searches
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).ti,ab.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	CORONARY DISEASE.kw.

#	Searches
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.ti,ab.
65	(complex$ adj10 congenital$ heart disease?).ti,ab.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).ti,ab.
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).ti,ab.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).ti,ab.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).ti,ab.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	(systemic$ adj3 analgesi$).ti,ab.
84	ANALGESICS, OPIOID.kw.
85	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
86	remifentanil.mp.
87	KETAMINE.kw.
88	ketamine.mp.
89	(inhal$ adj3 analgesi$).ti,ab.
90	NITROUS OXIDE.kw.
91	(nitrous oxide or N2O).mp.
92	laughing gas.ti,ab.
93	(gas adj2 air).ti,ab.
94	Entonox.mp.
95	Nitronox.mp.
96	sevoflurane.mp.

#	Searches
97	desflurane.mp.
98	((Non-pharma$ or Nonpharma$) adj3 analgesi$).ti,ab.
99	TRANSCUTANEOUS ELECTRIC NERVE STIMULATION.kw.
100	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).ti,ab.
101	TENS.ti,ab.
102	electroanalgesi$.ti,ab.
103	electroacupuncture.ti,ab.
104	ACUPUNCTURE THERAPY.kw.
105	ACUPUNCTURE ANALGESIA.kw.
106	acupuncture.ti,ab.
107	water papule?.ti,ab.
108	BATHS.kw.
109	birthing pool?.ti,ab.
110	MASSAGE.kw.
111	massag$.ti,ab.
112	reflexolog$.ti,ab.
113	AROMATHERAPY.kw.
114	aromatherap$.ti,ab.
115	hypnobirth$.ti,ab.
116	HOMEOPATHY.kw.
117	hom?eopath$.ti,ab.
118	or/83-117
119	ANALGESIA, EPIDURAL.kw.
120	INJECTIONS, EPIDURAL.kw.
121	((Spinal$ or spinous$) adj5 analges$).ti,ab.
122	epidural$.ti,ab.
123	CSE.ti,ab.
124	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
125	(neuraxial$ adj5 analges$).ti,ab.
126	or/119-125
127	RISK.kw.
128	RISK ASSESSMENT.kw.
129	risk?.ti,ab.
130	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS".kw.
131	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
132	harm$.ti,ab.
133	THERAPEUTIC USES.kw.
134	(therapeutic$ adj3 (effect? or use?)).ti,ab.
135	benefi$.ti,ab.
136	or/127-135

#	Searches
137	PAIN MANAGEMENT.kw.
138	82 and 118 and 126
139	82 and (118 or 126) and 136
140	82 and 137
141	or/138-140

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PREGNANCY.kw.
2	PERIPARTUM PERIOD.kw.
3	PARTURITION.kw.
4	LABOR, OBSTETRIC.kw.
5	OBSTETRIC LABOR, PREMATURE.kw.
6	pregnan$.tw,tx.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw,tx.
8	((during or giving or give) adj3 birth?).tw,tx.
9	or/1-8
10	PULMONARY VALVE STENOSIS.kw.
11	(pulmonary adj2 stenos$).tw,tx.
12	DUCTUS ARTERIOSUS, PATENT.kw.
13	(Paten$ adj2 ductus arteriosus).tw,tx.
14	MITRAL VALVE PROLAPSE.kw.
15	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
16	click murmur syndrome?.tw,tx.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
18	HEART SEPTAL DEFECTS, ATRIAL.kw.
19	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
21	(persist$ adj2 ostium primum).tw,tx.
22	anomal$ pulmonary venous drain$.tw,tx.
23	CARDIAC COMPLEXES, PREMATURE.kw.
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
25	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
26	"TETRALOGY OF FALLOT".kw.
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
28	ARRHYTHMIAS, CARDIAC.kw.
29	(arrhythmia? or dysrhythmia?).tw,tx.
30	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
31	(Bradycardia? or bradyarrhythmia?).tw,tx.
32	Brugada Syndrome.tw,tx.

#	Searches
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
34	Heart Block.tw,tx.
35	Long QT Syndrome.tw,tx.
36	Parasystole.tw,tx.
37	Pre-Excitation Syndrome?.tw,tx.
38	Tachycardia?.tw,tx.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.
40	CARDIOMYOPATHY, HYPERTROPHIC.kw.
41	(Hypertrophic adj2 cardiomyopath$).tw,tx.
42	AORTIC VALVE INSUFFICIENCY.kw.
43	MITRAL VALVE INSUFFICIENCY.kw.
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
46	MARFAN SYNDROME.kw.
47	(Marfan$ adj2 syndrome).tw,tx.
48	AORTIC DISEASES.kw.
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
50	Aortitis.tw,tx.
51	Loeys-Dietz Syndrome.tw,tx.
52	Leriche Syndrome.tw,tx.
53	AORTIC COARCTATION.kw.
54	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
55	HEART VALVE PROSTHESIS.kw.
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
57	"TRANSPOSITION OF GREAT VESSELS".kw.
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
59	FONTAN PROCEDURE.kw.
60	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
61	CORONARY DISEASE.kw.
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
63	HEART DEFECTS, CONGENITAL.kw.
64	Cyanotic heart disease?.tw,tx.
65	(complex$ adj10 congenital$ heart disease?).tw,tx.
66	PULMONARY HYPERTENSION.kw.
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
68	VENTRICULAR DYSFUNCTION.kw.
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
71	(CARDIOMYOPATHIES and TIME FACTORS).kw.
72	(previous$ adj5 cardiomyopath$).tw,tx.

#	Searches
73	MITRAL VALVE STENOSIS.kw.
74	(mitral adj2 stenos?s).tw,tx.
75	AORTIC VALVE STENOSIS.kw.
76	(aort$ adj2 stenos?s).tw,tx.
77	AORTIC COARCTATION.kw.
78	(Coarctation? adj3 aort$).tw,tx.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
82	or/80-81
83	(systemic$ adj3 analgesi$).tw,tx.
84	ANALGESICS, OPIOID.kw.
85	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
86	remifentanil.mp.
87	KETAMINE.kw.
88	ketamine.mp.
89	(inhal$ adj3 analgesi$).tw,tx.
90	NITROUS OXIDE.kw.
91	(nitrous oxide or N2O).mp.
92	laughing gas.tw,tx.
93	(gas adj2 air).tw,tx.
94	Entonox.mp.
95	Nitronox.mp.
96	sevoflurane.mp.
97	desflurane.mp.
98	((Non-pharma$ or Nonpharma$) adj3 analgesi$).tw,tx.
99	TRANSCUTANEOUS ELECTRIC NERVE STIMULATION.kw.
100	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).tw,tx.
101	TENS.tw,tx.
102	electroanalgesi$.tw,tx.
103	electroacupuncture.tw,tx.
104	ACUPUNCTURE THERAPY.kw.
105	ACUPUNCTURE ANALGESIA.kw.
106	acupuncture.tw,tx.
107	water papule?.tw,tx.
108	BATHS.kw.

#	Searches
109	birthing pool?.tw,tx.
110	MASSAGE.kw.
111	massag$.tw,tx.
112	reflexolog$.tw,tx.
113	AROMATHERAPY.kw.
114	aromatherap$.tw,tx.
115	hypnobirth$.tw,tx.
116	HOMEOPATHY.kw.
117	hom?eopath$.tw,tx.
118	or/83-117
119	ANALGESIA, EPIDURAL.kw.
120	INJECTIONS, EPIDURAL.kw.
121	((Spinal$ or spinous$) adj5 analges$).tw,tx.
122	epidural$.tw,tx.
123	CSE.tw,tx.
124	((central$ or regional$) adj5 neuraxial$ adj5 block$).tw,tx.
125	(neuraxial$ adj5 analges$).tw,tx.
126	or/119-125
127	RISK.kw.
128	RISK ASSESSMENT.kw.
129	risk?.tw,tx.
130	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS".kw.
131	(adverse$ adj3 (effect? or event? or reaction?)).tw,tx.
132	harm$.tw,tx.
133	THERAPEUTIC USES.kw.
134	(therapeutic$ adj3 (effect? or use?)).tw,tx.
135	benefi$.tw,tx.
136	or/127-135
137	PAIN MANAGEMENT.kw.
138	82 and 118 and 126
139	82 and (118 or 126) and 136
140	82 and 137
141	or/138-140

Database: Health Technology Assessment

#	Searches
1	PREGNANCY/
2	PERIPARTUM PERIOD/
3	PARTURITION/
4	exp LABOR, OBSTETRIC/
5	OBSTETRIC LABOR, PREMATURE/

#	Searches
6	pregnan$.tw.
7	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).tw.
8	((during or giving or give) adj3 birth?).tw.
9	or/1-8
10	PULMONARY VALVE STENOSIS/
11	(pulmonary adj2 stenos$).tw.
12	DUCTUS ARTERIOSUS, PATENT/
13	(Paten$ adj2 ductus arteriosus).tw.
14	MITRAL VALVE PROLAPSE/
15	(mitral valve? adj2 (prolapse? or floppy)).tw.
16	click murmur syndrome?.tw.
17	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
18	HEART SEPTAL DEFECTS, ATRIAL/
19	HEART SEPTAL DEFECTS, VENTRICULAR/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
21	(persist$ adj2 ostium primum).tw.
22	anomal$ pulmonary venous drain$.tw.
23	exp CARDIAC COMPLEXES, PREMATURE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
25	((Atrial or ventricular) adj2 extrasystole?).tw.
26	"TETRALOGY OF FALLOT"/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
28	exp ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).tw.
30	(Atrial adj2 (Fibrillation or Flutter)).tw.
31	(Bradycardia? or bradyarrhythmia?).tw.
32	Brugada Syndrome.tw.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
34	Heart Block.tw.
35	Long QT Syndrome.tw.
36	Parasystole.tw.
37	Pre-Excitation Syndrome?.tw.
38	Tachycardia?.tw.
39	(Ventricular adj2 (Fibrillation or Flutter)).tw.
40	exp CARDIOMYOPATHY, HYPERTROPHIC/
41	(Hypertrophic adj2 cardiomyopath$).tw.
42	AORTIC VALVE INSUFFICIENCY/
43	MITRAL VALVE INSUFFICIENCY/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.

#	Searches
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).tw.
48	exp AORTIC DISEASES/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
50	Aortitis.tw.
51	Loeys-Dietz Syndrome.tw.
52	Leriche Syndrome.tw.
53	AORTIC COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).tw.
55	HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
57	"TRANSPOSITION OF GREAT VESSELS"/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).tw.
61	exp CORONARY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
63	*HEART DEFECTS, CONGENITAL/
64	Cyanotic heart disease?.tw.
65	(complex$ adj10 congenital$ heart disease?).tw.
66	*PULMONARY HYPERTENSION/
67	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
68	exp VENTRICULAR DYSFUNCTION/
69	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
70	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
71	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
72	(previous$ adj5 cardiomyopath$).tw.
73	MITRAL VALVE STENOSIS/
74	(mitral adj2 stenos?s).tw.
75	exp AORTIC VALVE STENOSIS/
76	(aort$ adj2 stenos?s).tw.
77	AORTIC COARCTATION/
78	(Coarctation? adj3 aort$).tw.
79	or/10-78
80	9 and 79
81	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
82	or/80-81
83	(systemic$ adj3 analgesi$).tw.
84	exp ANALGESICS, OPIOID/

#	Searches
85	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
86	remifentanil.mp.
87	KETAMINE/
88	ketamine.mp.
89	(inhal$ adj3 analgesi$).tw.
90	exp NITROUS OXIDE/
91	(nitrous oxide or N2O).mp.
92	laughing gas.tw.
93	(gas adj2 air).tw.
94	Entonox.mp.
95	Nitronox.mp.
96	sevoflurane.mp.
97	desflurane.mp.
98	((Non-pharma$ or Nonpharma$) adj3 analgesi$).tw.
99	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/
100	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).tw.
101	TENS.tw.
102	electroanalgesi$.tw.
103	electroacupuncture.tw.
104	ACUPUNCTURE THERAPY/
105	ACUPUNCTURE ANALGESIA/
106	acupuncture.tw.
107	water papule?.tw.
108	BATHS/
109	birthing pool?.tw.
110	MASSAGE/
111	massag$.tw.
112	reflexolog$.tw.
113	AROMATHERAPY/
114	aromatherap$.tw.
115	hypnobirth$.tw.
116	HOMEOPATHY/
117	hom?eopath$.tw.
118	or/83-117
119	ANALGESIA, EPIDURAL/
120	INJECTIONS, EPIDURAL/

#	Searches
121	((Spinal$ or spinous$) adj5 analges$).tw.
122	epidural$.tw.
123	CSE.tw.
124	((central$ or regional$) adj5 neuraxial$ adj5 block$).tw.
125	(neuraxial$ adj5 analges$).tw.
126	or/119-125
127	RISK/
128	RISK ASSESSMENT/
129	risk?.tw.
130	"DRUG-RELATED SIDE EFFECTS AND ADVERSE REACTIONS"/
131	(adverse$ adj3 (effect? or event? or reaction?)).tw.
132	harm$.tw.
133	THERAPEUTIC USES/
134	(therapeutic$ adj3 (effect? or use?)).tw.
135	benefi$.tw.
136	or/127-135
137	exp ANALGESICS, OPIOID/ae [Adverse Effects]
138	exp ANALGESICS, OPIOID/tu [Therapeutic Use]
139	KETAMINE/ae [Adverse Effects]
140	KETAMINE/tu [Therapeutic Use]
141	NITROUS OXIDE/ae [Adverse Effects]
142	NITROUS OXIDE/tu [Therapeutic Use]
143	exp TRANSCUTANEOUS ELECTRIC NERVE STIMULATION/ae [Adverse Effects]
144	ACUPUNCTURE THERAPY/ae [Adverse Effects]
145	ACUPUNCTURE ANALGESIA/ae [Adverse Effects]
146	BATHS/ae [Adverse Effects]
147	MASSAGE/ae [Adverse Effects]
148	MASSAGE/tu [Therapeutic Use]
149	AROMATHERAPY/ae [Adverse Effects]
150	HOMEOPATHY/ae [Adverse Effects]
151	ANALGESIA, EPIDURAL/ae [Adverse Effects]
152	INJECTIONS, EPIDURAL/ae [Adverse Effects]
153	or/137-152
154	PAIN MANAGEMENT/
155	ANALGESIA, PATIENT-CONTROLLED/mt [Methods]
156	ANALGESIA, OBSTETRICAL/mt [Methods]
157	or/154-156
158	82 and 118 and 126
159	82 and (118 or 126) and 136
160	82 and 153

#	Searches
161	82 and 157
162	or/158-161

Database: Embase

#	Searches
1	*PREGNANCY/
2	*PERINATAL PERIOD/
3	exp *BIRTH/
4	exp *LABOR/
5	*PREMATURE LABOR/
6	*INTRAPARTUM CARE/
7	pregnan$.ti,ab.
8	(labo?r or childbirth or partu$ or intra?part$ or peri?part$).ti,ab.
9	((during or giving or give) adj3 birth?).ti,ab.
10	or/1-9
11	PULMONARY VALVE STENOSIS/
12	(pulmonary adj2 stenos$).ti,ab.
13	PATENT DUCTUS ARTERIOSUS/
14	(Paten$ adj2 ductus arteriosus).ti,ab.
15	MITRAL VALVE PROLAPSE/
16	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
17	click murmur syndrome?.ti,ab.
18	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
19	HEART SEPTUM DEFECT/
20	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
21	(persist$ adj2 ostium primum).ti,ab.
22	anomal$ pulmonary venous drain$.ti,ab.
23	EXTRASYSTOLE/
24	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
25	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
26	FALLOT TETRALOGY/su [Surgery]
27	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
28	exp *HEART ARRHYTHMIA/
29	(arrhythmia? or dysrhythmia?).ti,ab.
30	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
31	(Bradycardia? or bradyarrhythmia?).ti,ab.
32	Brugada Syndrome.ti,ab.
33	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
34	Heart Block.ti,ab.
35	Long QT Syndrome.ti,ab.

#	Searches
36	Parasystole.ti,ab.
37	Pre-Excitation Syndrome?.ti,ab.
38	Tachycardia?.ti,ab.
39	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
40	exp *HYPERTROPHIC CARDIOMYOPATHY/
41	(Hypertrophic adj2 cardiomyopath$).ti,ab.
42	AORTIC VALVE REGURGITATION/
43	MITRAL VALVE REGURGITATION/
44	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
45	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
46	MARFAN SYNDROME/
47	(Marfan$ adj2 syndrome).ti,ab.
48	exp *AORTA DISEASE/
49	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
50	Aortitis.ti,ab.
51	Loeys-Dietz Syndrome.ti,ab.
52	Leriche Syndrome.ti,ab.
53	AORTA COARCTATION/su [Surgery]
54	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
55	exp *HEART VALVE PROSTHESIS/
56	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
57	GREAT VESSELS TRANSPOSITION/
58	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
59	FONTAN PROCEDURE/
60	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
61	exp *CORONARY ARTERY DISEASE/
62	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
63	CYANOTIC HEART DISEASE/
64	Cyanotic heart disease?.ti,ab.
65	*CONGENITAL HEART DISEASE/
66	(complex$ adj10 congenital$ heart disease?).ti,ab.
67	*PULMONARY HYPERTENSION/
68	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
69	exp *HEART VENTRICLE FAILURE/
70	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
71	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
72	exp CARDIOMYOPATHY/ and TIME FACTOR/
73	(previous$ adj5 cardiomyopath$).ti,ab.
74	MITRAL VALVE STENOSIS/
75	(mitral adj2 stenos?s).ti,ab.

#	Searches
76	AORTA VALVE STENOSIS/
77	(aort$ adj2 stenos?s).ti,ab.
78	AORTA COARCTATION/
79	(Coarctation? adj3 aort$).ti,ab.
80	or/11-79
81	10 and 80
82	(systemic$ adj3 analgesi$).ti,ab.
83	exp NARCOTIC ANALGESIC AGENT/
84	(Opioid? or Alfentanil or Alphaprodine or Buprenorphine or Butorphanol or Codeine or Dextromoramide or Dextropropoxyphene or Dihydromorphine or Diphenoxylate or Enkephalin or Ethylketocyclazocine or Ethylmorphine or Etorphine or Fentanyl or Heroin or Hydrocodone or Hydromorphone or Levorphanol or Meperidine or Meptazinol or Methadone or Methadyl Acetate or Morphine or Nalbuphine or Opiate Alkaloid? or Opium or Oxycodone or Oxymorphone or Pentazocine or Phenazocine or Phenoperidine or Pirinitramide or Promedol or Sufentanil or Tilidine or Tramadol or pethidine or diamorphine).mp.
85	remifentanil.mp.
86	KETAMINE/
87	ketamine.mp.
88	(inhal$ adj3 analgesi$).ti,ab.
89	NITROUS OXIDE/
90	NITROUS OXIDE PLUS OXYGEN/
91	SEVOFLURANE/
92	DESFLURANE/
93	(nitrous oxide or N2O).mp.
94	laughing gas.ti,ab.
95	(gas adj2 air).ti,ab.
96	Entonox.mp.
97	Nitronox.mp.
98	sevoflurane.mp.
99	desflurane.mp.
100	((Non-pharma$ or Nonpharma$) adj3 analgesi$).ti,ab.
101	TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION/
102	((transcutaneous or percutaneous) adj3 (electric$ or nerve?) adj3 stimulat$).ti,ab.
103	TENS.ti,ab.
104	electroanalgesi$.ti,ab.
105	electroacupuncture.ti,ab.
106	ACUPUNCTURE/
107	ACUPUNCTURE ANALGESIA/
108	acupuncture.ti,ab.
109	water papule?.ti,ab.
110	BATH/
111	birthing pool?.ti,ab.

#	Searches
112	REFLEXOLOGY/
113	massag$.ti,ab.
114	reflexolog$.ti,ab.
115	AROMATHERAPY/
116	aromatherap$.ti,ab.
117	hypnobirth$.ti,ab.
118	HOMEOPATHY/
119	hom?eopath$.ti,ab.
120	or/82-119
121	EPIDURAL ANALGESIA/
122	EPIDURAL DRUG ADMINISTRATION/
123	((Spinal$ or spinous$) adj5 analges$).ti,ab.
124	epidural$.ti,ab.
125	CSE.ti,ab.
126	((central$ or regional$) adj5 neuraxial$ adj5 block$).ti,ab.
127	(neuraxial$ adj5 analges$).ti,ab.
128	or/121-127
129	*RISK/
130	*RISK ASSESSMENT/
131	risk?.ti,ab.
132	*ADVERSE DRUG REACTION/
133	*SIDE EFFECT/
134	(adverse$ adj3 (effect? or event? or reaction?)).ti,ab.
135	harm$.ti,ab.
136	*THERAPY/
137	(therapeutic$ adj3 (effect? or use?)).ti,ab.
138	benefi$.ti,ab.
139	or/129-138
140	exp NARCOTIC ANALGESIC AGENT/ae [Adverse Drug Reaction]
141	KETAMINE/ae [Adverse Drug Reaction]
142	NITROUS OXIDE/ae [Adverse Drug Reaction]
143	NITROUS OXIDE PLUS OXYGEN/ae [Adverse Drug Reaction]
144	SEVOFLURANE/ae [Adverse Drug Reaction]
145	DESFLURANE/ae [Adverse Drug Reaction]
146	ACUPUNCTURE/ae [Adverse Drug Reaction]
147	ACUPUNCTURE/th [Therapy]
148	ACUPUNCTURE ANALGESIA/ae [Adverse Drug Reaction]
149	BATH/ae [Adverse Drug Reaction]
150	BATH/th [Therapy]
151	AROMATHERAPY/ae [Adverse Drug Reaction]

#	Searches
152	HOMEOPATHY/ae [Adverse Drug Reaction]
153	EPIDURAL DRUG ADMINISTRATION/ae [Adverse Drug Reaction]
154	or/140-153
155	OBSTETRIC ANALGESIA/
156	81 and 120 and 128
157	81 and (120 or 128) and 139
158	81 and 154
159	81 and 155
160	or/156-159
161	limit 160 to english language
162	letter.pt. or LETTER/
163	note.pt.
164	editorial.pt.
165	CASE REPORT/ or CASE STUDY/
166	(letter or comment*).ti.
167	or/162-166
168	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
169	167 not 168
170	ANIMAL/ not HUMAN/
171	NONHUMAN/
172	exp ANIMAL EXPERIMENT/
173	exp EXPERIMENTAL ANIMAL/
174	ANIMAL MODEL/
175	exp RODENT/
176	(rat or rats or mouse or mice).ti.
177	or/169-176
178	161 not 177

Intrapartum care for women with cardiac disease – management of the third stage of labour

Database: Medline; Medline EPub Ahead of Print; and Medline In-Process & Other Non-Indexed Citations

#	Searches
1	PULMONARY VALVE STENOSIS/
2	(pulmonary adj2 stenos$).ti,ab.
3	DUCTUS ARTERIOSUS, PATENT/
4	(Paten$ adj2 ductus arteriosus).ti,ab.
5	MITRAL VALVE PROLAPSE/
6	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
7	click murmur syndrome?.ti,ab.

#	Searches
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
9	HEART SEPTAL DEFECTS, ATRIAL/
10	HEART SEPTAL DEFECTS, VENTRICULAR/
11	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
12	(persist$ adj2 ostium primum).ti,ab.
13	anomal$ pulmonary venous drain$.ti,ab.
14	exp CARDIAC COMPLEXES, PREMATURE/
15	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
16	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
17	"TETRALOGY OF FALLOT"/su [Surgery]
18	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
19	exp *ARRHYTHMIAS, CARDIAC/
20	(arrhythmia? or dysrhythmia?).ti,ab.
21	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
22	(Bradycardia? or bradyarrhythmia?).ti,ab.
23	Brugada Syndrome.ti,ab.
24	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
25	Heart Block.ti,ab.
26	Long QT Syndrome.ti,ab.
27	Parasystole.ti,ab.
28	Pre-Excitation Syndrome?.ti,ab.
29	Tachycardia?.ti,ab.
30	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
31	exp CARDIOMYOPATHY, HYPERTROPHIC/
32	(Hypertrophic adj2 cardiomyopath$).ti,ab.
33	AORTIC VALVE INSUFFICIENCY/
34	MITRAL VALVE INSUFFICIENCY/
35	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
36	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
37	MARFAN SYNDROME/
38	(Marfan$ adj2 syndrome).ti,ab.
39	exp AORTIC DISEASES/
40	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
41	Aortitis.ti,ab.
42	Loeys-Dietz Syndrome.ti,ab.
43	Leriche Syndrome.ti,ab.
44	AORTIC COARCTATION/su [Surgery]
45	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
46	HEART VALVE PROSTHESIS/
47	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.

#	Searches
48	"TRANSPOSITION OF GREAT VESSELS"/
49	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
50	FONTAN PROCEDURE/
51	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
52	exp CORONARY DISEASE/
53	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
54	*HEART DEFECTS, CONGENITAL/
55	Cyanotic heart disease?.ti,ab.
56	(complex$ adj10 congenital$ heart disease?).ti,ab.
57	*PULMONARY HYPERTENSION/
58	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
59	exp VENTRICULAR DYSFUNCTION/
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
62	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
63	(previous$ adj5 cardiomyopath$).ti,ab.
64	MITRAL VALVE STENOSIS/
65	(mitral adj2 stenos?s).ti,ab.
66	exp AORTIC VALVE STENOSIS/
67	(aort$ adj2 stenos?s).ti,ab.
68	AORTIC COARCTATION/
69	(Coarctation? adj3 aort$).ti,ab.
70	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
71	or/1-70
72	LABOR STAGE, THIRD/
73	((third or 3rd) adj5 stage? adj10 labo?r$).ti,ab.
74	(involution$ adj3 stage?).ti,ab.
75	or/72-74
76	((placenta? or membrane?) adj3 (expul$ or expel$)).ti,ab.
77	afterbirth?.ti,ab.
78	PLACENTA, RETAINED/
79	(placenta? adj3 retain$).ti,ab.
80	PLACENTA ACCRETA/
81	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).ti,ab.
82	or/76-81
83	POSTPARTUM HEMORRHAGE/
84	((Postpartum? or Post-partum?) adj3 h?emorrhag$).ti,ab.
85	or/83-84
86	UTERINE CONTRACTION/
87	((uterus or uterin$ or myometri$) adj3 contract$).ti,ab.

#	Searches
88	or/86-87
89	(activ$ adj3 manag$).ti,ab.
90	exp OXYTOCICS/
91	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
92	exp ANTIFIBRINOLYTIC AGENTS/
93	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
94	BREAST FEEDING/
95	(breastfeed$ or breastfed or breast feed$ or breast fed).ti,ab.
96	UMBILICAL CORD/
97	((Clamp$ or cut$ or sever$) adj3 cord?).ti,ab.
98	(cord? adj3 traction).ti,ab.
99	or/89-98
100	71 and 75
101	71 and (82 or 85 or 88) and 99
102	or/100-101
103	limit 102 to english language
104	LETTER/
105	EDITORIAL/
106	NEWS/
107	exp HISTORICAL ARTICLE/
108	ANECDOTES AS TOPIC/
109	COMMENT/
110	CASE REPORT/
111	(letter or comment*).ti.
112	or/104-111
113	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
114	112 not 113
115	ANIMALS/ not HUMANS/
116	exp ANIMALS, LABORATORY/
117	exp ANIMAL EXPERIMENTATION/
118	exp MODELS, ANIMAL/
119	exp RODENTIA/
120	(rat or rats or mouse or mice).ti.
121	or/114-120
122	103 not 121

Database: Cochrane Central Register of Controlled Trials

#	Searches
1	PULMONARY VALVE STENOSIS/
2	(pulmonary adj2 stenos$).ti,ab.
3	DUCTUS ARTERIOSUS, PATENT/
4	(Paten$ adj2 ductus arteriosus).ti,ab.
5	MITRAL VALVE PROLAPSE/
6	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
7	click murmur syndrome?.ti,ab,kw.
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
9	HEART SEPTAL DEFECTS, ATRIAL/
10	HEART SEPTAL DEFECTS, VENTRICULAR/
11	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
12	(persist$ adj2 ostium primum).ti,ab.
13	anomal$ pulmonary venous drain$.ti,ab,kw.
14	exp CARDIAC COMPLEXES, PREMATURE/
15	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
16	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
17	"TETRALOGY OF FALLOT"/su [Surgery]
18	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
19	exp *ARRHYTHMIAS, CARDIAC/
20	(arrhythmia? or dysrhythmia?).ti,ab,kw.
21	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
22	(Bradycardia? or bradyarrhythmia?).ti,ab,kw.
23	Brugada Syndrome.ti,ab,kw.
24	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
25	Heart Block.ti,ab,kw.
26	Long QT Syndrome.ti,ab,kw.
27	Parasystole.ti,ab,kw.
28	Pre-Excitation Syndrome?.ti,ab,kw.
29	Tachycardia?.ti,ab,kw.
30	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
31	exp CARDIOMYOPATHY, HYPERTROPHIC/
32	(Hypertrophic adj2 cardiomyopath$).ti,ab.
33	AORTIC VALVE INSUFFICIENCY/
34	MITRAL VALVE INSUFFICIENCY/
35	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
36	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
37	MARFAN SYNDROME/
38	(Marfan$ adj2 syndrome).ti,ab.
39	exp AORTIC DISEASES/

#	Searches
40	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
41	Aortitis.ti,ab,kw.
42	Loeys-Dietz Syndrome.ti,ab,kw.
43	Leriche Syndrome.ti,ab,kw.
44	AORTIC COARCTATION/su [Surgery]
45	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
46	HEART VALVE PROSTHESIS/
47	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
48	"TRANSPOSITION OF GREAT VESSELS"/
49	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
50	FONTAN PROCEDURE/
51	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
52	exp CORONARY DISEASE/
53	(Coronary adj2 (disease? or aneurysm? or arteriosclerosis or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
54	*HEART DEFECTS, CONGENITAL/
55	Cyanotic heart disease?.ti,ab,kw.
56	(complex$ adj10 congenital$ heart disease?).ti,ab.
57	*PULMONARY HYPERTENSION/
58	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
59	exp VENTRICULAR DYSFUNCTION/
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
62	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
63	(previous$ adj5 cardiomyopath$).ti,ab.
64	MITRAL VALVE STENOSIS/
65	(mitral adj2 stenos?s).ti,ab.
66	exp AORTIC VALVE STENOSIS/
67	(aort$ adj2 stenos?s).ti,ab.
68	AORTIC COARCTATION/
69	(Coarctation? adj3 aort$).ti,ab.
70	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
71	or/1-70
72	LABOR STAGE, THIRD/
73	((third or 3rd) adj5 stage? adj10 labo?r$).ti,ab.
74	(involution$ adj3 stage?).ti,ab.
75	or/72-74
76	((placenta? or membrane?) adj3 (expul$ or expel$)).ti,ab.
77	afterbirth?.ti,ab,kw.
78	PLACENTA, RETAINED/
79	(placenta? adj3 retain$).ti,ab.

#	Searches
80	PLACENTA ACCRETA/
81	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).ti,ab.
82	or/76-81
83	POSTPARTUM HEMORRHAGE/
84	((Postpartum? or Post-partum?) adj3 h?emorrhag$).ti,ab.
85	or/83-84
86	UTERINE CONTRACTION/
87	((uterus or uterin$ or myometri$) adj3 contract$).ti,ab.
88	or/86-87
89	(activ$ adj3 manag$).ti,ab.
90	exp OXYTOCICS/
91	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
92	exp ANTIFIBRINOLYTIC AGENTS/
93	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
94	BREAST FEEDING/
95	(breastfeed$ or breastfed or breast feed$ or breast fed).ti,ab,kw.
96	UMBILICAL CORD/
97	((Clamp$ or cut$ or sever$) adj3 cord?).ti,ab.
98	(cord? adj3 traction).ti,ab.
99	or/89-98
100	71 and 75
101	71 and (82 or 85 or 88) and 99
102	or/100-101

Database: Cochrane Database of Systematic Reviews

#	Searches
1	PULMONARY VALVE STENOSIS.kw.
2	(pulmonary adj2 stenos$).ti,ab.
3	DUCTUS ARTERIOSUS, PATENT.kw.
4	(Paten$ adj2 ductus arteriosus).ti,ab.
5	MITRAL VALVE PROLAPSE.kw.
6	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
7	click murmur syndrome?.ti,ab.
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
9	HEART SEPTAL DEFECTS, ATRIAL.kw.
10	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
11	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
12	(persist$ adj2 ostium primum).ti,ab.

#	Searches
13	anomal$ pulmonary venous drain$.ti,ab.
14	CARDIAC COMPLEXES, PREMATURE.kw.
15	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
16	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
17	"TETRALOGY OF FALLOT".kw.
18	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
19	ARRHYTHMIAS, CARDIAC.kw.
20	(arrhythmia? or dysrhythmia?).ti,ab.
21	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
22	(Bradycardia? or bradyarrhythmia?).ti,ab.
23	Brugada Syndrome.ti,ab.
24	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
25	Heart Block.ti,ab.
26	Long QT Syndrome.ti,ab.
27	Parasystole.ti,ab.
28	Pre-Excitation Syndrome?.ti,ab.
29	Tachycardia?.ti,ab.
30	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
31	CARDIOMYOPATHY, HYPERTROPHIC.kw.
32	(Hypertrophic adj2 cardiomyopath$).ti,ab.
33	AORTIC VALVE INSUFFICIENCY.kw.
34	MITRAL VALVE INSUFFICIENCY.kw.
35	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
36	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
37	MARFAN SYNDROME.kw.
38	(Marfan$ adj2 syndrome).ti,ab.
39	AORTIC DISEASES.kw.
40	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
41	Aortitis.ti,ab.
42	Loeys-Dietz Syndrome.ti,ab.
43	Leriche Syndrome.ti,ab.
44	AORTIC COARCTATION.kw.
45	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
46	HEART VALVE PROSTHESIS.kw.
47	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
48	"TRANSPOSITION OF GREAT VESSELS".kw.
49	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
50	FONTAN PROCEDURE.kw.
51	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
52	CORONARY DISEASE.kw.

#	Searches
53	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
54	HEART DEFECTS, CONGENITAL.kw.
55	Cyanotic heart disease?.ti,ab.
56	(complex$ adj10 congenital$ heart disease?).ti,ab.
57	PULMONARY HYPERTENSION.kw.
58	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
59	VENTRICULAR DYSFUNCTION.kw.
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
62	(CARDIOMYOPATHIES and TIME FACTORS).kw.
63	(previous$ adj5 cardiomyopath$).ti,ab.
64	MITRAL VALVE STENOSIS.kw.
65	(mitral adj2 stenos?s).ti,ab.
66	AORTIC VALVE STENOSIS.kw.
67	(aort$ adj2 stenos?s).ti,ab.
68	AORTIC COARCTATION.kw.
69	(Coarctation? adj3 aort$).ti,ab.
70	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
71	or/1-70
72	LABOR STAGE, THIRD.kw.
73	((third or 3rd) adj5 stage? adj10 labo?r$).ti,ab.
74	(involution$ adj3 stage?).ti,ab.
75	or/72-74
76	((placenta? or membrane?) adj3 (expul$ or expel$)).ti,ab.
77	afterbirth?.ti,ab.
78	PLACENTA, RETAINED.kw.
79	(placenta? adj3 retain$).ti,ab.
80	PLACENTA ACCRETA.kw.
81	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).ti,ab.
82	or/76-81
83	POSTPARTUM HEMORRHAGE.kw.
84	((Postpartum? or Post-partum?) adj3 h?emorrhag$).ti,ab.
85	or/83-84
86	UTERINE CONTRACTION.kw.
87	((uterus or uterin$ or myometri$) adj3 contract$).ti,ab.
88	or/86-87
89	(activ$ adj3 manag$).ti,ab.
90	OXYTOCICS.kw.

#	Searches
91	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
92	ANTIFIBRINOLYTIC AGENTS.kw.
93	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
94	BREAST FEEDING.kw.
95	(breastfeed$ or breastfed or breast feed$ or breast fed).ti,ab.
96	UMBILICAL CORD.kw.
97	((Clamp$ or cut$ or sever$) adj3 cord?).ti,ab.
98	(cord? adj3 traction).ti,ab.
99	or/89-98
100	71 and 75
101	71 and (82 or 85 or 88) and 99
102	or/100-101

Database: Database of Abstracts of Reviews of Effects

#	Searches
1	PULMONARY VALVE STENOSIS.kw.
2	(pulmonary adj2 stenos$).tw,tx.
3	DUCTUS ARTERIOSUS, PATENT.kw.
4	(Paten$ adj2 ductus arteriosus).tw,tx.
5	MITRAL VALVE PROLAPSE.kw.
6	(mitral valve? adj2 (prolapse? or floppy)).tw,tx.
7	click murmur syndrome?.tw,tx.
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw,tx.
9	HEART SEPTAL DEFECTS, ATRIAL.kw.
10	HEART SEPTAL DEFECTS, VENTRICULAR.kw.
11	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw,tx.
12	(persist$ adj2 ostium primum).tw,tx.
13	anomal$ pulmonary venous drain$.tw,tx.
14	CARDIAC COMPLEXES, PREMATURE.kw.
15	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw,tx.
16	((Atrial or ventricular) adj2 extrasystole?).tw,tx.
17	"TETRALOGY OF FALLOT".kw.
18	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw,tx.
19	ARRHYTHMIAS, CARDIAC.kw.
20	(arrhythmia? or dysrhythmia?).tw,tx.
21	(Atrial adj2 (Fibrillation or Flutter)).tw,tx.
22	(Bradycardia? or bradyarrhythmia?).tw,tx.
23	Brugada Syndrome.tw,tx.

#	Searches
24	(premature adj2 (atrial or ventricular) adj2 contraction?).tw,tx.
25	Heart Block.tw,tx.
26	Long QT Syndrome.tw,tx.
27	Parasystole.tw,tx.
28	Pre-Excitation Syndrome?.tw,tx.
29	Tachycardia?.tw,tx.
30	(Ventricular adj2 (Fibrillation or Flutter)).tw,tx.
31	CARDIOMYOPATHY, HYPERTROPHIC.kw.
32	(Hypertrophic adj2 cardiomyopath$).tw,tx.
33	AORTIC VALVE INSUFFICIENCY.kw.
34	MITRAL VALVE INSUFFICIENCY.kw.
35	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw,tx.
36	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw,tx.
37	MARFAN SYNDROME.kw.
38	(Marfan$ adj2 syndrome).tw,tx.
39	AORTIC DISEASES.kw.
40	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw,tx.
41	Aortitis.tw,tx.
42	Loeys-Dietz Syndrome.tw,tx.
43	Leriche Syndrome.tw,tx.
44	AORTIC COARCTATION.kw.
45	(Coarctation? adj10 (repair$ or surgery)).tw,tx.
46	HEART VALVE PROSTHESIS.kw.
47	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw,tx.
48	"TRANSPOSITION OF GREAT VESSELS".kw.
49	(Transpos$ adj2 great adj2 (vessels or arteries)).tw,tx.
50	FONTAN PROCEDURE.kw.
51	(Fontan$ adj2 (circulat$ or procedure?)).tw,tx.
52	CORONARY DISEASE.kw.
53	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw,tx.
54	HEART DEFECTS, CONGENITAL.kw.
55	Cyanotic heart disease?.tw,tx.
56	(complex$ adj10 congenital$ heart disease?).tw,tx.
57	PULMONARY HYPERTENSION.kw.
58	(Pulmonary adj2 arter$ adj2 hypertens$).tw,tx.
59	VENTRICULAR DYSFUNCTION.kw.
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw,tx.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw,tx.
62	(CARDIOMYOPATHIES and TIME FACTORS).kw.
63	(previous$ adj5 cardiomyopath$).tw,tx.

#	Searches
64	MITRAL VALVE STENOSIS.kw.
65	(mitral adj2 stenos?s).tw,tx.
66	AORTIC VALVE STENOSIS.kw.
67	(aort$ adj2 stenos?s).tw,tx.
68	AORTIC COARCTATION.kw.
69	(Coarctation? adj3 aort$).tw,tx.
70	PREGNANCY COMPLICATIONS, CARDIOVASCULAR.kw.
71	or/1-70
72	LABOR STAGE, THIRD.kw.
73	((third or 3rd) adj5 stage? adj10 labo?r$).tw,tx.
74	(involution$ adj3 stage?).tw,tx.
75	or/72-74
76	((placenta? or membrane?) adj3 (expul$ or expel$)).tw,tx.
77	afterbirth?.tw,tx.
78	PLACENTA, RETAINED.kw.
79	(placenta? adj3 retain$).tw,tx.
80	PLACENTA ACCRETA.kw.
81	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).tw,tx.
82	or/76-81
83	POSTPARTUM HEMORRHAGE.kw.
84	((Postpartum? or Post-partum?) adj3 h?emorrhag$).tw,tx.
85	or/83-84
86	UTERINE CONTRACTION.kw.
87	((uterus or uterin$ or myometri$) adj3 contract$).tw,tx.
88	or/86-87
89	(activ$ adj3 manag$).tw,tx.
90	OXYTOCICS.kw.
91	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
92	ANTIFIBRINOLYTIC AGENTS.kw.
93	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
94	BREAST FEEDING.kw.
95	(breastfeed$ or breastfed or breast feed$ or breast fed).tw,tx.
96	UMBILICAL CORD.kw.
97	((Clamp$ or cut$ or sever$) adj3 cord?).tw,tx.
98	(cord? adj3 traction).tw,tx.
99	or/89-98
100	71 and 75
101	71 and (82 or 85 or 88) and 99

#	Searches
102	or/100-101

Database: Health Technology Assessment

#	Searches
1	PULMONARY VALVE STENOSIS/
2	(pulmonary adj2 stenos$).tw.
3	DUCTUS ARTERIOSUS, PATENT/
4	(Paten$ adj2 ductus arteriosus).tw.
5	MITRAL VALVE PROLAPSE/
6	(mitral valve? adj2 (prolapse? or floppy)).tw.
7	click murmur syndrome?.tw.
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).tw.
9	HEART SEPTAL DEFECTS, ATRIAL/
10	HEART SEPTAL DEFECTS, VENTRICULAR/
11	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).tw.
12	(persist$ adj2 ostium primum).tw.
13	anomal$ pulmonary venous drain$.tw.
14	exp CARDIAC COMPLEXES, PREMATURE/
15	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).tw.
16	((Atrial or ventricular) adj2 extrasystole?).tw.
17	"TETRALOGY OF FALLOT"/su [Surgery]
18	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).tw.
19	exp *ARRHYTHMIA/
20	(arrhythmia? or dysrhythmia?).tw.
21	(Atrial adj2 (Fibrillation or Flutter)).tw.
22	(Bradycardia? or bradyarrhythmia?).tw.
23	Brugada Syndrome.tw.
24	(premature adj2 (atrial or ventricular) adj2 contraction?).tw.
25	Heart Block.tw.
26	Long QT Syndrome.tw.
27	Parasystole.tw.
28	Pre-Excitation Syndrome?.tw.
29	Tachycardia?.tw.
30	(Ventricular adj2 (Fibrillation or Flutter)).tw.
31	exp CARDIOMYOPATHY, HYPERTROPHIC/
32	(Hypertrophic adj2 cardiomyopath$).tw.
33	AORTIC VALVE INSUFFICIENCY/
34	MITRAL VALVE INSUFFICIENCY/
35	((mitral or aort$) adj2 (regurg$ or incompeten$)).tw.
36	((mitral or aort$) adj2 valv$ adj2 insufficien$).tw.

#	Searches
37	MARFAN SYNDROME/
38	(Marfan$ adj2 syndrome).tw.
39	exp AORTIC DISEASES/
40	(aort$ adj2 (disease? or aneurysm? or ruptur$)).tw.
41	Aortitis.tw.
42	Loeys-Dietz Syndrome.tw.
43	Leriche Syndrome.tw.
44	AORTIC COARCTATION/su [Surgery]
45	(Coarctation? adj10 (repair$ or surgery)).tw.
46	HEART VALVE PROSTHESIS/
47	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).tw.
48	"TRANSPOSITION OF GREAT VESSELS"/
49	(Transpos$ adj2 great adj2 (vessels or arteries)).tw.
50	FONTAN PROCEDURE/
51	(Fontan$ adj2 (circulat$ or procedure?)).tw.
52	exp CORONARY DISEASE/
53	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).tw.
54	*HEART DEFECTS, CONGENITAL/
55	Cyanotic heart disease?.tw.
56	(complex$ adj10 congenital$ heart disease?).tw.
57	*PULMONARY HYPERTENSION/
58	(Pulmonary adj2 arter$ adj2 hypertens$).tw.
59	exp VENTRICULAR DYSFUNCTION/
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).tw.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).tw.
62	exp *CARDIOMYOPATHIES/ and TIME FACTORS/
63	(previous$ adj5 cardiomyopath$).tw.
64	MITRAL VALVE STENOSIS/
65	(mitral adj2 stenos?s).tw.
66	exp AORTIC VALVE STENOSIS/
67	(aort$ adj2 stenos?s).tw.
68	AORTIC COARCTATION/
69	(Coarctation? adj3 aort$).tw.
70	PREGNANCY COMPLICATIONS, CARDIOVASCULAR/
71	or/1-70
72	LABOR STAGE, THIRD/
73	((third or 3rd) adj5 stage? adj10 labo?r$).tw.
74	(involution$ adj3 stage?).tw.
75	or/72-74
76	((placenta? or membrane?) adj3 (expul$ or expel$)).tw.

#	Searches
77	afterbirth?.tw.
78	PLACENTA, RETAINED/
79	(placenta? adj3 retain$).tw.
80	PLACENTA ACCRETA/
81	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).tw.
82	or/76-81
83	POSTPARTUM HEMORRHAGE/
84	((Postpartum? or Post-partum?) adj3 h?emorrhag$).tw.
85	or/83-84
86	UTERINE CONTRACTION/
87	((uterus or uterin$ or myometri$) adj3 contract$).tw.
88	or/86-87
89	(activ$ adj3 manag$).tw.
90	exp OXYTOCICS/
91	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
92	exp ANTIFIBRINOLYTIC AGENTS/
93	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
94	BREAST FEEDING/
95	(breastfeed$ or breastfed or breast feed$ or breast fed).tw.
96	UMBILICAL CORD/
97	((Clamp$ or cut$ or sever$) adj3 cord?).tw.
98	(cord? adj3 traction).tw.
99	or/89-98
100	71 and 75
101	71 and (82 or 85 or 88) and 99
102	or/100-101

Database: Embase

#	Searches
1	PULMONARY VALVE STENOSIS/
2	(pulmonary adj2 stenos$).ti,ab.
3	PATENT DUCTUS ARTERIOSUS/
4	(Paten$ adj2 ductus arteriosus).ti,ab.
5	MITRAL VALVE PROLAPSE/
6	(mitral valve? adj2 (prolapse? or floppy)).ti,ab.
7	click murmur syndrome?.ti,ab.
8	(Repair$ adj3 lesion? adj3 (heart? or cardiac)).ti,ab.
9	HEART SEPTUM DEFECT/

#	Searches
10	((atrial or ventricul$ or intraventricul$) adj2 septal adj2 defect$).ti,ab.
11	(persist$ adj2 ostium primum).ti,ab.
12	anomal$ pulmonary venous drain$.ti,ab.
13	EXTRASYSTOLE/
14	((Atrial or ventricular or supraventricular) adj2 (ectopic or premature) adj2 (beat? or complex$ or complice?)).ti,ab.
15	((Atrial or ventricular) adj2 extrasystole?).ti,ab.
16	FALLOT TETRALOGY/su [Surgery]
17	(tetralogy adj2 Fallot$ adj10 (repair$ or surgery)).ti,ab.
18	exp *HEART ARRHYTHMIA/
19	(arrhythmia? or dysrhythmia?).ti,ab.
20	(Atrial adj2 (Fibrillation or Flutter)).ti,ab.
21	(Bradycardia? or bradyarrhythmia?).ti,ab.
22	Brugada Syndrome.ti,ab.
23	(premature adj2 (atrial or ventricular) adj2 contraction?).ti,ab.
24	Heart Block.ti,ab.
25	Long QT Syndrome.ti,ab.
26	Parasystole.ti,ab.
27	Pre-Excitation Syndrome?.ti,ab.
28	Tachycardia?.ti,ab.
29	(Ventricular adj2 (Fibrillation or Flutter)).ti,ab.
30	exp *HYPERTROPHIC CARDIOMYOPATHY/
31	(Hypertrophic adj2 cardiomyopath$).ti,ab.
32	AORTIC VALVE REGURGITATION/
33	MITRAL VALVE REGURGITATION/
34	((mitral or aort$) adj2 (regurg$ or incompeten$)).ti,ab.
35	((mitral or aort$) adj2 valv$ adj2 insufficien$).ti,ab.
36	MARFAN SYNDROME/
37	(Marfan$ adj2 syndrome).ti,ab.
38	exp *AORTA DISEASE/
39	(aort$ adj2 (disease? or aneurysm? or ruptur$)).ti,ab.
40	Aortitis.ti,ab.
41	Loeys-Dietz Syndrome.ti,ab.
42	Leriche Syndrome.ti,ab.
43	AORTA COARCTATION/su [Surgery]
44	(Coarctation? adj10 (repair$ or surgery)).ti,ab.
45	exp *HEART VALVE PROSTHESIS/
46	((heart or cardiac) adj3 valve? adj5 (prosthe$ or mechanical or replace$)).ti,ab.
47	GREAT VESSELS TRANSPOSITION/
48	(Transpos$ adj2 great adj2 (vessels or arteries)).ti,ab.
49	FONTAN PROCEDURE/

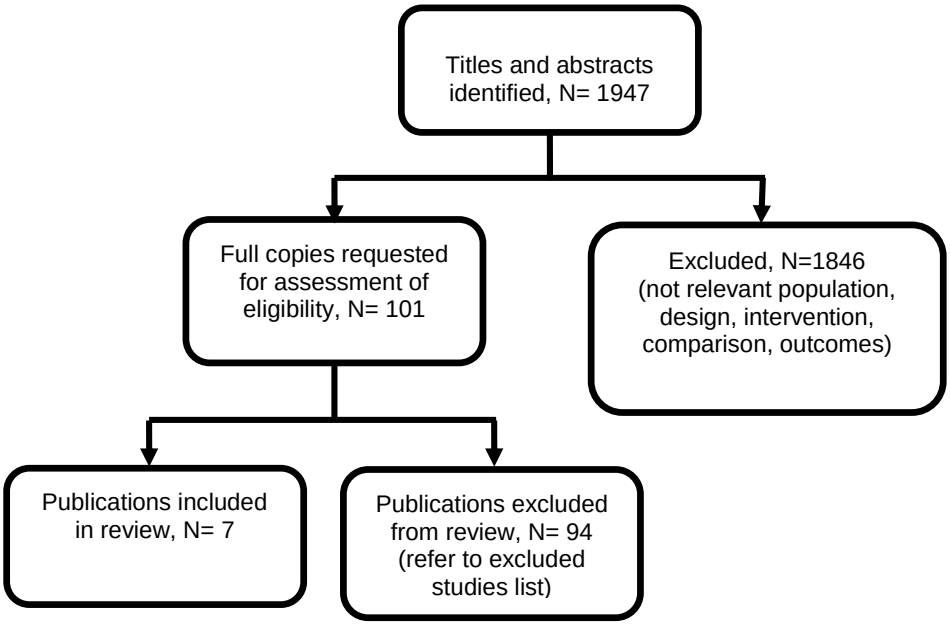
#	Searches
50	(Fontan$ adj2 (circulat$ or procedure?)).ti,ab.
51	exp *CORONARY ARTERY DISEASE/
52	(Coronary adj2 (disease? or aneurysm? or arterioscleros?s or occlusion? or stenos?s or restenos?s or thrombos?s or vasospasm?)).ti,ab.
53	CYANOTIC HEART DISEASE/
54	Cyanotic heart disease?.ti,ab.
55	*CONGENITAL HEART DISEASE/
56	(complex$ adj10 congenital$ heart disease?).ti,ab.
57	*PULMONARY HYPERTENSION/
58	(Pulmonary adj2 arter$ adj2 hypertens$).ti,ab.
59	exp *HEART VENTRICLE FAILURE/
60	((left or right) adj2 ventric$ adj2 (impair$ or systemic$ or dysfuncti$)).ti,ab.
61	(systemic$ adj2 ventric$ adj2 dysfuncti$).ti,ab.
62	exp CARDIOMYOPATHY/ and TIME FACTOR/
63	(previous$ adj5 cardiomyopath$).ti,ab.
64	MITRAL VALVE STENOSIS/
65	(mitral adj2 stenos?s).ti,ab.
66	AORTA VALVE STENOSIS/
67	(aort$ adj2 stenos?s).ti,ab.
68	AORTA COARCTATION/
69	(Coarctation? adj3 aort$).ti,ab.
70	or/1-69
71	LABOR STAGE 3/
72	((third or 3rd) adj5 stage? adj10 labo?r$).ti,ab.
73	(involution$ adj3 stage?).ti,ab.
74	or/71-73
75	((placenta? or membrane?) adj3 (expul$ or expel$)).ti,ab.
76	afterbirth?.ti,ab.
77	RETAINED PLACENTA/
78	(placenta? adj3 retain$).ti,ab.
79	PLACENTA ACCRETA/
80	(placenta? adj3 (accreta$ or increta$ or precreta$ or adherent)).ti,ab.
81	or/75-80
82	POSTPARTUM HEMORRHAGE/
83	((Postpartum? or Post-partum?) adj3 h?emorrhag$).ti,ab.
84	or/82-83
85	UTERUS CONTRACTION/
86	((uterus or uterin$ or myometri$) adj3 contract$).ti,ab.
87	or/85-86
88	(activ$ adj3 manag$).ti,ab.
89	exp UTEROTONIC AGENT/

#	Searches
90	(Uterotonic? or Oxytocic? or Carboprost or Dinoprost or Dinoprostone or Ergonovine or Ergotamine or Methylergonovine or Misoprostol or Oxytocin or Quipazine or Sparteine or Vasotocin or hemabate or syntometrine or syntocinon or ergometrine).mp.
91	exp ANTIFIBRINOLYTIC AGENT/
92	(antifibrinolytic? or anti-fibrinolytic? or Aminocaproic Acid or Tranexamic Acid or Vitamin K? or alpha-2-Antiplasmin).mp.
93	BREAST FEEDING/
94	(breastfeed$ or breastfed or breast feed$ or breast fed).ti,ab.
95	UMBILICAL CORD/
96	((Clamp$ or cut$ or sever$) adj3 cord?).ti,ab.
97	(cord? adj3 traction).ti,ab.
98	or/88-97
99	70 and 74
100	70 and (81 or 84 or 87) and 98
101	or/99-100
102	limit 101 to english language
103	letter.pt. or LETTER/
104	note.pt.
105	editorial.pt.
106	CASE REPORT/ or CASE STUDY/
107	(letter or comment*).ti.
108	or/103-107
109	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
110	108 not 109
111	ANIMAL/ not HUMAN/
112	NONHUMAN/
113	exp ANIMAL EXPERIMENT/
114	exp EXPERIMENTAL ANIMAL/
115	ANIMAL MODEL/
116	exp RODENT/
117	(rat or rats or mouse or mice).ti.
118	or/110-117
119	102 not 118

Appendix C – Clinical evidence study selection

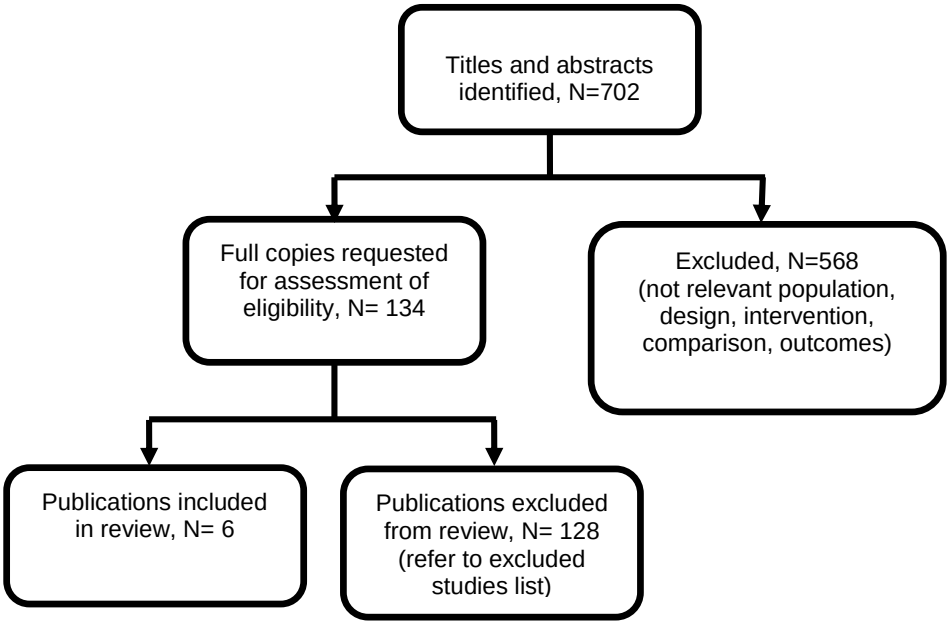
Intrapartum care for women with cardiac disease – stratification of risk

Figure 1. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – stratification of risk



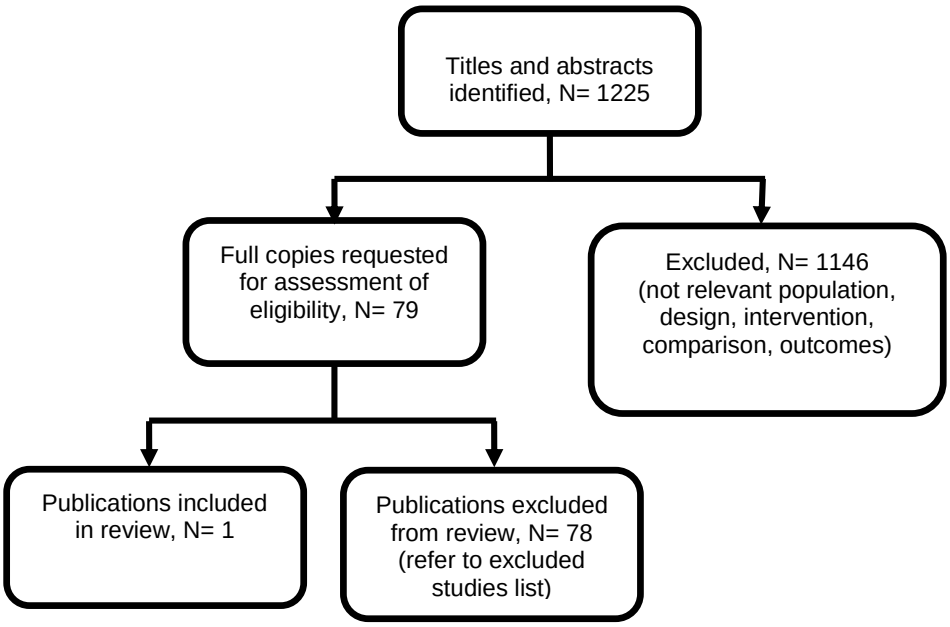
Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Figure 2. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease



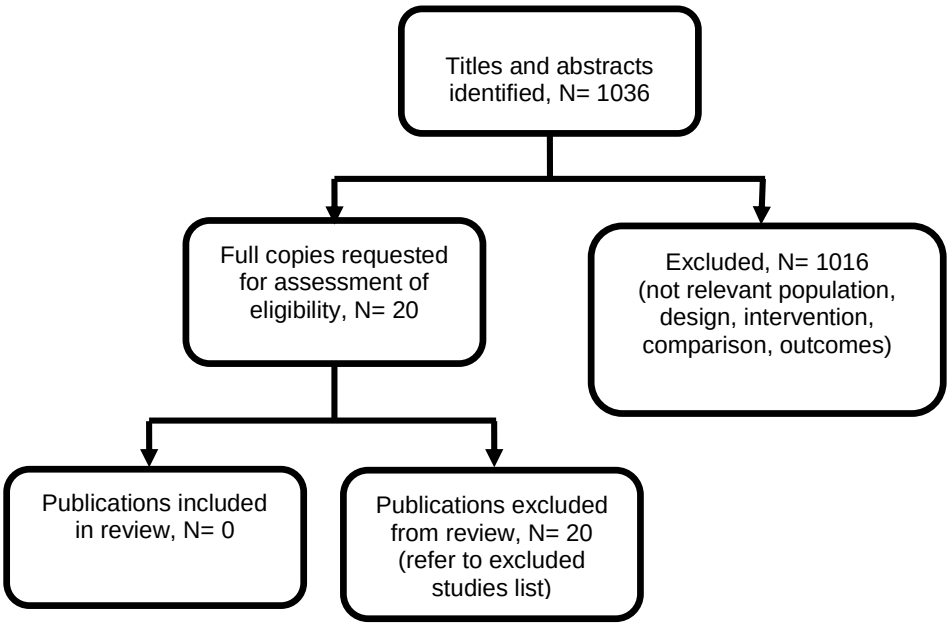
Intrapartum care for women with cardiac disease – mode of birth

Figure 3. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – mode of birth



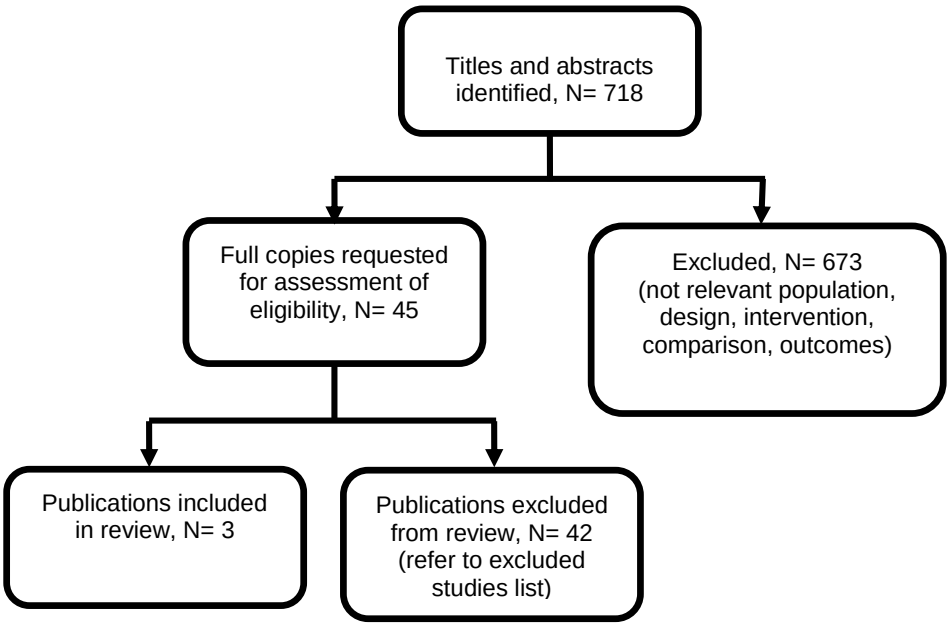
Intrapartum care for women with cardiac disease – fluid management

Figure 4. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – fluid management



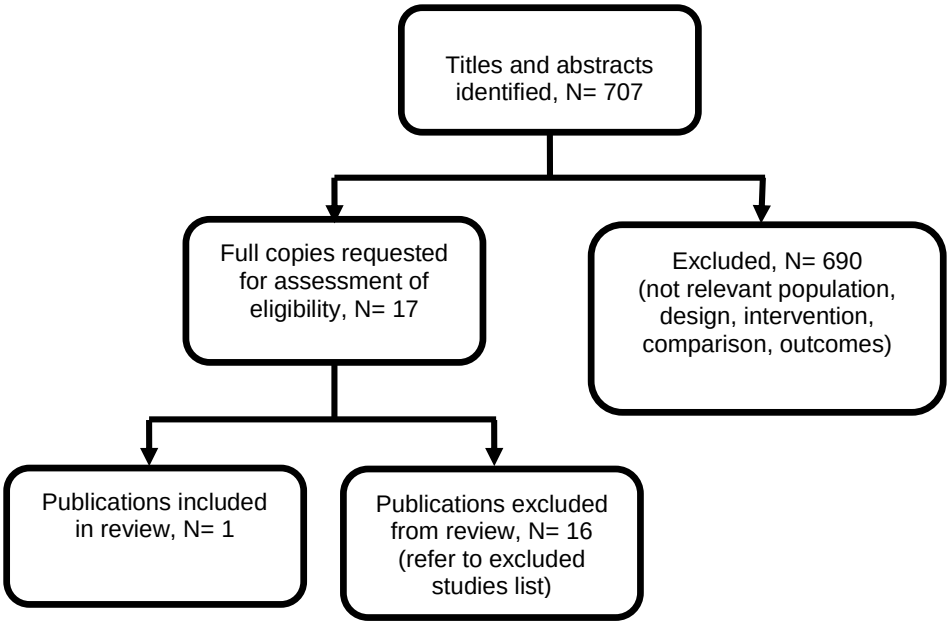
Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Figure 5. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy



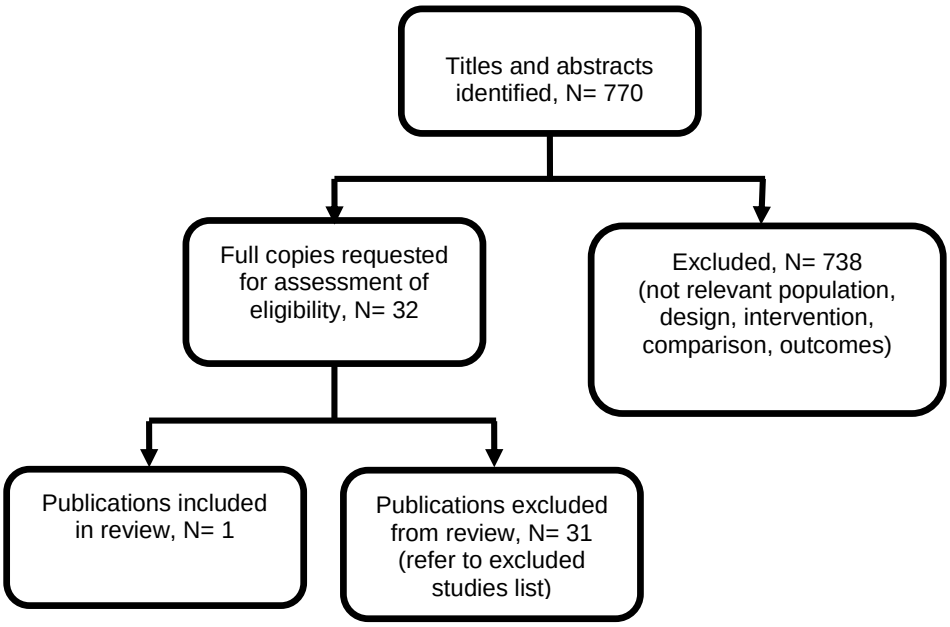
Intrapartum care for women with cardiac disease – management of cardiomyopathy

Figure 6. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – management of cardiomyopathy



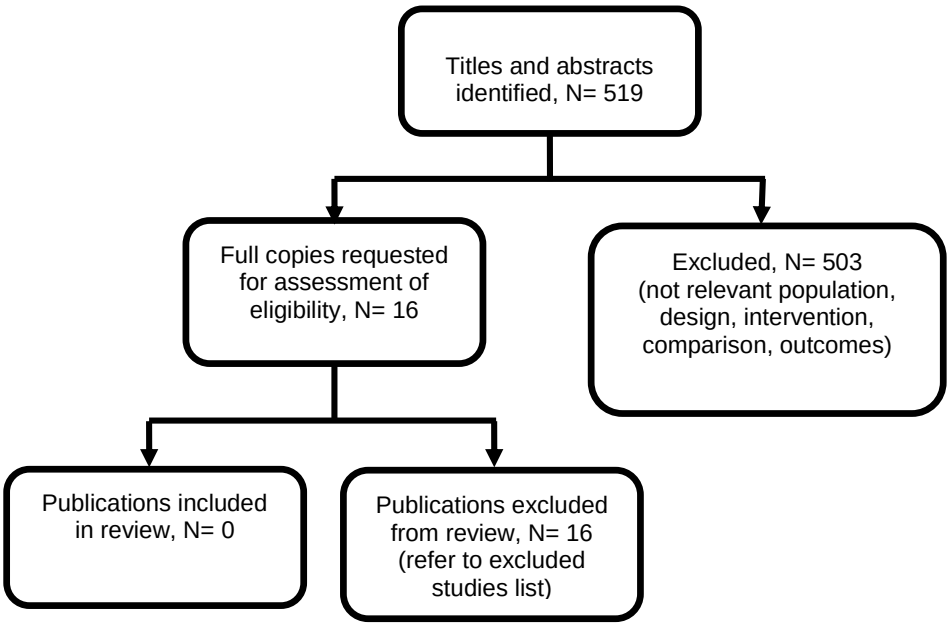
Intrapartum care for women with cardiac disease – anaesthesia

Figure 7. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – anaesthesia



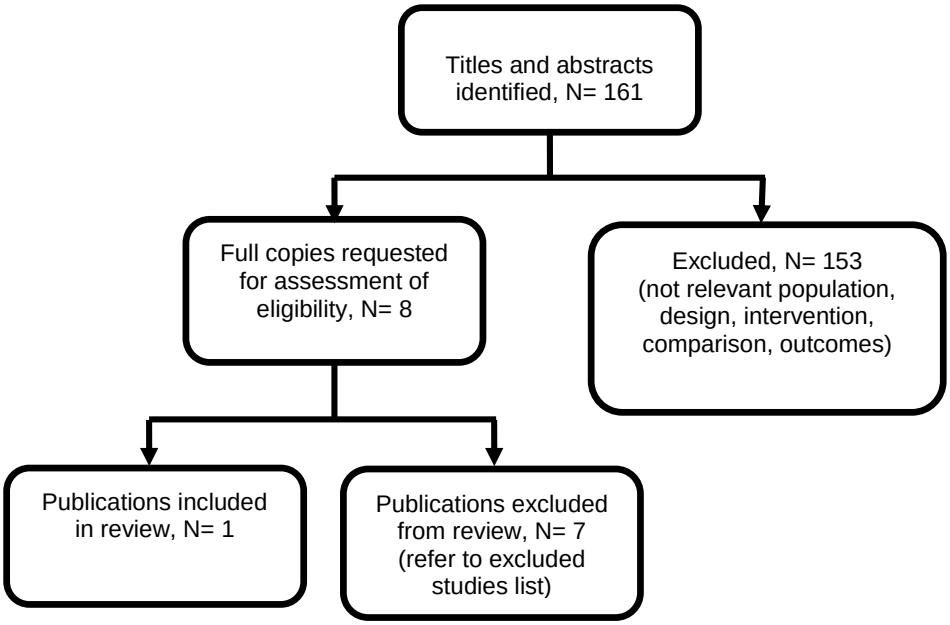
Intrapartum care for women with cardiac disease – analgesia

Figure 8. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – analgesia



Intrapartum care for women with cardiac disease – management of the third stage of labour

Figure 9. Flow diagram of clinical evidence study selection for Intrapartum care for women with cardiac disease – management of third stage of labour



Appendix D – Excluded studies

Intrapartum care for women with cardiac disease – stratification of risk

Clinical studies

Study	Reason for exclusion
Allyn, J., Guglielminotti, J., Omnes, S., Guezouli, L., Egan, M., Jondeau, G., Longrois, D., Montravers, P., Marfan's syndrome during pregnancy: anesthetic management of delivery in 16 consecutive patients, Anesthesia & Analgesia, 116, 392-8, 2013	Study design; non-comparative observational study
Authors/Task Force, members, Elliott, P. M., Anastasakis, A., Borger, M. A., Borggrefe, M., Cecchi, F., Charron, P., Hagege, A. A., Lafont, A., Limongelli, G., Mahrholdt, H., McKenna, W. J., Mogensen, J., Nihoyannopoulos, P., Nistri, S., Pieper, P. G., Pieske, B., Rapezzi, C., Rutten, F. H., Tillmanns, C., Watkins, H., 2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: the Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC), European Heart Journal, 35, 2733-79, 2014	Study design; guidelines
Autore, C., Conte, M. R., Piccininno, M., Bernabo, P., Bonfiglio, G., Bruzzi, P., Spirito, P., Risk associated with pregnancy in hypertrophic cardiomyopathy, Journal of the American College of Cardiology, 40, 1864-9, 2002	Comparison outside of scope; pregnant women vs. general population
Avila, W. S., Rossi, E. G., Ramires, J. A. F., Grinberg, M., Bortolotto, M. R. L., Zugaib, M., Da Luz, P. L., Pregnancy in patients with heart disease: Experience with 1,000 cases, Clinical Cardiology, 26, 135-142, 2003	The study aimed to determine the association between type of heart disease and pregnancy outcomes, instead of risk factors
Beaton, A., Okello, E., Destigter, K., Scheel, A., Perlman, L., Sable, C., Impact of rheumatic heart disease on maternal outcomes in pregnancy: Leveraging existing infrastructure to address a critical knowledge gap, Global Heart, 1), e75, 2016	Conference proceedings
Bhattacharyya, A., Basra, S. S., Sen, P., Kar, B., Peripartum cardiomyopathy: a review, Texas Heart Institute Journal, 39, 8-16, 2012	Study design; non-systematic review
Billebeau, Gilles, Etienne, Martin, Cheikh-Khelifa, Riadh, Vauthier-Brouzes, Daniele, Gandjbakhch, Estelle, Isnard, Richard, Nizard, Jacky, Komajda, Michel, Dommergues, Marc, Charron, Philippe, Pregnancy in women with a cardiomyopathy:	Outcomes outside of scope

Study	Reason for exclusion
Outcomes and predictors from a retrospective cohort, Archives of cardiovascular diseases, 2017	
Biteker, M., Duran, N., Kaya, H., Yildiz, M., Gokdeniz, T., Gunduz, S., Tanboga, I. H., Kahveci, G., Akgun, T., Ozkan, M., Predictive value of n-terminal pro-B-type natriuretic peptide and echocardiographic paramaters in patients with peripartum cardiomyopathy, European Heart Journal, 30, 447-448, 2009	Conference proceedings
Bope, N., Shahid, J., Koutrolou-Sotiropoulou, P., Miller, C., Parikh, P., Stergiopoulos, K., Impact of cardiomyopathy on clinical outcomes in pregnant women with heart disease, Journal of Cardiac Failure, 1), S35, 2013	Conference proceedings
Bouhout, I., Poirier, N., Mazine, A., Dore, A., Mercier, L. A., Leduc, L., El-Hamamsy, I., Cardiac, obstetric, and fetal outcomes during pregnancy after biological or mechanical aortic valve replacement, Canadian Journal of Cardiology, 30, 801-7, 2014	Study design; descriptive study
Castanho, A. Q. D. S., Martins, M. D. G., Silva, A. A. C. D., Rios, L. T. M., Pinto, K. L., Carvalho, V. D. S., Deus, L. B. D. D., Oliveira Neto, V. B. D., Cardiopathy and pregnancy: Maternal results, Journal of Perinatal Medicine. Conference: 10th World Congress of Perinatal Medicine, 39, 2011	Conference proceedings
Cauldwell, M., Von Klemperer, K., Uebing, A., Swan, L., Steer, P. J., Babu-Narayan, S. V., Gatzoulis, M. A., Johnson, M. R., A cohort study of women with a Fontan circulation undergoing preconception counselling, Heart, 102, 534-540, 2016	No data reporting the predictive value of risk factors for outcomes of interest
Cauldwell, Matthew, Von Klemperer, Kate, Uebing, Anselm, Swan, Lorna, Steer, Philip J., Gatzoulis, Michael, Johnson, Mark R., Why is post-partum haemorrhage more common in women with congenital heart disease?, International journal of cardiology, 218, 285-290, 2016	Outcomes outside of scope; post-partum haemorrhage
Chugh,R., Management of pregnancy in patients with congenital heart disease and systemic ventricular failure, Progress in Pediatric Cardiology, #19, 47-60, 2004	Study design; non-systematic review
Curtis,S.L., Marsden-Williams,J., Sullivan,C., Sellers,S.M., Trinder,J., Scrutton,M., Stuart,A.G., Current trends in the management of heart disease in pregnancy, International Journal of Cardiology, 133, 62-69, 2009	Wrong intervention; management included interventions outside of scope
Dobbenga-Rhodes, Y. A., Prive, A. M., Assessment and evaluation of the woman with	Study design; non-systematic review

Study	Reason for exclusion
cardiac disease during pregnancy, Journal of Perinatal & Neonatal Nursing, 20, 295-302, 2006	
Dorbala,S., Brozena,S., Zeb,S., Galatro,K., Homel,P., Ren,J.F., Chaudhry,F.A., Risk stratification of women with peripartum cardiomyopathy at initial presentation: a dobutamine stress echocardiography study, Journal of the American Society of Echocardiography, 18, 45-48, 2005	Population outside of scope; women with peripartum cardiomyopathy (PPCM) vs. women without PPCM
Drenthen, W., Pieper, P. G., Ploeg, M., Voors, A. A., Roos-Hesselink, J. W., Mulder, B. J. M., Vliegen, H. W., Sollie, K. M., Ebels, T., Van Veldhuisen, D. J., Risk of complications during pregnancy after Senning or Mustard (atrial) repair of complete transposition of the great arteries, European Heart Journal, 26, 2588-2595, 2005	Study design; descriptive study
Emmanuel, Y., Thorne, S. A., Heart disease in pregnancy, Best Practice and Research: Clinical Obstetrics and Gynaecology, 29, 579-597, 2015	Study design; non-systematic review
English, K., Ulivi, G., Oliver, J., Winfield, S., Everett, T., Simms, A., Lansbury, A., Aortic stenosis in pregnancy outcomes of a combined cardiac & obstetric antenatal clinic, Cardiology in the Young, 27, S97, 2017	Conference proceedings
Estensen, M. E., Langesaeter, E., Gullestad, L., Aakhus, S., Skulstad, H., Peripartum cardiomyopathy-evaluation of left ventricular reserve capacity by ergometric stressechocardiography 9-12 months postpartum, European Heart Journal Cardiovascular Imaging, 13, i155, 2012	Conference proceedings
Fett,J.D., Carraway,R.D., Perry,H., Dowell,D.L., Emerging insights into peripartum cardiomyopathy, Journal of Health, Population and Nutrition, 21, 1-7, 2003	Comparison outside of scope; women with peripartum cardiomyopathy (PPCM) vs. women without PPCM
Fu, Q., Lin, J., Risk factors for heart failure during pregnancy among Chinese women with cardiac disease, International Journal of Gynecology and Obstetrics, 130, 266-269, 2015	The outcome, heart failure, was not explicitly defined and was not clear enough to justify whether it was similar to one of the critical outcomes, severe maternal morbidity
Furenas, E., Eriksson, P., Wennerholm, U. B., Dellborg, M., Effect of maternal age and cardiac disease severity on outcome of pregnancy in women with congenital heart disease, International Journal of Cardiology, 243, 197-203, 2017	Outcomes outside of scope
Garg, L., Garg, J., Krishnamoorthy, P., Ahnert, A., Shah, N., Dusaj, R. S., Bozorgnia, B., The Influence of Pregnancy in Patients with Congenital Long QT Syndrome, Cardiology in Review, 31, 31, 2016	Study design; non-systematic review

Study	Reason for exclusion
Goldberg, L. A., Gleason, L. P., Ruckdeschel, E. S., Bhamare, T., Drajpuch, D., Hirshberg, A., Partington, S. L., Rogers, R., Srinivas, S. K., Stokes, N., Tobin, L., Levine, L. D., Kim, Y. Y., Risk assessment in pregnant women with congenital heart disease, Circulation, 134, 2016	Conference proceedings
Goya, M., Casellas, M., Merced, C., Pijuan-Domenech, A., Galian, L., Dos, L., Casaldaliga, J., Subirana, M., Pedrosa, V., Rojas, M., Martinez, C., Ferreira, I., Monts, M., Gascon, A., Mendoza, M., Baro, F., Suy, A., Lopez-Gil, V., Manrique, S., Tornos, P., Garcia-Dorado, D., Carreras, E., Cabero, L., Predictors of obstetric complications in women with heart disease, Journal of Maternal-Fetal and Neonatal Medicine, 29, 2306-2311, 2016	No data reporting the predictive value of risk factors for the outcomes of interest in the protocol
Grewal, J., Silversides, C. K., Colman, J. M., Pregnancy in women with heart disease. risk assessment and management of heart failure, Heart Failure Clinics, 10, 117-129, 2014	Study design; non-systematic review
Hameed, A. B., Lawton, E. S., McCain, C. L., Morton, C. H., Mitchell, C., Main, E. K., Foster, E., Pregnancy-related cardiovascular deaths in California: beyond peripartum cardiomyopathy, American Journal of Obstetrics & Gynecology, 213, 379.e1-10, 2015	Population outside of scope; cardiovascular pregnancy-related deaths
Hameed,A., Karaalp,I.S., Tummala,P.P., Wani,O.R., Canetti,M., Akhter,M.W., Goodwin,I., Zapadinsky,N., Elkayam,U., The effect of valvular heart disease on maternal and fetal outcome of pregnancy, Journal of the American College of Cardiology, 37, 893-899, 2001	Comparison outside of scope; pregnant women with valvular heart disease vs. pregnant women with non-valvular heart disease
Hasanaj, Q., Wilson, B. J., Little, J., Montazeri, Z., Carroll, J. C., Cihr Emerging Team in Genomics in Screening, Family history: impact on coronary heart disease risk assessment beyond guideline-defined factors, Public Health Genomics, 16, 208-14, 2013	Population outside of scope; women did not have cardiac disease
Hilfiker-Kleiner, D., Haghikia, A., Nonhoff, J., Bauersachs, J., Peripartum cardiomyopathy: current management and future perspectives, European Heart Journal, 36, 1090-7, 2015	Study design; non-systematic review
Huang, G. Y., Zhang, L. Y., Long-Le, M. A., Wang, L. X., Clinical characteristics and risk factors for peripartum cardiomyopathy, African Health Sciences, 12, 26-31, 2012	Population outside of scope; women with PPCM following delivery vs. women without PPCM following delivery
Jadhav, S. P., Pregnancy and congenital heart disease, Pediatric Radiology, 45, S63-S64, 2015	Conference proceedings
Jastrow, N., Meyer, P., Khairy, P., Mercier, L. A., Dore, A., Marcotte, F., Leduc, L., Prediction of complications in pregnant women with cardiac	Study design; descriptive study

Study	Reason for exclusion
diseases referred to a tertiary center, International Journal of Cardiology, 151, 209-13, 2011	
Jimenez-Juan, L., Krieger, E. V., Valente, A. M., Geva, T., Wintersperger, B. J., Moshonov, H., Siu, S. C., Colman, J. M., Silversides, C. K., Wald, R. M., Cardiovascular magnetic resonance imaging predictors of pregnancy outcomes in women with coarctation of the aorta, European Heart Journal Cardiovascular Imaging, 15, 299-306, 2014	No data reporting the predictive value of risk factors for outcomes of interest
Johnson-Coyle, L., Jensen, L., Sobey, A., American College of Cardiology, Foundation, American Heart, Association, Peripartum cardiomyopathy: review and practice guidelines, American Journal of Critical Care, 21, 89-98, 2012	Study design; guidelines
Juan, L. J., Krieger, E., Valente, A. M., Ley-Zaporozhan, J., Moshonov, H., Wintersperger, B. J., Silversides, C., Siu, S., Crean, A. M., Ley, S., Colman, J. M., Nguyen, E. T., Paul, N. S., Sermer, M., Wald, R. M., Aortic dimensions on cardiovascular magnetic resonance imaging relate to pregnancy outcomes in women with coarctation of the aorta: A multicenter study, Journal of Cardiovascular Magnetic Resonance. Conference: 15th Annual SCMR Scientific Sessions, 14, 2012	Conference proceedings
Juan, L. J., Valente, A. M., Wintersperger, B. J., Silversides, C., Crean, A. M., Colman, J. M., Nguyen, E. T., Geva, T., Wald, R. M., Relationship between cardiac magnetic resonance imaging parameters and pregnancy outcomes in women post mustard repair: A multi-center study, Journal of Cardiovascular Magnetic Resonance, 15, 433-434, 2013	Conference proceedings
Kamiya,C.A., Iwamiya,T., Neki,R., Katsuragi,S., Kawasaki,K., Miyoshi,T., Sasaki,Y., Osato,K., Murohara,T., Ikeda,T., Outcome of pregnancy and effects on the right heart in women with repaired tetralogy of fallot, Circulation Journal, 76, 957-963, 2012	Outcomes outside of scope; cardiac events
Kampman, M. A. M., Balci, A., Mulder, B. J. M., Van Dijk, A. P. J., Roos-Hesselink, J. W., Sollie-Szarynska, K. M., Ludwig-Ruitenberg, M., Van Melle, J. P., Van Veldhuisen, D. J., Pieper, P. G., Nt-proBNP predicts cardiovascular complications in pregnant women with congenital heart disease, European Heart Journal, 34, 378, 2013	Conference proceedings
Kampman, M. A., Balci, A., Groen, H., van Dijk, A. P., Roos-Hesselink, J. W., van Melle, J. P., Sollie-Szarynska, K. M., Wajon, E. M., Mulder, B. J., van Veldhuisen, D. J., Pieper, P. G., Zahara Ii investigators, Cardiac function and cardiac events 1-year postpartum in women with congenital heart	Study design; non-comparative descriptive study

Study	Reason for exclusion
disease, American Heart Journal, 169, 298-304, 2015	
Kampman, M. A., Siegmund, A. S., Bilardo, C. M., van Veldhuisen, D. J., Balci, A., Oudijk, M. A., Groen, H., Mulder, B. J., Roos-Hesselink, J. W., Sieswerda, G., de Laat, M. W., Sollie-Szarynska, K. M., Pieper, P. G., Uteroplacental Doppler flow and pregnancy outcome in women with tetralogy of Fallot, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 49, 231-239, 2017	Comparison outside of scope; study compared pregnant women with tetralogy of Fallot with healthy pregnant women
Karaye, K. M., Lindmark, K., Henein, M. Y., Electrocardiographic predictors of peripartum cardiomyopathy, Cardiovascular Journal of Africa, 27, 66-70, 2016	Population outside of scope; women with peripartum cardiomyopathy (PPCM), not women with previous PPCM
Koutrolou-Sotiropoulou, P., Parikh, P. B., Miller, C., Lima, F. V., Butler, J., Stergiopoulos, K., Impact of Heart Disease on Maternal and Fetal Outcomes in Pregnant Women, American Journal of Cardiology, 116, 474-80, 2015	Comparison outside of scope; pregnant women with cardiomyopathy or other heart disease compared with healthy pregnant women
Kumari, M., Tang, W. H., Maroo, A. P., Natriuretic peptide testing in high-risk pregnancy: a preventive opportunity?, Current Heart Failure Reports, 11, 471-6, 2014	Study design; non-systematic review
Kuperstein, R., Cahan, T., Yoeli-Ullman, R., Ben Zekry, S., Shinfeld, A., Simchen, M. J., Risk of Aortic Dissection in Pregnant Patients With the Marfan Syndrome, American Journal of Cardiology, 30, 30, 2016	Study design; non-comparative observational study
Langford,E.J., Makharia,M.K., Langford,K.S., Cardiac disease in pregnancy: A District General Hospital perspective, British Journal of Cardiology, 16, 98-101, 2009	Study design; descriptive study
Lewey, J., Haythe, J., Cardiomyopathy in pregnancy, Seminars in Perinatology, 38, 309-17, 2014	Study design; non-systematic review
Li, J. M., Nguyen, C., Joglar, J. A., Hamdan, M. H., Page, R. L., Frequency and outcome of arrhythmias complicating admission during pregnancy: experience from a high-volume and ethnically-diverse obstetric service, Clinical Cardiology, 31, 538-41, 2008	Study design; descriptive study
Li, W., Li, H., Long, Y., Clinical Characteristics and Long-term Predictors of Persistent Left Ventricular Systolic Dysfunction in Peripartum Cardiomyopathy, Canadian Journal of Cardiology, 32, 362-368, 2016	Population is women with peripartum cardiomyopathy (PPCM) not women with previous PPCM
Liu, H., Huang, T. T., Lin, J. H., Risk factors and risk index of cardiac events in pregnant women	Outcome was outside of interest

Study	Reason for exclusion
with heart disease, Chinese Medical Journal, 125, 3410-5, 2012	
Liu,H., Huang,T., Zhao,W., Shen,Y., Lin,J., Pregnancy outcomes and relative risk factors among Chinese women with congenital heart disease, International Journal of Gynecology and Obstetrics, 120, 245-248, 2013	Population is women with peripartum cardiomyopathy (PPCM) not women with previous PPCM
Lumsden, R. H., Barasa, F. A., Park, L. P., Ochieng, C. B., Alera, J. M., Christoffersen-Deb, A., Bloomfield, G. S., Defining and predicting the burden and risk of cardiac disease in pregnancy in Kenya: A retrospective review of all cases from 2011-2015, Circulation, 136, 2017	Conference abstract publication only
Martins, L. C., Freire, C. M. V., Capurucu, C. A. B., Nunes, M. C. P., Rezende, C. A. L., Risk prediction of cardiovascular complications in pregnant women with heart disease, Arquivos Brasileiros de Cardiologia, 106, 289-296, 2016	Validation study of CARPREG predicting cardiovascular complication (which was not direct outcome of interest)
McKellar, S. H., MacDonald, R. J., Michelena, H. I., Connolly, H. M., Sundt, T. M., 3rd, Frequency of cardiovascular events in women with a congenitally bicuspid aortic valve in a single community and effect of pregnancy on events, American Journal of Cardiology, 107, 96-9, 2011	Non-comparative study
McLaughlin, L., Khan, A., Anbazhagan, A., Cooke, I., Management of pregnant women with pre-existing cardiac conditions within a tertiary centre, BJOG: An International Journal of Obstetrics and Gynaecology, 123, 131-132, 2016	Conference abstract
Melao, F., Ribeiro, V., Cruz, C., Maciel, M. J., Pregnancy outcome and offspring risk in congenital heart disease: A single experience in a tertiay center, European Heart Journal Cardiovascular Imaging, 14, ii162, 2013	Conference abstract
Ntiloudi, D., Zegkos, T., Bazmpani, M. A., Parcharidou, D., Panagiotidis, T., Hadjimiltiades, S., Karvounis, H., Giannakoulas, G., Pregnancy outcome in women with congenital heart disease: A single-center experience, Hellenic Journal of Cardiology, 2018	Descriptive study of women with congenital heart disease
Ntiloudi, D., Zegkos, T., Koutsakis, A., Giannakoulas, G., Karvounis, H., Pregnancy in Patients With Congenital Heart Disease: A Contemporary Challenge, Cardiology in Review, 25, 326-330, 2017	Review
Ntiloudi, Despina, Zegkos, Thomas, Bazmpani, Maria Anna, Parcharidou, Despoina, Panagiotidis, Theofilos, Hadjimiltiades, Stavros, Karvounis, Haralambos, Giannakoulas, George, Pregnancy outcome in women with congenital heart disease: A single-center experience, Hellenic journal of	Descriptive study

Study	Reason for exclusion
cardiology : HJC = Hellenike kardiologike epitheorese, 2017	
Ntusi, N. B. A., Mayosi, B. M., Risk factors for disease development and predictors of outcome in peripartum cardiomyopathy, European Heart Journal, 31, 27, 2010	Conference abstract
Old, A., Arya, R., Macleod, K., Verma, A., Chattington, P., Five-year experience of maternal cardiac disease in a district general Hospital 2008-2012, Archives of Disease in Childhood: Fetal and Neonatal Edition, 99, A125-A126, 2014	Conference abstract
Oudijk, M., Kampman, M. A. M., Bilardo, K. M., Balci, A., Mulder, B. J. M., Roos-Hesselink, J. W., De Laat, M. W. M., Sollie-Szarynska, K. M., Van Veldhuisen, D. J., Pieper, E. G., Right ventricular function is associated with impaired uteroplacental circulation in pregnant women with Tetralogy of Fallot, American Journal of Obstetrics and Gynecology, 214, S422, 2016	Abstract publication only
Pandit,V., Shetty,S., Kumar,A., Sagir,A., Incidence and outcome of peripartum cardiomyopathy from a tertiary hospital in South India, Tropical Doctor, 39, 168-169, 2009	Population is women with peripartum cardiomyopathy (PPCM), not women with previous PPCM
Petelenz, T., Singer, K., Cekanski, A., Fiutowski, L., Slominska-Petelenz, T., Poreba, R., Czyz, Z., Lewicki, A., Krol, M., Pregnancy and delivery prognostic risk score for women with congenital heart disease and acquired valvular heart disease, Wiadomosci Lekarskie, 50, 287-94, 1997	Article in Polish
Pieper, P. G., Walker, F., Pregnancy in women with hypertrophic cardiomyopathy, Netherlands Heart Journal, 21, 14-18, 2013	Non-systematic review
Prasad, A. K., Ventura, H. O., Valvular heart disease and pregnancy. A high index of suspicion is important to reduce risks, Postgraduate Medicine, 110, 69-72, 75-6, 82-3, passim, 2001	Narrative review
Rigato, I., Rigato, S., Steriotis, A. K., Zorzi, A., Basso, C., Thiene, G., Iliceto, S., Corrado, D., Bauce, B., Is pregnancy associated with an increased risk of arrhythmias and disease progression in arrhythmogenic right ventricular cardiomyopathy?, Circulation. Conference: American Heart Association, 126, 2012	Conference abstract
Rigato, I., Zardo, S., Steriotis, A. K., Basso, C., Daliento, L., Thiene, G., Iliceto, S., Corrado, D., Bauce, B., Pregnancy in women with arrhythmogenic right ventricular cardiomyopathy, European Heart Journal, 33, 365, 2012	Conference abstract
Roche-Kelly, E., Nelson-Piercy, C., Managing cardiovascular disease during pregnancy: best	Full-text article was unavailable

Study	Reason for exclusion
practice to optimize outcomes, Future Cardiology, 10, 421-33, 2014	
Sabanayagam, A., Agarwal, A., MacCain, C., Lawton, E., Main, E., Hameed, A., Harris, I., Foster, E., Mortality in pregnant women with congenital heart disease: A subanalysis of the california pregnancy-associated mortality review, Journal of the American College of Cardiology, 69, 606, 2017	Conference abstract publication only
sermer, M., Colman, J., Siu, S., Pregnancy complicated by heart disease: a review of Canadian experience, Journal of Obstetrics & Gynaecology, 23, 540-4, 2003	Comparison to women without cardiac disease
Seth, R., Moss, A. J., McNitt, S., Zareba, W., Andrews, M. L., Qi, M., Robinson, J. L., Goldenberg, I., Ackerman, M. J., Benhorin, J., Kaufman, E. S., Locati, E. H., Napolitano, C., Priori, S. G., Schwartz, P. J., Towbin, J. A., Vincent, G. M., Zhang, L., Long QT syndrome and pregnancy, Journal of the American College of Cardiology, 49, 1092-8, 2007	Comparison to a non-pregnant population
Sidlik,R., Sheiner,E., Levy,A., Wiznitzer,A., Effect of maternal congenital heart defects on labor and delivery outcome: a population-based study, Journal of Maternal-Fetal and Neonatal Medicine, 20, 211-216, 2007	Comparison with women who do not have a cardiac condition
Singh,M., Bolger,A., Khare,M., Multidisciplinary management of heart disease in pregnancy: A single centre experience, Archives of Disease in Childhood: Fetal and Neonatal Edition, 96, Fa111-, 2011	Conference abstract
Siu, S. C. B., Sermer, M., Mason, J., Wald, R., Colman, J., Silversides, C., Twenty year trends in maternal and perinatal complications in pregnant women with heart disease, Journal of the American College of Cardiology, 69, 566, 2017	Abstract publication only
Siu, S. C., Colman, J. M., Sorensen, S., Smallhorn, J. F., Farine, D., Amankwah, K. S., Spears, J. C., Sermer, M., Adverse neonatal and cardiac outcomes are more common in pregnant women with cardiac disease, Circulation, 105, 2179-84, 2002	Comparison to women who do not have heart disease.
Siu, S. C., Grewal, J., Sermer, M., Mason, J., Kiess, M., Wald, R., Colman, J., Silversides, C., Comprehensive prediction of cardiac outcomes in pregnant women with heart disease, Circulation, 136, 2017	Conference abstract publication only
Siu, S. C., Sermer, M., Colman, J. M., Alvarez, A. N., Mercier, L. A., Morton, B. C., Kells, C. M., Bergin, M. L., Kiess, M. C., Marcotte, F., Taylor, D. A., Gordon, E. P., Spears, J. C., Tam, J. W.,	Validation study of CARPREG risk assessment tool for cardiac event (not direct outcome of interest)

Study	Reason for exclusion
Amankwah, K. S., Smallhorn, J. F., Farine, D., Sorensen, S., Cardiac Disease in Pregnancy, Investigators, Prospective multicenter study of pregnancy outcomes in women with heart disease, Circulation, 104, 515-21, 2001	
Suwanrath, C., Thongphanang, P., Pinjaroen, S., Validation ofmodified WHO classification in pregnant women with heart disease in a tertiary care center in southern Thailand, Journal of Obstetrics and Gynaecology Research, 43, 81-82, 2017	Abstract publication only
Suwanrath, C., Thongphanang, P., Pinjaroen, S., Suwanugsorn, S., Validation of modified world health organization classification for pregnant women with heart disease in a tertiary care center in southern Thailand, International Journal of Women's Health, 10, 47-53, 2018	Descriptive study of pregnancy risk among women with heart disease by WHO classification
Tan, G., Chan, J. Y. S., Maternal outcomes and risk assessment in pregnancies associated with structural heart diseases: A single tertiary centre experience, Journal of the American College of Cardiology, 67, 952, 2016	Abstract publication only
Thangaroopan,M., Wald,R.M., Silversides,C.K., Mason,J., Smallhorn,J.F., Sermer,M., Colman,J.M., Siu,S.C., Incremental diagnostic yield of pediatric cardiac assessment after fetal echocardiography in the offspring of women with congenital heart disease: a prospective study, Pediatrics, 121, e660-e665, 2008	Comparison of fetal and paediatric detection of congenital heart disease
Umeda, H., Ota, T., Misumida, N., Hayashi, K., Komoriya, Y., Ishiki, R., Sugino, S., Iwase, M., Inagaki, H., Murohara, T., Impact of high risk pregnancy on left ventricular function during peripartum period: from the Toyota peripartum cardiomyopathy study, European Heart Journal, 32, 289, 2011	Conference abstract
Van Hagen, I. M., Boersma, E., Johnson, M. R., Thorne, S. A., Parsonage, W. A., Escribano Subias, P., Lesniak-Sobelga, A., Irtyuga, O., Sorour, K. A., Taha, N., Maggioni, A. P., Hall, R., Roos-Hesselink, J. W., Global cardiac risk assessment in the Registry of Pregnancy and Cardiac disease: Results of a registry from the European Society of Cardiology, European Journal of Heart Failure, 18, 523-533, 2016	Outcome was outside of this review's interest
Van Hagen, I. M., Roos-Hesselink, J. W., Donvito, V., Liptai, C., Morissens, M., Murphy, D. J., Galian, L., Bazargani, N. M., Cornette, J., Hall, R., Johnson, M. R., Incidence and predictors of obstetric and fetal complications in women with structural heart disease, Heart, 103, 1610-1618, 2017	The risk factors and outcomes were outside of the protocol

Study	Reason for exclusion
Varlet, E., Nizard, J., Duthoit, G., Fressart, V., Badenco, N., Waintraub, X., Chastre, T., Maupain, C., Hidden-Lucet, F., Gandjbakhch, E., Arrhythmogenic right ventricular dysplasia during pregnancy : Retrospective study of 21 patients, Europace, 17, iii227, 2015	Conference abstract
Vereczkey, A., Czeizel, A. E., Birth outcomes and risk or protective factors of ventricular Septal defects during pregnancy, Birth Defects Research Part A - Clinical and Molecular Teratology, 103 (5), 420, 2015	Conference abstract
Wallis,H., Thorne,S., Congenital heart disease and pregnancy, Women's health, 2, 743-752, 2006	Narrative review
Warnes, C. A., Pregnancy and Delivery in Women With Congenital Heart Disease, Circulation Journal, 79, 1416-21, 2015	Non-systematic review
Weiss, B. M., Atanassoff, P. G., Cyanotic congenital heart disease and pregnancy: natural selection, pulmonary hypertension, and anesthesia, Journal of Clinical Anesthesia, 5, 332-41, 1993	Narrative review
Yap, S. C., Drenthen, W., Pieper, P. G., Moons, P., Mulder, B. J. M., Mostert, B., Vliegen, H. W., van Dijk, A. P. J., Meijboom, F. J., Steegers, E. A. P., Roos-Hesselink, J. W., Risk of complications during pregnancy in women with congenital aortic stenosis, International Journal of Cardiology, 126, 240-246, 2008	Severity of aortic stenosis was assessed by doppler which was not considered in the protocol
Zhang, F., Xuebin,, The reasearch into the clinical characteristics of peripartum cardiomyopathy, Heart, 98, E165-E166, 2012	Conference abstract

Economic studies

2 See Supplement 2 (Health economics) for details of economic evidence reviews and health
3 economic modelling.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Clinical studies

Study	Reason for exclusion
Abildgaard, U., Sandset, P. M., Hammerstrom, J., Gjestvang, F. T., Tveit, A., Management of pregnant women with mechanical heart valve prosthesis: thromboprophylaxis with low molecular weight heparin, Thrombosis Research, 124, 262-7, 2009	Included in Xu 2016 systematic review
Akhtar,R.P., Abid,A.R., Zafar,H., Cheema,M.A., Khan,J.S., Anticoagulation in pregnancy with mechanical heart valves: 10-year experience, Asian Cardiovascular and Thoracic Annals, 15, 497-501, 2007	Included in Xu 2016 systematic review
Al-Ahmad, A. M., Hartnett-Daudelin, D., Salem, D. N., Antithrombotic therapy for prosthetic valves: routine treatment and special considerations, Current Cardiology Reports, 3, 85-9, 2001	Study design; non-systematic review (antithrombotic treatment in patients with prosthetic valves)
Al-Lawati, A. A., Venkitraman, M., Al-Delaime, T., Valliathu, J., Pregnancy and mechanical heart valves replacement; dilemma of anticoagulation, European Journal of Cardio-Thoracic Surgery, 22, 223-7, 2002	Included in Xu 2016 systematic review
Anonymous,, ACOG Committee opinion, No. 276, October 2002. Safety of lovenox in pregnancy, International Journal of Gynecology and Obstetrics, 79, 299-300, 2002	Duplicate reference
Arnaout, M. S., Kazma, H., Khalil, A., Shasha, N., Nasrallah, A., Karam, K., Alam, S. E., Is there a safe anticoagulation protocol for pregnant women with prosthetic valves?, Clinical & Experimental Obstetrics & Gynecology, 25, 101-4, 1998	Outcomes outside of scope
Ashour, Z. A., Shawky, H. A., Hassan Hussein, M., Outcome of pregnancy in women with mechanical valves, Texas Heart Institute Journal, 27, 240-5, 2000	Included in Xu 2016 systematic review
Ayad, S. W., Hassanein, M. M., Mohamed, E. A., Gohar, A. M., Maternal and fetal outcomes in pregnant women with a prosthetic mechanical heart valve, Clinical Medicine Insights: Cardiology, 10, 11-17, 2016	Comparison outside of scope; comparison is by valve replacement site
Ayhan, A., Yapar, E. G., Yuce, K., Kisnisci, H. A., Nazli, N., Ozmen, F., Pregnancy and its complications after cardiac valve replacement, International Journal of Gynaecology & Obstetrics, 35, 117-22, 1991	Included in Xu 2016 systematic review
Ayhan,A., Yucel,A., Bildirici,I., Dogan,R., Feto-maternal morbidity and mortality after cardiac valve replacement, Acta Obstetricia et Gynecologica Scandinavica, 80, 713-718, 2001	Better quality data already included

Study	Reason for exclusion
Badduke, B. R., Jamieson, W. R., Miyagishima, R. T., Munro, A. I., Gerein, A. N., MacNab, J., Tyers, G. F., Pregnancy and childbearing in a population with biologic valvular prostheses, Journal of Thoracic & Cardiovascular Surgery, 102, 179-86, 1991	Comparison outside of scope; pregnant vs. non-pregnant women
Barbour, L. A., Pickard, J., Controversies in thromboembolic disease during pregnancy: a critical review, Obstetrics & Gynecology, 86, 621-33, 1995	Study design; narrative review (diagnosis, treatment and complications of thromboembolism in pregnancy)
Basude, S., Hein, C., Curtis, S. L., Clark, A., Trinder, J., Low-molecular-weight heparin or warfarin for anticoagulation in pregnant women with mechanical heart valves: what are the risks? A retrospective observational study, BJOG: An International Journal of Obstetrics & Gynaecology, 119, 1008-13; discussion 1012-3, 2012	Included in Xu 2016 systematic review
Ben Ismail, M., Abid, F., Trabelsi, S., Taktak, M., Fekih, M., Cardiac valve prostheses, anticoagulation, and pregnancy, British Heart Journal, 55, 101-5, 1986	Better quality data already included
Benatta, N., Batouche, D. D., Anticoagulation's problematic during pregnancy in carriers of mechanical heart prostheses, Archives of Cardiovascular Diseases Supplements, 9, 75-76, 2017	Conference proceedings
Berresheim, M., Wilkie, J., Nerenberg, K. A., Ibrahim, Q., Bungard, T. J., A case series of LMWH use in pregnancy: should trough anti-Xa levels guide dosing?, Thrombosis Research, 134, 1234-40, 2014	Included in Xu 2016 systematic review
Bhutta, S. Z., Aziz, S., Korejo, R., Pregnancy following cardiac surgery, JPMA - Journal of the Pakistan Medical Association, 53, 407-13, 2003	Included in Xu 2016 systematic review
Bian, C., Qi, X., Li, L., Zhao, J., Liu, X., Anticoagulant management of pregnant women with mechanical heart valve replacement during perioperative period, Archives of Gynecology & Obstetrics, 293, 69-74, 2016	Better quality data already included
Bian, Ce, Qi, Xiaorong, Li, Li, Zhao, Jitong, Liu, Xinghui, Anticoagulant management of pregnant women with mechanical heart valve replacement during perioperative period, Archives of Gynecology and Obstetrics, 293, 69-74, 2016	Study design; retrospective review
Born, D., Martinez, E. E., Almeida, P. A., Santos, D. V., Carvalho, A. C., Moron, A. F., Miyasaki, C. H., Moraes, S. D., Ambrose, J. A., Pregnancy in patients with prosthetic heart valves: the effects of anticoagulation on mother, fetus, and neonate, American Heart Journal, 124, 413-7, 1992	Included in Xu 2016 systematic review
Caruso, A., de Carolis, S., Ferrazzani, S., Paradisi, G., Pomini, F., Pompei, A., Pregnancy outcome in women with cardiac valve prosthesis,	Comparison outside of scope; no drug A vs. drug B comparison

Study	Reason for exclusion
European Journal of Obstetrics, Gynecology, & Reproductive Biology, 54, 7-11, 1994	
Casanegra, P., Aviles, G., Maturana, G., Dubernet, J., Cardiovascular management of pregnant women with a heart valve prosthesis, American Journal of Cardiology, 36, 802-6, 1975	Included in Xu 2016 systematic review
Chan, W. S., Anand, S., Ginsberg, J. S., Anticoagulation of pregnant women with mechanical heart valves: a systematic review of the literature, Archives of Internal Medicine, 160, 191-6, 2000	More recent systematic review included
Chaudhary, R. K., Nepal, C., Khanal, N., Pathak, R., Giri, S., Bhatt, V. R., Management and outcome of heparin-induced thrombocytopenia in pregnancy: A systematic review, Cardiovascular and Hematological Agents in Medicinal Chemistry, 13, 92-97, 2015	Population outside of scope; case series of women with heparin induced thrombocytopenia
Chen, W. W., Chan, C. S., Lee, P. K., Wang, R. Y., Wong, V. C., Pregnancy in patients with prosthetic heart valves: an experience with 45 pregnancies, Quarterly Journal of Medicine, 51, 358-65, 1982	Included in Xu 2016 systematic review
Cotrufo, M., De Feo, M., De Santo, L. S., Romano, G., Della Corte, A., Renzulli, A., Gallo, C., Risk of warfarin during pregnancy with mechanical valve prostheses, Obstetrics & Gynecology, 99, 35-40, 2002	Included in Xu 2016 systematic review
De Santo, L. S., Romano, G., Della Corte, A., D'Oria, V., Nappi, G., Giordano, S., Cotrufo, M., De Feo, M., Mechanical aortic valve replacement in young women planning on pregnancy: maternal and fetal outcomes under low oral anticoagulation, a pilot observational study on a comprehensive pre-operative counseling protocol, Journal of the American College of Cardiology, 59, 1110-5, 2012	Presents results of use of pre-operative counselling protocol to guide choice of replacement valves
Della Corte, A., De Feo, M., Romano, G., Amarelli, C., De Santo, L. S., Nappi, G., Scardone, M., Cotrufo, M., Risk of warfarin anticoagulation in pregnant patients with mechanical heart valve prostheses, Journal of Heart Valve Disease, 13 Suppl 1, S90, 2004	Study design; non-systematic review
Descarries, L. M., Leduc, L., Khairy, P., Mercier, L. A., Low-molecular-weight heparin in pregnant women with prosthetic heart valves, Journal of Heart Valve Disease, 15, 679-85, 2006	Study design; case series (n=5 women)
Deviri, E., Levinsky, L., Yechezkel, M., Levy, M. J., Pregnancy after valve replacement with porcine xenograft prosthesis, Surgery, Gynecology & Obstetrics, 160, 437-43, 1985	Better quality data already included
Donvito, V., Maina, A., Arrotta, M., Bordese, R., Cicogna, L., Comoglio, F. M., Gollo, E., Montali, N., Todros, T., Anticoagulation in pregnant patients with mechanical heart valves, Italian Journal of Medicine, 10, 38, 2016	Conference proceedings

Study	Reason for exclusion
D'Souza, R., Ostro, J., Shah, P. S., Silversides, C. K., Malinowski, A., Murphy, K. E., Sermer, M., Shehata, N., Anticoagulation for pregnant women with mechanical heart valves: A systematic review andmeta-Analysis, European Heart Journal, 38, 1509-1516, 2017	Systematic review and included studies being checked for relevancy
D'Souza, Rohan, Ostro, Jackie, Shah, Prakesh S., Silversides, Candice K., Malinowski, Ann, Murphy, Kellie E., Sermer, Mathew, Shehata, Nadine, Anticoagulation for pregnant women with mechanical heart valves: a systematic review and meta-analysis, European Heart Journal, 38, 1509-1516, 2017	Systematic review; included studies being checked for relevancy
Duhl, A. J., Low-molecular-weight heparins for the prevention and treatment of venous thromboembolism in at-risk pregnant women: a review, Journal of Reproductive Medicine, 53, 657-66, 2008	Study design; non-systematic review
Elkayam, U., Singh, H., Irani, A., Akhter, M. W., Anticoagulation in pregnant women with prosthetic heart valves, Journal of Cardiovascular Pharmacology & Therapeutics, 9, 107-15, 2004	Study design; non-systematic review
Fedrick, J., Butler, N. R., Warfarin anticoagulation and pregnancy, Lancet, 1, 192, 1971	Study design; letter to the editor
Garcez, Juliane Dantas Seabra, Rosa, Vitor Emer Egypto, Lopes, Antonio Sergio de Santis Andrade, Accorsi, Tarso Augusto Duenhas, Fernandes, Joao Ricardo Cordeiro, Pomerantzeff, Pablo Maria, Avila, Walkiria Samuel, Tarasoutchi, Flavio, Patient Management with Metallic Valve Prosthesis during Pregnancy and Postpartum Period, Arquivos brasileiros de cardiologia, 105, 426-9, 2015	Study design; review
Geelani, M. A., Singh, S., Verma, A., Nagesh, A., Betigeri, V., Nigam, M., Anticoagulation in patients with mechanical valves during pregnancy, Asian Cardiovascular & Thoracic Annals, 13, 30-3, 2005	Included in Xu 2016 systematic review
Ginsberg, J. S., Turpie, A. G. G., Thromboembolism and pregnancy, International Angiology, 20, 103-109, 2001	Study design; editorial
Goland, S., Schwartzenberg, S., Fan, J., Kozak, N., Khatri, N., Elkayam, U., Monitoring of anti-Xa in pregnant patients with mechanical prosthetic valves receiving low-molecular-weight heparin: peak or trough levels?, Journal of Cardiovascular Pharmacology & Therapeutics, 19, 451-6, 2014	Included in Xu 2016 systematic review
Greer, I. A., Venous thromboembolism and anticoagulant therapy in pregnancy, Gender Medicine, 2 Suppl A, S10-7, 2005	Study design; non-systematic review
Guidozzi, F., Pregnancy in patients with prosthetic cardiac valves, South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde, 65, 961-3, 1984	Included in Xu 2016 systematic review

Study	Reason for exclusion
Hassouna, A., Allam, H., Oral anticoagulation therapy during pregnancy in patients with mechanical mitral valves: a prospective study, Cardiovascular Surgery, 9, 478-81, 2001	Included in Xu 2016 systematic review
Hassouna, A., Ammar, A., Elnahas, Y., Toema, A., Allam, H., Limited dose warfarin throughout pregnancy in high-risk patients with mechanical valves: A randomized clinical trial, Egyptian Heart Journal, 67, 115-22, 2015	Comparison outside of scope; pregnant vs. non-pregnant women
Higgins, J. R., Management of valvular heart disease, Thrombosis Research, 115 Suppl 1, 32-4, 2005	Study design; non-systematic review
Hirsh, J., Cade, J. F., O'Sullivan, E. F., Clinical experience with anticoagulant therapy during pregnancy, British Medical Journal, 1, 270-3, 1970	Only 3 women from included 14 had prosthetic heart valves
Hui, C., Tan, P. S., Mok, Z. W., Tan, L. K., Mechanical prosthetic heart valves in pregnancy - The Singapore experience, BJOG: An International Journal of Obstetrics and Gynaecology, 125, 118, 2018	Conference proceedings
Huttel, E., Padberg, S., Meister, R., Beck, E., Schaefer, C., Pregnancy outcome of first trimester exposure to the vitamin K antagonist phenprocoumon depends on duration of treatment, Thrombosis and Haemostasis, 117, 870-879, 2017	Indications of phenprocoumon were not specific for prosthetic heart valve alone and the study compared with normal non-exposed pregnancy
Ibarra Perez, C., Arevalo Toledo, N., Alvarez De La Cadena, O., Noriega Guerra, L., The course of pregnancy in patients with artificial heart valves, American Journal of Medicine, 61, 504-512, 1976	Included in Xu 2016 systematic review
Iliuta, L., Candea, V., Vasilescu, A., Moldovan, H., Gherghiceanu, D. P., Macarie, C., Fraxiparine versus unfractionated heparin for the perioperative anticoagulant therapy in patients undergoing mechanical prosthetic heart valve replacement, Archives of the Balkan Medical Union, 38, 141-8, 2003	Full text unavailable
Iturbe-Alessio, I., Fonseca, M. C., Mutchinik, O., Santos, M. A., Zajarias, A., Salazar, E., Risks of anticoagulant therapy in pregnant women with artificial heart valves, New England Journal of Medicine, 315, 1390-3, 1986	Included in Xu 2016 systematic review
Izaguirre, R., De La Pena, A., Ramirez, A., Cortina, E., Huerta, M., Salazar, E., Anti-Xa activity with low-molecular-weight heparin, enoxaparin, during pregnancy in women with mechanical heart valves, Proceedings of the Western Pharmacology Society, 45, 127-8, 2002	Case series n=9 women
James, A. H., Brancazio, L. R., Gehrig, T. R., Wang, A., Ortel, T. L., Low-molecular-weight heparin for thromboprophylaxis in pregnant women with mechanical heart valves, Journal of Maternal-Fetal & Neonatal Medicine, 19, 543-9, 2006	More recent systematic review included(Xu 2016)

Study	Reason for exclusion
Javares, T., Coto, E. O., Maiques, V., Rincon, A., Such, M., Caffarena, J. M., Pregnancy after heart valve replacement, International Journal of Cardiology, 5, 731-43, 1984	Included in Xu 2016 systematic review
Kalcik, M., Bayam, E., Yesin, M., Gunduz, S., Gursoy, M. O., Karakoyun, S., Cersit, S., Kilicgedik, A., Guner, A., Kalkan, S., Erdem, A., Demirbag, R., Ozkan, M., Comparison of different anticoagulation regimens in pregnant patients with mechanical prosthetic heart valves, European Heart Journal, 38, 1271-1272, 2017	Conference abstract publication only
Kanhere, Anjali Vivek, Kanhere, Vivek Madhav, Pregnancy After Cardiac Surgery, Journal of obstetrics and gynaecology of India, 66, 10-5, 2016	Review
Kashfi, F., Samiei, N., Khamoushi, A. J., Hosseini, S., Ghavidel, A. A., Taheripanah, R., Pregnancy after mechanical mitral valve replacement, Iranian Red Crescent Medical Journal, 14, 2012	Patient population is included within the prospective Khamoushi 2011 study
Kataoka, G., Asano, R., Sato, A., Tatsuishi, W., Nakano, K., Outcomes of prosthetic valve replacement in women of child-bearing age, Surgery Today, 47, 755-761, 2017	Information on coagulation was inadequate
Kawamata,K., Neki,R., Yamanaka,K., Endo,S., Fukuda,H., Ikeda,T., Douchi,T., Risks and pregnancy outcome in women with prosthetic mechanical heart valve replacement, Circulation Journal, 71, 211-213, 2007	Included in Xu 2016 systematic review)
Khader, K. A., Saad, A. S., Abdelshafy, M., Pregnancy Outcome in Women with Mechanical Prosthetic Heart Valves Treated with Unfractionated Heparin (UFH) or Enoxaparin, Journal of Obstetrics & Gynaecology of India, 66, 321-6, 2016	Full text unavailable
Khamooshi, A. J., Kashfi, F., Hoseini, S., Tabatabaei, M. B., Javadpour, H., Noohi, F., Anticoagulation for prosthetic heart valves in pregnancy. Is there an answer?, Asian Cardiovascular & Thoracic Annals, 15, 493-6, 2007	Included in Xu 2016 systematic review
Kim, B. J., An, S. J., Shim, S. S., Jun, J. K., Yoon, B. H., Syn, H. C., Park, J. S., Pregnancy outcomes in women with mechanical heart valves, Journal of Reproductive Medicine, 51, 649-54, 2006	Better quality data already included
Kim, K. H., Dong, S. J., Ahn, H., Anticoagulation in pregnant women with a bileaflet mechanical cardiac valve replacement, Heart Surgery Forum, 10, 181-184, 2007	Included in Xu 2016 systematic review
Laros, R. K., Jr., Hage, M. L., Hayashi, R. H., Pregnancy and heart valve prostheses, Obstetrics & Gynecology, 35, 241-7, 1970	Narrative paper about 2 cases and a very short description of 22 cases of women with prosthetic cardiac valves
Larrea, J. L., Nunez, L., Reque, J. A., Gil Aguado, M., Matarros, R., Minguez, J. A., Pregnancy and	Better quality data already included

Study	Reason for exclusion
mechanical valve prostheses: a high-risk situation for the mother and the fetus, Annals of Thoracic Surgery, 36, 459-63, 1983	
Lecuru,F., Desnos,M., Taurelle,R., Anticoagulant therapy in pregnancy. Report of 54 cases, Acta Obstetricia et Gynecologica Scandinavica, 75, 217-221, 1996	Not population of interest - women requiring anticoagulation, not all women had prosthetic valves
Lee, C. N., Wu, C. C., Lin, P. Y., Hsieh, F. J., Chen, H. Y., Pregnancy following cardiac prosthetic valve replacement, Obstetrics & Gynecology, 83, 353-6, 1994	Included in Xu 2016 systematic review
Lee, P. K., Wang, R. Y., Chow, J. S., Cheung, K. L., Wong, V. C., Chan, T. K., Combined use of warfarin and adjusted subcutaneous heparin during pregnancy in patients with an artificial heart valve, Journal of the American College of Cardiology, 8, 221-4, 1986	Retrospective case series - better quality data already included
Lee,J.H., Park,N.H., Keum,D.Y., Choi,S.Y., Kwon,K.Y., Cho,C.H., Low molecular weight heparin treatment in pregnant women with a mechanical heart valve prosthesis, Journal of Korean Medical Science, 22, 258-261, 2007	Included in Xu 2016 systematic review
Lesniak-Sobelga, A. M., Kostkiewicz, M., Wisniowska-Smialek, S., Holcman, K., Hlawaty, M., Biernacka-Fijalkowska, B., Rubis, P., Podolec, P., Pregnancy and fetal outcome in patients with implanted mechanical prostheses-29 years experience, European Heart Journal, 37, 1368-1369, 2016	Conference abstract publication
Lesniak-Sobelga, A., Tracz, W., Kostkiewicz, M., Clinical and echocardiographic assessment of pregnant patients with prosthetic and homograft heart valves: Maternal and fetal outcome, Acta Cardiologica, 62, 637-638, 2007	Conference abstract publication only
Limet, R., Grondin, C. M., Cardiac valve prostheses, anticoagulation, and pregnancy, Annals of Thoracic Surgery, 23, 337-341, 1977	Included in Xu 2016 systematic review
Lu, E., Shatzel, J. J., Salati, J., Deloughery, T. G., The Safety of Low-Molecular-Weight Heparin during and after Pregnancy, Obstetrical and Gynecological Survey, 72, 721-729, 2017	Review of guidelines
Lu, Z., Zhuang, X., Feifei, L., Comparison of two anticoagulation strategies for pregnant women with mechanical valves, Journal of the American College of Cardiology, 70, C154, 2017	Conference abstract publication only
Lutz,D.J., Noller,K.L., Spittell,J.A.,Jr., Danielson,G.K., Fish,C.R., Pregnancy and its complications following cardiac valve prostheses, American Journal of Obstetrics and Gynecology, 131, 460-468, 1978	Included in Xu 2016 systematic review
Malekzadeh-Milani, S., Ladouceur, M., Gaillard, T., Khimoud, D., Pontnau, F., Iserin, L., Nizard, J., Boudjemline, Y., Pregnancy in women with	Conference abstract publication

Study	Reason for exclusion
percutaneous pulmonary valve implantation, Cardiology in the Young, 26, S119, 2016	
Malik, H. T., Sepehripour, A. H., Shipolini, A. R., McCormack, D. J., Is there a suitable method of anticoagulation in pregnant patients with mechanical prosthetic heart valves?, Interactive Cardiovascular and Thoracic Surgery, 15, 484-488, 2012	More recent systematic review included (Xu 2016)
Matorras, R., Reque, J. A., Usandizaga, J. A., Prosthetic heart valve and pregnancy. A study of 59 cases, Gynecologic and Obstetric Investigation, 19, 21-31, 1985	Included in Xu 2016 systematic review
McLintock,C., McCowan,L.M., North,R.A., Maternal complications and pregnancy outcome in women with mechanical prosthetic heart valves treated with enoxaparin, BJOG: An International Journal of Obstetrics and Gynaecology, 116, 1585-1592, 2009	Included in Xu 2016
Meschengieser, S., Fondevila, C., Santarelli, M., Lazzari, M., Anticoagulation in pregnant women with mechanical heart valve prostheses, Heart, 82, 23-26, 1999	The study compared oral anticoagulants with heparin in first trimester (<24 weeks gestation)
Meschengieser,S.S., Fondevila,C.G., Santarelli,M.T., Lazzari,M.A., Anticoagulation in pregnant women with mechanical heart valve prostheses, Heart, 82, 23-26, 1999	Included in Xu 2016 systematic review
Mihaljevic,T., Paul,S., Leacche,M., Rawn,J.D., Cohn,L.H., Byrne,J.G., Valve replacement in women of childbearing age: influences on mother, fetus and neonate, Journal of Heart Valve Disease, 14, 151-157, 2005	Included in Xu 2016 systematic review
Moinipoor, A. A., Shamlou, A. S., Lotfalizadeh, M., Esfehanizadeh, J., Mottahedi, B., Hosseini, H., Evaluation of last guidelines and studies about the best treatment with anticoagulant during pregnancy in woman with mechanical heart valves, Iranian Journal of Obstetrics, Gynecology and Infertility, 18, 15-19, 2015	Full text unavailable
Monteiro, A. V., Rebelo, J., Patricio, L., Campos, A., Borges, A., Ferreira, R. C., Ten Years' Experience of Pregnancy Outcomes in Women with Cardiac Valvulopathies: Are Valve Prostheses Worst?, Journal of Heart Valve Disease, 24, 368-75, 2015	No comparison of interest - comparison of women with valvular heart prostheses and women with valvular heart disease
Monteiro, Andre Viveiros, Rebelo, Joana, Patricio, Lino, Campos, Ana, Borges, Augusta, Ferreira, Rui Cruz, Ten Years' Experience of Pregnancy Outcomes in Women with Cardiac Valvulopathies: Are Valve Prostheses Worst?, The Journal of heart valve disease, 24, 368-75, 2015	Retrospective study
Nanas, J. N., Kontoyannis, S. A., Mitsibounas, D. N., Stamatelopoulos, S. F., Thrombolytic treatment for thrombosis of a mitral valve	A case report (n=1)

Study	Reason for exclusion
prosthesis during pregnancy, Intensive Care Medicine, 27, 1668-1669, 2001	
Nassar, A. H., Hobeika, E. M., Abd Essamad, H. M., Taher, A., Khalil, A. M., Usta, I. M., Pregnancy outcome in women with prosthetic heart valves, American Journal of Obstetrics & Gynecology, 191, 1009-13, 2004	Included in Xu 2016 systematic review
Oakley, C., Doherty, P., Proceedings: Pregnancy after valve replacement, British Heart Journal, 38, 876, 1976	Duplicate reference
O'Neill, H., Blake, S., Sugrue, D., Macdonald, D., Problems in the management of patients with artificial valves during pregnancy, British Journal of Obstetrics & Gynaecology, 89, 940-3, 1982	Included in Xu 2016 systematic review
Oran, B., Lee-Parritz, A., Ansell, J., Low molecular weight heparin for the prophylaxis of thromboembolism in women with prosthetic mechanical heart valves during pregnancy, Thrombosis & Haemostasis, 92, 747-51, 2004	More recent systematic review included (Xu 2016)
Pajszczyk-Kieszkiewicz, T., Krzeminska-Pakula, M., Kowalska-Koprek, U., Zaslonka, J., Zaslonka, A., Pregnancy in women with valvular prostheses--follow-up observations, Zeitschrift fur Kardiologie, 75 Suppl 2, 308-11, 1986	Duplicate reference
Pandey, U., To study the maternal and neonatal outcomes of pregnancies complicated by rheumatic heart disease, International Journal of Infertility and Fetal Medicine, 5, 92-94, 2014	Retrospective study
Parry, H., English, K., Oliver, J., Cullington, D., Ciantar, E., Simpson, N., Winfield, S., Norfolk, D., Are complications during pregnancy in women with mechanical heart valves influenced by their choice of anticoagulation?, Heart, 103, A57, 2017	Conference abstract publication only
Pavunkumar, P., Venugopal, P., Kaul, U., Iyer, K. S., Das, B., Sampathkumar, A., Airon, B., Rao, I. M., Sharma, M. L., Bhatia, M. L., Gopinath, N., Pregnancy in patients with prosthetic cardiac valve. A 10-year experience, Scandinavian Journal of Thoracic and Cardiovascular Surgery, 22, 19-22, 1988	Included in Xu 2016 systematic review
Plesinac, S. D., Darko, P. V., Pilic, I. Z., Babovic, I. R., Anticoagulation therapy during pregnancy of patients with artificial heart valves: fetomaternal outcome, Archives of Gynecology & Obstetrics, 274, 141-5, 2006	Not the comparison of interest: ethylbiscumacetate (Pelenthan) used
Popelova, J., Zatocil, T., Vavera, Z., Palecek, T., Ostransky, J., Lhotsky, J., Rubacek, M., Gebauer, R., Mechanical heart valve prosthesis in pregnancy - multicenter retrospective observational study, Cor et Vasa.	Better quality data already included
Pridmore, B. R., Murray, K. H., McAllen, P. M., The management of anticoagulant therapy during and after pregnancy, British Journal of Obstetrics & Gynaecology, 82, 740-4, 1975	Not the population of interest - no women with prosthetic heart valves included

Study	Reason for exclusion
Quinn, J., Von Klemperer, K., Brooks, R., Peebles, D., Walker, F., Cohen, H., Use of high intensity adjusted dose low molecular weight heparin in women with mechanical heart valves during pregnancy: a single-center experience, Haematologica, 94, 1608-12, 2009	Included in Xu 2016 systematic review
Rowan, J. A., McCowan, L. M., Raudkivi, P. J., North, R. A., Enoxaparin treatment in women with mechanical heart valves during pregnancy, American Journal of Obstetrics & Gynecology, 185, 633-7, 2001	Included in Xu 2016 systematic review
Sadler, L., McCowan, L., White, H., Stewart, A., Bracken, M., North, R., Pregnancy outcomes and cardiac complications in women with mechanical, bioprosthetic and homograft valves, BJOG: An International Journal of Obstetrics & Gynaecology, 107, 245-53, 2000	Included in Xu 2016 systematic review
Saeed, C. R., Frank, J. B., Pravin, M., Aziz, R. H., Serasheini, M., Dominique, T. G., A prospective trial showing the safety of adjusted-dose enoxaparin for thromboprophylaxis of pregnant women with mechanical prosthetic heart valves, Clinical & Applied Thrombosis/Hemostasis, 17, 313-9, 2011	Included in Xu 2016 systematic review
Salazar, E., Izaguirre, R., Verdejo, J., Mutchinick, O., Elkayam, U., Failure of adjusted doses of subcutaneous heparin to prevent thromboembolic phenomena in pregnant patients with mechanical cardiac valve prostheses, Journal of the American College of Cardiology, 27, 1698-1706, 1996	Included in Xu 2016 systematic review
Salazar,E., Zajarias,A., Gutierrez,N., Iturbe,I., The problem of cardiac valve prostheses, anticoagulants, and pregnancy, Circulation, 70, I169-I177, 1984	Included in Xu 2016 systematic review
Samiei, N., Kashfi, F., Khamoushi, A., Hosseini, S., Ghavidel, A. A., Taheripanah, R., Mirmesdagh, Y., Pregnancy outcome after mechanical mitral valve replacement: A prospective study, Journal of Tehran University Heart Center, 7, 117-20, 2012	Included in Xu 2016 systematic review
Sbarouni, E., Oakley, C. M., Outcome of pregnancy in women with valve prostheses, British Heart Journal, 71, 196-201, 1994	Included in Xu 2016 systematic review
Seshadri, N., Goldhaber, S. Z., Elkayam, U., Grimm, R. A., Groce, J. B., 3rd, Heit, J. A., Spinler, S. A., Turpie, A. G., Bosker, G., Klein, A. L., The clinical challenge of bridging anticoagulation with low-molecular-weight heparin in patients with mechanical prosthetic heart valves: an evidence-based comparative review focusing on anticoagulation options in pregnant and nonpregnant patients, American Heart Journal, 150, 27-34, 2005	A narrative review about anticoagulation with low-molecular-weight heparin in patients with mechanical prosthetic heart valves

Study	Reason for exclusion
Shannon, M. S., Edwards, M. B., Long, F., Taylor, K. M., Bagger, J. P., De Swiet, M., Anticoagulant management of pregnancy following heart valve replacement in the United Kingdom, 1986-2002, Journal of Heart Valve Disease, 17, 526-32, 2008	Included in Xu 2016 systematic review
Shapiro, N. L., Kominiarek, M. A., Nutescu, E. A., Chevalier, A. B., Hibbard, J. U., Dosing and monitoring of low-molecular-weight heparin in high-risk pregnancy: Single-center experience, Pharmacotherapy, 31, 678-685, 2011	Not population of interest - women requiring anticoagulation, not all have valve prosthesis
Sheikhzadeh, A., Ghabusi, P., Hakim, S., Wendler, G., Sarram, M., Tarbiat, S., Congestive heart failure in valvular heart disease in pregnancies with and without valvular prostheses and anticoagulant therapy, Clinical Cardiology, 6, 465-70, 1983	Not the comparison of interest: pregnant women with valvular disease without valve replacement and without anticoagulant therapy vs women with prosthetic valve replacement and under anti-coagulation therapy
Sillesen,M., Hjortdal,V., Vejlstrup,N., Sorensen,K., Pregnancy with prosthetic heart valves - 30 years' nationwide experience in Denmark, European Journal of Cardio-thoracic Surgery, 40, 448-454, 2011	Not the comparison on interest (drug A vs drug B)
Snape, E., Thachil, J., Clarke, B., Vause, S., Anti-Xa based dose changes during low molecular weight heparin anticoagulation for mechanical prosthetic heart valves during pregnancy, Journal of Obstetrics and Gynaecology, 1-2, 2018	Case series (evidence for LMWH was already available from comparative studies)
Srivastava, A. R., Modi, P., Sahi, S., Niwariya, Y., Singh, H., Banerjee, A., Anticoagulation for pregnant patients with mechanical heart valves, Annals of Cardiac Anaesthesia, 10, 95-107, 2007	A narrative review about risk assessment, anticoagulants and complications in women with mechanical valves
Srivastava,A.K., Gupta,A.K., Singh,A.V., Husain,T., Effect of oral anticoagulant during pregnancy with prosthetic heart valve, Asian Cardiovascular and Thoracic Annals, 10, 306-309, 2002	Not the comparison on interest (drug A vs drug B)
Steinberg, Zachary L., Dominguez-Islas, Clara P., Otto, Catherine M., Stout, Karen K., Krieger, Eric V., Maternal and Fetal Outcomes of Anticoagulation in Pregnant Women With Mechanical Heart Valves, Journal of the American College of Cardiology, 69, 2681-2691, 2017	Systematic review: included studies being checked for relevancy
Suri,V., Keepanasseril,A., Aggarwal,N., Chopra,S., Bagga,R., Sikka,P., Vijayvergiya,R., Mechanical valve prosthesis and anticoagulation regimens in pregnancy: a tertiary centre experience, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 159, 320-323, 2011	Included in Xu 2016 systematic review
Tanaka, H., Tanaka, K., Kamiya, C., Iwanaga, N., Katsuragi, S., Yoshimatsu, J., Analysis of anticoagulant therapy by unfractionated heparin during pregnancy after mechanical valve replacement, Circulation Journal, 78, 878-81, 2014	Included in Xu 2016 systematic review

Study	Reason for exclusion
Tounsi, A. , Abid, D., Louati, D., Mallek, S., Akrout, M., Abid, L., Abdennadher, M., Frikha, I., Chaabene, K., Hentati, M., Kammoun, S., Anticoagulation in Pregnant Women with Mechanical Heart Valve Prostheses: 25-Year Experience at a Tertiary Care Hospital in a Developing Country, World Journal of Cardiovascular Diseases, 4, 287-293, 2014	Comparison of acenocoumarol with UFH in first trimester (i.e. < 12 weeks gestation)
van Hagen, I. M., Roos-Hesselink, J. W., Ruys, T. P., Merz, W. M., Goland, S., Gabriel, H., Lelonek, M., Trojnarska, O., Al Mahmeed, W. A., Balint, H. O., Ashour, Z., Baumgartner, H., Boersma, E., Johnson, M. R., Hall, R., Ropac Investigators, the, EURObservational Research Programme Team, Pregnancy in Women With a Mechanical Heart Valve: Data of the European Society of Cardiology Registry of Pregnancy and Cardiac Disease (ROPAC), Circulation, 132, 132-42, 2015	Included in Xu 2016 systematic review
Verhamme, Peter, Herregods, Marie-Christine, Van de Werf, Frans, Anticoagulation of pregnant women with mechanical heart valves: protecting mother or child?, European Heart Journal, 38, 1517-1519, 2017	Review
Vitali, E., Donatelli, F., Quaini, E., Groppelli, G., Pellegrini, A., Pregnancy in patients with mechanical prosthetic heart valves. Our experience regarding 98 pregnancies in 57 patients, Journal of Cardiovascular Surgery, 27, 221-7, 1986	Included in Xu 2016 systematic review
Vural,K.M., Ozatik,M.A., Uncu,H., Emir,M., Yurdagok,O., Sener,E., Tasdemir,O., Pregnancy after mechanical mitral valve replacement, Journal of Heart Valve Disease, 12, 370-376, 2003	Better quality data already included
Wang, E. H., Marnoch, C. A., Khurana, R., Sia, W., Yuksel, N., Haemorrhagic complications of peripartum anticoagulation: A retrospective chart review, Obstetric Medicine, 7, 77-83, 2014	Not clear how many (if any at all) women with prosthetic heart valves were included
Wang, Erica Hz, Marnoch, Catherine A., Khurana, Rshmi, Sia, Winnie, Yuksel, Nese, Haemorrhagic complications of peripartum anticoagulation: A retrospective chart review, Obstetric medicine, 7, 77-83, 2014	Retrospective chart review
Wang, J., Li, K., Li, H., Zhu, W., Sun, H., Lu, C., Comparison of anticoagulation regimens for pregnant women with prosthetic heart valves: A meta-analysis of prospective studies, Cardiovascular Therapeutics, 35, e12292, 2017	Systematic review and included studies being checked for relevancy
Wang, Jing, Li, Kangqi, Li, Hongyan, Zhu, Weiwei, Sun, Haiyan, Lu, Congxiao, Comparison of Anticoagulation Regimens for Pregnant Women with Prosthetic Heart Valves: A Meta-analysis of Prospective Studies, Cardiovascular therapeutics, 2017	Systematic review: included studies being checked for relevancy

Study	Reason for exclusion
Wang, R. Y., Lee, P. K., Chow, J. S., Chen, W. W., Efficacy of low-dose, subcutaneously administered heparin in treatment of pregnant women with artificial heart valves, Medical Journal of Australia, 2, 126-8, 1983	No relevant comparison - all women received the same anticoagulant therapy
Yarrington, Christina D., Valente, Anne Marie, Economy, Katherine E., Cardiovascular Management in Pregnancy: Antithrombotic Agents and Antiplatelet Agents, Circulation, 132, 1354-64, 2015	Review
Yinon, Y., Siu, S. C., Warshafsky, C., Maxwell, C., McLeod, A., Colman, J. M., Sermer, M., Silversides, C. K., Use of low molecular weight heparin in pregnant women with mechanical heart valves, American Journal of Cardiology, 104, 1259-63, 2009	Included in Xu 2016 systematic review

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – mode of birth

Clinical studies

Study	Reason for exclusion
Asfour,V., Murphy,M.O., Attia,R., Is vaginal delivery or caesarean section the safer mode of delivery in patients with adult congenital heart disease?, Interactive Cardiovascular and Thoracic Surgery, 17, 144-150, 2013	Systematic review; no relevant studies included
Autore, C., Conte, M. R., Piccininno, M., Bernabo, P., Bonfiglio, G., Bruzzi, P., Spirito, P., Risk associated with pregnancy in hypertrophic cardiomyopathy, Journal of the American College of Cardiology, 40, 1864-9, 2002	Comparison outside of scope; pregnant women hypertrophic cardiomyopathy vs. general population
Avila, W. S., Rossi, E. G., Ramires, J. A., Grinberg, M., Bortolotto, M. R., Zugaib, M., da Luz, P. L., Pregnancy in patients with heart disease: experience with 1,000 cases, Clinical Cardiology, 26, 135-42, 2003	Study design; case series
Benatta, N., Batouche, D., Cardiac complications of deliverance and modality of delivery in mitral stenosis about 83 cases, Archives of Cardiovascular Diseases Supplements, 10, 70-71, 2018	Conference proceedings
Bharti, R., Sharma, M., Gaikwad, H. S., Tripathi, V., Ahmed, A., Batra, A., Evaluation of maternal and fetal outcome in pregnancy with congenital heart disease, Indian Journal of Public Health Research and Development, 3, 246-249, 2012	Full text article unavailable
Boyle, R. K., Anaesthesia in parturients with heart disease: a five year review in an Australian tertiary	Comparison outside of scope

Study	Reason for exclusion
hospital, International Journal of Obstetric Anesthesia, 12, 173-7, 2003	
Cauldwell, M., Steer, P., Coats, L., Hodson, K., Head, C., Jakes, A., Bonner, S., Maudin, L., Abraham, D., English, K., Walker, N., Simpson, M., Bolger, A., Siddiqui, F., Johnson, M., Pregnancy outcomes in a cohort of women with a Fontan repair: A UK multicentre study, European Heart Journal, 38, 212, 2017	The study did not report the reason for the choice of mode of birth
Cauldwell, M., Von Klemperer, K., Uebing, A., Swan, L., Steer, P. J., Gatzoulis, M., Johnson, M. R., Why is post-partum haemorrhage more common in women with congenital heart disease?, International Journal of Cardiology, 218, 285-90, 2016	Outcomes not linked to C-section intervention
Chhetri, S., Shrestha, N. R., Pilgrim, T., Pregnancy complicated by heart disease in Nepal, Heart Asia, 6, 26-9, 2014	Intervention data not linked to cardiac factors and outcome not disaggregated by intervention
Chhetri, Shailaja, Shrestha, Nikesh Raj, Pilgrim, Thomas, Pregnancy complicated by heart disease in Nepal, Heart Asia, 6, 26-9, 2014	The study did not report the reason for the choice of mode of birth and the study was conducted in a low resource country
Constantine, A. H., Kempny, A., Swan, L., Gatzoulis, M. A., Wort, S. J., Dimopoulos, K., Pregnancy in adults with congenital heart disease in England: Birth rate and delivery practices between 1997 and 2014, European Heart Journal, 38, 212, 2017	Conference proceedings
Desai,D.K., Adanlawo,M., Naidoo,D.P., Moodley,J., Kleinschmidt,I., Mitral stenosis in pregnancy: a four-year experience at King Edward VIII Hospital, Durban, South Africa, BJOG: An International Journal of Obstetrics and Gynaecology, 107, 953-958, 2000	Indications for intervention were obstetric not cardiac
Diao, M., Ndiaye, M. B., Mbaye, A., Bodian, M., Dia, M. M., Sarr, M., Kane, A., Monsuez, J. J., Ba, S. A., Pregnancy in women with heart disease in sub-Saharan Africa la grossesse des femmes atteintes de cardiopathie en Afrique subsaharienne, Archives of Cardiovascular Diseases, 104, 370-374, 2011	Case series, outcomes not disaggregated by intervention
Dolgun, Z. N., Inan, C., Sayin, N. C., Maternal and fetal outcomes in pregnancies with pulmonary hypertension: Experience of a tertiary center, Taiwanese Journal of Obstetrics and Gynecology, 57, 13-17, 2018	The study did not report the reason for the choice of mode of birth
Doshi,H.U., Oza,H.V., Tekani,H., Modi,K., Cardiac disease in pregnancy - Maternal and perinatal outcome, Journal of the Indian Medical Association, 108, 278-282, 2010	Indications for caesarean section were obstetric not cardiac
Easter, S. R., Rouse, C. E., Duarte, V. E., Schreier, J., Singh, M., Valente, A. M., Economy, K. E., Planned mode of delivery and maternal morbidity in women with cardiac disease in	Conference proceedings

Study	Reason for exclusion
pregnancy, American Journal of Obstetrics and Gynecology, 218, S468-S469, 2018	
English, K., Ulivi, G., Oliver, J., Winfield, S., Everett, T., Simms, A., Lansbury, A., Aortic stenosis in pregnancy outcomes of a combined cardiac & obstetric antenatal clinic, Cardiology in the Young, 27, S97, 2017	Conference proceedings
Fraser, D., Cracked pitchers, Proceedings of the Royal Society of Medicine, 64, 629-32, 1971	Study design; case series
Furenas, E., Eriksson, P., Wennerholm, U. B., Dellborg, M., Effect of maternal age and cardiac disease severity on outcome of pregnancy in women with congenital heart disease, International Journal of Cardiology, 243, 197-203, 2017	Outcomes were not disaggregated by mode of birth
Goya, M., Casellas, M., Merced, C., Pijuan-Domenech, A., Galian, L., Dos, L., Casaldaliga, J., Subirana, M., Pedrosa, V., Rojas, M., Martinez, C., Ferreira, I., Monts, M., Gascon, A., Mendoza, M., Baro, F., Suy, A., Lopez-Gil, V., Manrique, S., Tornos, P., Garcia-Dorado, D., Carreras, E., Cabero, L., Predictors of obstetric complications in women with heart disease, Journal of Maternal-Fetal and Neonatal Medicine, 29, 2306-2311, 2016	Intervention is unclear and outcomes not reported by intervention group
Grassmann, C., Henry, O., Peripartum outcomes and the anaesthetic management of parturients with mild to moderate congenital heart disease, Anaesthesia, 72, 54, 2017	Conference proceedings
Grewal, J., Siu, S. C., Ross, H. J., Mason, J., Balint, O. H., Sermer, M., Colman, J. M., Silversides, C. K., Pregnancy outcomes in women with dilated cardiomyopathy, Journal of the American College of Cardiology, 55, 45-52, 2009	No relevant comparison; caesarean section was not performed for cardiac indications in any of the women
Grigoriu, A. C., Colman, J., Silversides, C. K., Wald, R., Siu, S. C., Sermer, M., Marfan syndrome and pregnancy: Clinical implications and management, Fetal and Maternal Medicine Review, 21, 225-241, 2010	Full text article not available
Hawes, R., Wilson, V., Newton, R., Ten Klooster, L., Kiely, D., Condliffe, R., Elliot, C., Gandhi, S., Safe delivery of parturients with pulmonary hypertension: 16 years' experience in a national specialist referral centre, Anaesthesia, 72, 56, 2017	Conference proceedings
Hidano,G., Uezono,S., Terui,K., A retrospective survey of adverse maternal and neonatal outcomes for parturients with congenital heart disease, International Journal of Obstetric Anesthesia, 20, 229-235, 2011	Intervention is unclear, outcomes are not presented by intervention group
Hrycyk, J., Kaemmerer, H., Nagdyman, N., Hamann, M., Schneider, K. T. M., Kuschel, B., Mode of delivery and pregnancy outcome in	Study design; case series

Study	Reason for exclusion
women with congenital heart disease, PLoS ONE, 11, e0167820, 2016	
Isogai, T., Matsui, H., Tanaka, H., Kohyama, A., Fushimi, K., Yasunaga, H., Clinical features and peripartum outcomes in pregnant women with cardiac disease: a nationwide retrospective cohort study in Japan, Heart and Vessels, 1-13, 2018	The study did not report the reason for mode of birth
Iung, B., Cormier, B., Elias, J., Michel, P. L., Nallet, O., Porte, J. M., Sananes, S., Uzan, S., Vahanian, A., Acar, J., Usefulness of percutaneous balloon commissurotomy for mitral stenosis during pregnancy, American Journal of Cardiology, 73, 398-400, 1994	No outcomes reported
Kaleschke, G., Baumgartner, H., Pregnancy and heart disease: Pregnancy in congenital and valvular heart disease, Heart, 97, 1803-1809, 2011	Study design; non-systematic review
Khairy, P., Ouyang, D. W., Fernandes, S. M., Lee-Parritz, A., Economy, K. E., Landzberg, M. J., Pregnancy outcomes in women with congenital heart disease, Circulation, 113, 517-24, 2006	No relevant comparison
Kinsella, C., Thorne, S. A., Clift, P. F., Hudsmith, L. E., Bowater, S., Vasallo Peraza, R., Perez Torga, J. E., Roman Rubio, P. A., Managing delivery in women with congenital heart disease: Results from the Cuban National Programme for Pregnancy and Heart Disease, Heart, 104, A11, 2018	Conference proceedings
Krul, S. P. J., Van Der Smagt, J. J., Van Den Berg, M. P., Sollie, K. M., Pieper, P. G., Van Spaendonck-Zwarts, K. Y., Systematic review of pregnancy in women with inherited cardiomyopathies, European Journal of Heart Failure, 13, 584-594, 2011	Systematic review; no relevant studies included
Lawley, C. M., Lain, S. J., Algert, C. S., Ford, J. B., Figtree, G. A., Roberts, C. L., Prosthetic heart valves in pregnancy, outcomes for women and their babies: A systematic review and meta-analysis, BJOG: An International Journal of Obstetrics and Gynaecology, 122, 1446-1455, 2015	Systematic review; no relevant studies included
Lesniak-Sobelga, A. M., Kostkiewicz, M., Wisniowska-Smialek, S., Holcman, K., Hlawaty, M., Podolec, P., Paul, J., Echocardiographic study of pregnant patients with bicuspid aortic valve, European Heart Journal Cardiovascular Imaging, 18, 2017	Conference proceedings
Lesniak-Sobelga, A., Tracz, W., Kostkiewicz, M., Clinical and echocardiographic assessment of pregnant patients with prosthetic and homograft heart valves: Maternal and fetal outcome, Acta Cardiologica, 62, 637-638, 2007	Outcomes not disaggregated by intervention
Li, W., Li, H., Long, Y., Clinical Characteristics and Long-term Predictors of Persistent Left	Outcomes not disaggregated by intervention

Study	Reason for exclusion
Ventricular Systolic Dysfunction in Peripartum Cardiomyopathy, Canadian Journal of Cardiology, 32, 362-368, 2016	
Lima, F. V., Koutrolou-Sotiropoulou, P., Yen, T. Y., Stergiopoulos, K., Clinical characteristics and outcomes in pregnant women with Ebstein anomaly at the time of delivery in the USA: 2003-2012, Archives of Cardiovascular Diseases, 109, 390-8, 2016	Outcomes not disaggregated by intervention. C-section comparison with healthy control
Ma, L., Liu, W., Huang, Y., Perioperative management for parturients with pulmonary hypertension: experience with 30 consecutive cases.[Erratum appears in Front Med. 2013 Sep;7(3):395], Fronteras en Medicina, 6, 307-10, 2012	Outcomes not disaggregated by intervention. Study design; case series
Maki, J., Hiramatu, Y., Masuyama, H., Akagi, T., The perinatal outcomes of pregnant women with heart disease in Okayama University Hospital and towards the future, Journal of Obstetrics and Gynaecology Research, 43, 59-60, 2017	Conference proceedings
McFaul, P. B., Dornan, J. C., Lamki, H., Boyle, D., Pregnancy complicated by maternal heart disease. A review of 519 women, British Journal of Obstetrics & Gynaecology, 95, 861-7, 1988	Study design; case series
Meijer, J. M., Pieper, P. G., Drenthen, W., Voors, A. A., Roos-Hesselink, J. W., Van Dijk, A. P. J., Mulder, B. J. M., Ebels, T., Van Veldhuisen, D. J., Pregnancy, fertility, and recurrence risk in corrected tetralogy of Fallot, Heart, 91, 801-805, 2005	Some details on C-section for cardiac reasons but not linked to outcomes
Meng, M. L., Landau, R., Viktorsdottir, O., Banayan, J., Grant, T., Bateman, B., Smiley, R., Reitman, E., Pulmonary hypertension in pregnancy a report of 49 cases at four tertiary north American sites, Obstetrics and Gynecology, 129, 511-520, 2017	Study design; non-comparative study
Michaelson-Cohen,R., Elstein,D., Ioscovich,A., Armon,S., Schimmel,M.S., Butnaru,A., Samueloff,A., Grisaru-Granovsky,S., Severe heart disease complicating pregnancy does not preclude a favourable pregnancy outcome: 15 years' experience in a single centre, Journal of Obstetrics and Gynaecology, 31, 597-602, 2011	Outcomes not linked to intervention
Milleron, O., Baghdadi, D., Langeois, M., Spentchian, M., Arnoult, F., Delorme, G., Jondeau, G., Aortic dissection in Marfan syndrome: Is Bicuspid aortic valve a risk factor?, European Heart Journal, 37, 451-452, 2016	Conference proceedings
Monagle, John, Manikappa, Shashikanth, Ingram, Brendan, Malkoutzis, Vangy, Pulmonary hypertension and pregnancy: the experience of a tertiary institution over 15 years, Annals of cardiac anaesthesia, 18, 153-60, 2015	Study design; non-comparative study

Study	Reason for exclusion
Naguib,M.A., Dob,D.P., Gatzoulis,M.A., A functional understanding of moderate to complex congenital heart disease and the impact of pregnancy. Part II: tetralogy of Fallot, Eisenmenger's syndrome and the Fontan operation, International Journal of Obstetric Anesthesia, 19, 306-312, 2010	Study design; non-systematic review
Niswonger,J.W., Langmade,C.F., Cardiovascular changes in vaginal deliveries and cesarean sections, American Journal of Obstetrics and Gynecology, 107, 337-344, 1970	Population outside of scope
Oakley, G. D., McGarry, K., Limb, D. G., Oakley, C. M., Management of pregnancy in patients with hypertrophic cardiomyopathy, British Medical Journal, 1, 1749-50, 1979	Study design; case series
Ouyang,D.W., Khairy,P., Fernandes,S.M., Landzberg,M.J., Economy,K.E., Obstetric outcomes in pregnant women with congenital heart disease, International Journal of Cardiology, 144, 195-199, 2010	No relevant comparison (risk factors for adverse obstetric events), all C-sections were for obstetric reasons except 1
Owens, A., Lima, F. V., Nie, L., Yang, J., Avila, C., Stergiopoulos, K., Impact of heart disease during pregnancy on maternal cardiac and obstetric outcomes, Obstetrics and Gynecology, 129, 130S, 2017	Conference proceedings
Pieper,P.G., Balci,A., Aarnoudse,J.G., Kampman,M.A.M., Sollie,K.M., Groen,H., Mulder,B.J.M., Oudijk,M.A., Roos-Hesselink,J.W., Cornette,J., Van Dijk,A.P.J., Spaanderman,M.E., Drenthen,W., Van Veldhuisen,D.J., Uteroplacental blood flow, cardiac function, and pregnancy outcome in women with congenital heart disease, Circulation, 128, 2478-2487, 2013	No relevant comparison
Pippen, J., Koonce, J., Frischhertz, B., Markham, L., Thompson, J., Maternal and neonatal outcomes in women with congenital heart disease at a single academic center, Obstetrics and Gynecology, 129, 130S, 2017	Abstract publication only
Puri, V. K., Isser, H. S., Cardiac diseases and pregnancy, Journal of Internal Medicine of India, 1, 31-37, 1998	Narrative review
Radetskaya, L., Makatsariya, A., Hemorrhage risk evaluation during pregnancy and caesarean section in patients with mesenchymal dyplasia (Marfan syndrome, Ehlers-Danloss syndrome, hereditary hemorrhagic telangiectasia), Thrombosis Research, 151, S108-S109, 2017	Abstract publication only
Richards,N.A., Yentis,S.M., Anaesthesia, analgesia and peripartum management in women with pre-existing cardiac and respiratory disease, Fetal and Maternal Medicine Review, 17, 327-347, 2006	Narrative review
Robertson,J.E., Silversides,C.K., Mah,M.L., Kulikowski,J., Maxwell,C., Wald,R.M.,	No relevant comparison

Study	Reason for exclusion
Colman,J.M., Siu,S.C., Sermer,M., A contemporary approach to the obstetric management of women with heart disease, Journal of Obstetrics and Gynaecology Canada: JOGC, 34, 812-819, 2012	
Roos-Hesselink, J. W., Ruys, T. P. E., Stein, J. I., Thilen, U., Webb, G. D., Niwa, K., Kaemmerer, H., Baumgartner, H., Budts, W., Maggioni, A. P., Tavazzi, L., Taha, N., Johnson, M. R., Hall, R., Outcome of pregnancy in patients with structural or ischaemic heart disease: Results of a registry of the European Society of Cardiology, European Heart Journal, 34, 657-665, 2013	No relevant comparison
Sepehripour, A. H., Lo, T. T., Shipolini, A. R., McCormack, D. J., Can pregnant women be safely placed on cardiopulmonary bypass?, Interactive Cardiovascular & Thoracic Surgery, 15, 1063-70, 2012	Irrelevant intervention
Sharma, P., Obstetric outcome in patients with rheumatic heart disease: Experience of a tertiary hospital, Nepalese Heart Journal, 14, 31-34, 2017	Descriptive study
Sharshiner, R., Pare, E., Burchill, L. J., Broberg, C. S., Khan, A., Mode of delivery in women with congenital heart disease: A survey of congenital cardiac health care providers, American Journal of Obstetrics and Gynecology, 216 (1 Supplement 1), S407, 2017	Abstract publication only
Sharshiner, R., Pare, E., Clennon, E. K., Bullard, K. A., Caughey, A. B., Does mode of delivery in women with congenital heart disease vary by cardiac lesion?, American Journal of Obstetrics and Gynecology, 216, S520-S521, 2017	Abstract publication only
Sidlik,R., Sheiner,E., Levy,A., Wiznitzer,A., Effect of maternal congenital heart defects on labor and delivery outcome: a population-based study, Journal of Maternal-Fetal and Neonatal Medicine, 20, 211-216, 2007	Mode of birth as outcome with frequency presented by Congenital Heart Disease vs Control women
Sillesen,M., Hjortdal,V., Vejlstrup,N., Sorensen,K., Pregnancy with prosthetic heart valves - 30 years' nationwide experience in Denmark, European Journal of Cardio-thoracic Surgery, 40, 448-454, 2011	Mode of birth data presented for women with mechanical valves vs control group, and outcomes not presented by intervention group
Singh, A., Agrawal, S., Samra, K., Saluja, S., Tariq, U., Garg, L., Aurshiya, R., Fegley, M., Manda, Y., Nanda, S., Shirani, J., Childbirth related complications in women with hypertrophic cardiomyopathy, Journal of the American College of Cardiology, 69, 834, 2017	Abstract publication only
Sorel Goland, S., Van Hagen, I. M., Elbaz-Greener, G., Elkayam, U., Shotan, A., Merz, W. M., Enar, S. C., Gaisin, I. R., Pieper, P. G., Johnson, M. R., Hall, R., Blatt, A., Roos-Hesselink, J. W., Pregnancy in women with hypertrophic cardiomyopathy: Data from the	Abstract publication only

Study	Reason for exclusion
European Society of Cardiology initiated Registry of Pregnancy and Cardiac disease (ROPAC), European Journal of Heart Failure, 19, 82, 2017	
Thaman,R., Varnava,A., Hamid,M.S., Firoozi,S., Sachdev,B., Condon,M., Gimeno,J.R., Murphy,R., Elliott,P.M., McKenna,W.J., Pregnancy related complications in women with hypertrophic cardiomyopathy, Heart, 89, 752-756, 2003	No relevant intervention; case series
Thurman, R., Zaffar, N., Sayyar, P., Sermer, M., Siu, S., Silversides, C., D'Souza, R., Labour profile and outcomes in pregnant women with cardiac disease, American Journal of Obstetrics and Gynecology, 216 (1 Supplement 1), S459-S460, 2017	Abstract publication only
Tsuda,E., Ishihara,Y., Kawamata,K., Tsukano,S., Negi,R., Echigo,S., Chiba,Y., Pregnancy and delivery in patients with coronary artery lesions caused by Kawasaki disease, Heart, 91, 1481-1482, 2005	Case series
Ulivi, G., Everett, T., English, K., Winfield, S., Aortic stenosis in pregnancy: Outcomes of a combined cardiac and antenatal clinic, BJOG: An International Journal of Obstetrics and Gynaecology, 124, 104, 2017	Abstract publication only
Vasu,S., Stergiopoulos,K., Valvular heart disease in pregnancy, Hellenic Journal of Cardiology, 50, 498-510, 2009	Narrative review
Veille,J.C., Mertz,H., Cardiac disorders in pregnancy, Contemporary Clinical Gynecology and Obstetrics, 1, 325-334, 2002	Narrative review and case reports
Warrick, C. M., Hart, J. E., Lynch, A. M., Hawkins, J. A., Bucklin, B. A., Prevalence and descriptive analysis of congenital heart disease in parturients: obstetric, neonatal, and anesthetic outcomes, Journal of Clinical Anesthesia, 27, 492-8, 2015	No relevant comparison
Warrick, Christine M., Hart, Jan E., Lynch, Anne M., Hawkins, Joy A., Bucklin, Brenda A., Prevalence and descriptive analysis of congenital heart disease in parturients: obstetric, neonatal, and anesthetic outcomes, Journal of clinical anesthesia, 27, 492-8, 2015	Outcomes were not aggregated by mode of birth
Wasim, T., Amer, W., Majrroh, A., Siddiq, S., Foetomaternal outcome of pregnancy with cardiac disease, JPMA - Journal of the Pakistan Medical Association, 58, 175-8, 2008	No relevant comparison
Wolff,G.A., Weitzel,N.S., Management of acquired cardiac disease in the obstetric patient, Seminars in Cardiothoracic and Vascular Anesthesia, 15, 85-97, 2011	Narrative review
Wong, V. C., Wang, R. Y., Tse, T. F., Pregnancy and Takayasu's arteritis, American Journal of Medicine, 75, 597-601, 1983	No relevant comparison
Yadav, V., Sharma, J. B., Mishra, S., Kriplani, A., Bhatla, N., Kachhawa, G., Kumari, R., Karthik,,	Outcomes were not aggregated by mode of birth

Study	Reason for exclusion
Kriplani, I., Maternal and fetal outcome in operated vs non-operated cases of congenital heart disease cases in pregnancy, Indian Heart Journal, 70, 82-86, 2018	
Yuan, S. M., Cardiac myxoma in pregnancy: a comprehensive review, Revista Brasileira de Cirurgia Cardiovascular: Orgao Oficial da Sociedade Brasileira de Cirurgia Cardiovascular, 30, 386-94, 2015	No intervention of interest

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – fluid management

Clinical studies

Study	Reason for exclusion
Avila, W. S., Amaral, F. M. C., Ramires, J. A. F., Rossi, E. G., Grinberg, M., Bortolotto, M. R. L., Mady, C., Krieger, J. E., Zugaib, M., Influence of pregnancy on clinical course and fetal outcome of women with hypertrophic cardiomyopathy. [Portuguese, English], Arquivos Brasileiros de Cardiologia, 88, 423-428+480-485, 2007	Descriptive study of women with cardiac disease
Baris, L., Roos-Hesselink, J. W., Pregnancy in women with congenital heart disease: Need for new techniques in hemodynamic monitoring, International Journal of Cardiology, 2018	A full-text copy of the article could not be obtained
Bauce, B., Daliento, L., Frigo, G., Russo, G., Nava, A., Pregnancy in women with arrhythmogenic right ventricular cardiomyopathy/dysplasia, European Journal of Obstetrics, Gynecology, & Reproductive Biology, 127, 186-9, 2006	ECG and Echocardiogram were used before and after delivery
Benedetto, C., Marozio, L., Zonca, M., Giarola, M., Maula, V., Melzi, E., Chiarolini, L., Ciochetto, D., Micheletti, L., Coppo, F., 24h monitoring of blood pressure in pregnancy: clinical advantages, Chronobiologia, 21, 113-6, 1994	Women without any cardiac disease
Canobbio,M.M., Morris,C.D., Graham,T.P., Landzberg,M.J., Pregnancy outcomes after atrial repair for transposition of the great arteries, American Journal of Cardiology, 98, 668-672, 2006	The study did not report on cardiac monitoring method
Carlin, A. J., Alfirevic, Z., Gyte, G. M., Interventions for treating peripartum cardiomyopathy to improve outcomes for women and babies, Cochrane Database of Systematic Reviews, CD008589, 2010	Interventions were bromocriptine and standard heart failure therapy

Study	Reason for exclusion
Dildy, G. A., Cotton, D. B., Hemodynamic changes in pregnancy and pregnancy complicated by hypertension, Acute Care, 14-15, 26-46, 1988	Women without any cardiac disease
Duan, R., Xu, X., Wang, X., Yu, H., You, Y., Liu, X., Xing, A., Zhou, R., Xi, M., Pregnancy outcome in women with Eisenmenger's syndrome: a case series from west China, BMC Pregnancy & Childbirth, 16, 356, 2016	Insufficient (n<15) case series of women with cardiac disease
Ford,L., Abdullahi,A., Anjorin,F.I., Danbauchi,S.S., Isa,M.S., Maude,G.H., Parry,E.H., The outcome of peripartum cardiac failure in Zaria, Nigeria, Qjm, 91, 93-103, 1998	The pregnancy outcomes were not studied
Liu, H., Huang, T. T., Lin, J. H., Risk factors and risk index of cardiac events in pregnant women with heart disease, Chinese Medical Journal, 125, 3410-5, 2012	Same study as Liu 2013
Liu, S., Elkayam, U., Naqvi, T. Z., Echocardiography in Pregnancy: Part 1, Current Cardiology Reports, 18 (9) (no pagination), 2016	Literature review
Liu,H., Huang,T., Zhao,W., Shen,Y., Lin,J., Pregnancy outcomes and relative risk factors among Chinese women with congenital heart disease, International Journal of Gynecology and Obstetrics, 120, 245-248, 2013	Cardiac monitoring method was unclear
Oakley, C., Child, A., Jung, B., Presbitero, P., Tornos, P., Klein, W., Alonso Garcia, M. A., Blomstrom-Lundqvist, C., De Backer, G., Dargie, H., Deckers, J., Flather, M., Hradec, J., Mazzotta, G., Oto, A., Parkhomenko, A., Silber, S., Torbicki, A., Trappe, H. J., Dean, V., Poumeyrol-Jumeau, D., Expert consensus document on management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology, European Heart Journal, 24, 761-781, 2003	Guideline
Presbitero, P., Somerville, J., Stone, S., Aruta, E., Spiegelhalter, D., Rabajoli, F., Pregnancy in cyanotic congenital heart disease. Outcome of mother and fetus, Circulation, 89, 2673-6, 1994	No cardiac monitoring was performed
Robertson,J.E., Silversides,C.K., Mah,M.L., Kulikowski,J., Maxwell,C., Wald,R.M., Colman,J.M., Siu,S.C., Sermer,M., A contemporary approach to the obstetric management of women with heart disease, Journal of Obstetrics and Gynaecology Canada: JOGC, 34, 812-819, 2012	Not all the women with cardiac disease had cardiac monitoring and the criteria for cardiac monitoring were not reported
Rosenthal, M. H., Intrapartum intensive care management of the cardiac patient, Clinical Obstetrics & Gynecology, 24, 789-807, 1981	Literature review
Shim, W. J., Role of echocardiography in the management of cardiac disease in women, Journal of Cardiovascular Ultrasound, 22, 173-179, 2014	Literature review

Study	Reason for exclusion
Ueland, K., Intrapartum management of the cardiac patient, Clinics in Perinatology, 8, 155-64, 1981	Literature review and author's opinion article
Wald, R. M., Silversides, C. K., Kingdom, J., Toi, A., Lau, C. S., Mason, J., Colman, J. M., Sermer, M., Siu, S. C., Maternal Cardiac Output and Fetal Doppler Predict Adverse Neonatal Outcomes in Pregnant Women With Heart Disease, Journal of the American Heart Association, 4, 2015	Descriptive study of women with cardiac disease
Yuqi, Liu, Tan, Guoliang, Chengming, Shang, Xuri, Sun, The ICU Is Becoming a Main Battlefield for Severe Maternal Rescue in China: An 8-Year Single-Center Clinical Experience, Critical care medicine, 45, e1106-e1110, 2017	The outcomes were not aggregated by intervention of interest

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Clinical studies

Study	Reason for exclusion
Anguita Sanchez, M., Luque Moreno, A., Paredes Hurtado, N., Castillo Dominguez, J. C., Diagnostic protocol for cardiomyopathy in pregnancy, Medicine (Spain), 12, 2589-2592, 2017	Unable to obtain full text article
Arora, N. P., Mohamad, T., Mahajan, N., Danrad, R., Kottam, A., Li, T., Afonso, L. C., Cardiac magnetic resonance imaging in peripartum cardiomyopathy, American Journal of the Medical Sciences, 347, 112-7, 2014	No comparative echocardigraphy data to evaluate the predictive value of symptoms of heart failure
Avila Samuel, W., Gouveia, A. M. M., Rossi, E. G., Barreto, A. C. P., Zugaib, M., Grinberg, M., Ramires, J. A. F., Value of natriuretic peptides and proinflammatory cytokines for heart failure diagnosis during pregnancy, European Heart Journal, 31, 949, 2010	Conference abstract
Barbosa, M. M., Freire, C. M. V., Nascimento, B. R., Rochitte, C. E., Silva, M. C., Siqueira, M. H. A., Nunes, M. C. P., Rest left ventricular function and contractile reserve by dobutamine stress echocardiography in peripartum cardiomyopathy, Revista Portuguesa de Cardiologia, 31, 287-293, 2012	Population do not meet inclusion criteria
Barone-Rochette,G., Rodiere,M., Lantuejoul,S., Value of cardiac MRI in peripartum cardiomyopathy, Archives of cardiovascular diseases, 104, 263-264, 2011	Study design does not meet inclusion criteria - case report

Study	Reason for exclusion
Biteker, M., Duran, N., Kaya, H., Yildiz, M., Gokdeniz, T., Gunduz, S., Tanboga, I. H., Kahveci, G., Akgun, T., Ozkan, M., Predictive value of n-terminal pro-B-type natriuretic peptide and echocardiographic paramaters in patients with peripartum cardiomyopathy, European Heart Journal, 30, 447-448, 2009	Conference abstract
Biteker, M., Ilhan, E., Basaran, O., Dogan, V., Ozlek, E., Ozlek, B., Celik, O., Prognostic value of biomarkers in peripartum cardiomyopathy, Anatolian Journal of Cardiology, 18, 15, 2017	Conference abstract
Biteker, M., Ilhan, E., Biteker, G., Duman, D., Bozkurt, B., Delayed recovery in peripartum cardiomyopathy: an indication for long-term follow-up and sustained therapy, European Journal of Heart Failure, 14, 895-901, 2012	Outcomes do not meet inclusion criteria
Blatt,A., Svirski,R., Morawsky,G., Uriel,N., Neeman,O., Sherman,D., Vered,Z., Krakover,R., Short and long-term outcome of pregnant women with preexisting dilated cardiomypathy: an NTproBNP and echocardiography-guided study, Israel Medical Association Journal: Imaj, 12, 613-616, 2010	The outcome data was not presented in a format which allowed extraction
Blauwet, L. A., Libhaber, E., Forster, O., Tibazarwa, K., Mebazaa, A., Hilfiker-Kleiner, D., Sliwa, K., Predictors of outcome in 176 South African patients with peripartum cardiomyopathy, Heart, 99, 308-13, 2013	The study looked at the predictors of left ventricular recovery rather than diagnosis
Blauwet, Lori A., Delgado-Montero, Antonia, Ryo, Keiko, Marek, Josef J., Alharethi, Rami, Mather, Paul J., Modi, Kalgi, Sheppard, Richard, Thohan, Vinay, Pisarcik, Jessica, McNamara, Dennis M., Gorcsan, John, 3rd, Ipac Investigators*, Right Ventricular Function in Peripartum Cardiomyopathy at Presentation Is Associated With Subsequent Left Ventricular Recovery and Clinical Outcomes, Circulation. Heart failure, 9, 2016	The study looked at the predictors of left ventricular recovery rather than diagnosis
Briasoulis, A., Mocanu, M., Marinescu, K., Qaqi, O., Palla, M., Telila, T., Afonso, L., Longitudinal systolic strain profiles and outcomes in peripartum cardiomyopathy, Echocardiography, 33, 1354-1360, 2016	This study looked at the predictors of left ventricular recovery rather than diagnosis
Caforio, A. L. P., Fett, J. D., Cooper, L. T., Ansari, A. A., Angelini, A., Bottaro, S., Loddo, I., Bagato, F., Thiene, G., Iliceto, S., Serum anti-heart autoantibodies: Evidence for autoimmunity in haitian patients with peripartum cardiomyopathy, European Heart Journal, 32, 602, 2011	Conference abstract
Chapa,J.B., Heiberger,H.B., Weinert,L., Decara,J., Lang,R.M., Hibbard,J.U., Prognostic	No relevant outcome data were presented

Study	Reason for exclusion
value of echocardiography in peripartum cardiomyopathy, Obstetrics and Gynecology, 105, 1303-1308, 2005	
Damp, J., Givertz, M. M., Semigran, M., Alharethi, R., Ewald, G., Felker, G. M., Bozkurt, B., Boehmer, J., Haythe, J., Skopicki, H., Hanley-Yanez, K., Pisarcik, J., Halder, I., Gorcsan, J., Rana, S., Arany, Z., Fett, J. D., McNamara, D. M., Relaxin-2 and Soluble Flt1 Levels in Peripartum Cardiomyopathy. Results of the Multicenter IPAC Study, JACC: Heart Failure, 4, 380-388, 2016	Did not include the predictive values
Damp, Julie, Givertz, Michael M., Semigran, Marc, Alharethi, Rami, Ewald, Gregory, Felker, G. Michael, Bozkurt, Biykem, Boehmer, John, Haythe, Jennifer, Skopicki, Hal, Hanley-Yanez, Karen, Pisarcik, Jessica, Halder, Indrani, Gorcsan, John, 3rd, Rana, Sarosh, Arany, Zoltan, Fett, James D., McNamara, Dennis M., Ipac Investigators, Relaxin-2 and Soluble Flt1 Levels in Peripartum Cardiomyopathy: Results of the Multicenter IPAC Study, JACC. Heart failure, 4, 380-8, 2016	No relevant prognostic tests were included
Ersboll, A. S., Damm, P., Gustafsson, F., Vejlstrup, N. G., Johansen, M., Peripartum cardiomyopathy: a systematic literature review, Acta Obstetricia et Gynecologica Scandinavica, 95, 1205-1219, 2016	Systematic review - references checked for inclusion
Ferrero, S., Colombo, B. M., Fenini, F., Abbamonte, L. H., Arena, E., Peripartum cardiomyopathy: A review, Minerva Ginecologica, 55, 139-158, 2003	Narrative literature review
Fett, J. D., Earlier detection can help avoid many serious complications of peripartum cardiomyopathy, Future Cardiology, 9, 809-16, 2013	Population did not meet the inclusion criteria
Fett, J. D., Peripartum cardiomyopathy: challenges in diagnosis and management, Expert Review of Cardiovascular Therapy, 14, 1035-41, 2016	Opinion paper
Fett,J.D., Christie,L.G., Carraway,R.D., Murphy,J.G., Five-year prospective study of the incidence and prognosis of peripartum cardiomyopathy at a single institution, Mayo Clinic Proceedings, 80, 1602-1606, 2005	No relevant prognostic test were included
Goland,S., Modi,K., Bitar,F., Janmohamed,M., Mirocha,J.M., Czer,L.S., Illum,S., Hatamizadeh,P., Elkayam,U., Clinical profile and predictors of complications in peripartum cardiomyopathy, Journal of Cardiac Failure, 15, 645-650, 2009	No relevant outcomes were reported
Gunderson,E.P., Croen,L.A., Chiang,V., Yoshida,C.K., Walton,D., Go,A.S., Epidemiology	No relevant prognostic tests were included

Study	Reason for exclusion
of peripartum cardiomyopathy: incidence, predictors, and outcomes, Obstetrics and Gynecology, 118, 583-591, 2011	
Gurkan, U., Akgoz, H., Aksoy, S., Can Gurkan, O., Osken, A., Unal Dayi, S., Oz, D., Haci, R., Value of the neutrophil-to-lymphocyte ratio in predicting left ventricular recovery in patients with peripartum cardiomyopathy, Wiener Klinische Wochenschrift, 129, 893-899, 2017	Population did not meet inclusion criteria
Habli,M., O'Brien,T., Nowack,E., Khoury,S., Barton,J.R., Sibai,B., Peripartum cardiomyopathy: prognostic factors for long-term maternal outcome, American Journal of Obstetrics and Gynecology, 199, 415-415, 2008	No relevant outcome data presented
Haghikia, A., Kaya, Z., Schwab, J., Westenfeld, R., Ehlermann, P., Bachelier, K., Oettl, R., von Kaisenberg, C. S., Katus, H. A., Bauersachs, J., Hilfiker-Kleiner, D., Evidence of autoantibodies against cardiac troponin I and sarcomeric myosin in peripartum cardiomyopathy, Basic Research in Cardiology, 110, no pagination, 2015	No relevant outcome data were presented
Haghikia, A., Rontgen, P., Vogel-Claussen, J., Hilfiker-Kleiner, D., Bauersachs, J., Characterization of peripartum cardiomyopathy by cardiovascular magnetic resonance imaging, Journal of Cardiovascular Magnetic Resonance, 17, no pagination, 2015	Conference abstract
Hu,C.L., Li,Y.B., Zou,Y.G., Zhang,J.M., Chen,J.B., Liu,J., Tang,Y.H., Tang,Q.Z., Huang,C.X., Troponin T measurement can predict persistent left ventricular dysfunction in peripartum cardiomyopathy, Heart, 93, 488-490, 2007	No relevant prognostic tests were included
Isogai, T., Matsui, H., Tanaka, H., Fushimi, K., Yasunaga, H., In-hospital management and outcomes in patients with peripartum cardiomyopathy: a descriptive study using a national inpatient database in Japan, Heart and Vessels, 1-8, 2017	No relevant outcome data were presented
Katsuragi,S., Omoto,A., Kamiya,C., Ueda,K., Sasaki,Y., Yamanaka,K., Neki,R., Yoshimatsu,J., Niwa,K., Ikeda,T., Risk factors for maternal outcome in pregnancy complicated with dilated cardiomyopathy, Journal of Perinatology, 32, 170-175, 2012	No relevant outcome data were presented
Khan, S., Melikian, N., Mushemi-Blake, S., Jouhra, F., Dennes, W., Monaghan, M., Shah, A., Echocardiographic evaluation of post-partum ventricular remodelling-implications for the detection of cardiac disease, Heart, 100, no pagination, 2014	No relevant outcome data were presented

Study	Reason for exclusion
Kucia, A., Arstall, M., Dekker, G., Peripartum takotsubo cardiomyopathy, Heart Lung and Circulation, 24, S388, 2015	Conference abstract
Li, W., Li, H., Long, Y., Clinical Characteristics and Long-term Predictors of Persistent Left Ventricular Systolic Dysfunction in Peripartum Cardiomyopathy, Canadian Journal of Cardiology, 32, 362-368, 2016	No relevant prognostic tests included
Lu, C. H., Lee, W. C., Wu, M., Chen, S. W., Yeh, J. K., Cheng, C. W., Wu, K. P., Wen, M. S., Chen, T. H., Wu, V. C., Comparison of clinical outcomes in peripartum cardiomyopathy and age-matched dilated cardiomyopathy: A 15-year nationwide population-based study in Asia, Medicine, 96, e6898, 2017	No relevant outcome data reported
McNamara, D. M., Elkayam, U., Alharethi, R., Damp, J., Hsich, E., Ewald, G., Modi, K., Alexis, J. D., Ramani, G. V., Semigran, M. J., Haythe, J., Markham, D. W., Marek, J., Gorcsan, J., 3rd, Wu, W. C., Lin, Y., Halder, I., Pisarcik, J., Cooper, L. T., Fett, J. D., Ipac Investigators, Clinical Outcomes for Peripartum Cardiomyopathy in North America: Results of the IPAC Study (Investigations of Pregnancy-Associated Cardiomyopathy), Journal of the American College of Cardiology, 66, 905-14, 2015	No relevant outcome data reported
Munir, Rubab, Hussain, Sajjad, Kayani, Azhar Mahmood, Peripartum Cardiomyopathy in a Pakistani Cohort, Journal of the College of Physicians and Surgeons--Pakistan : JCPSP, 26, 740-3, 2016	Study design does not meet inclusion criteria - descriptive study
O'Connell,J.B., Costanzo-Nordin,M.R., Subramanian,R., Robinson,J.A., Wallis,D.E., Scanlon,P.J., Gunnar,R.M., Peripartum cardiomyopathy: clinical, hemodynamic, histologic and prognostic characteristics, Journal of the American College of Cardiology, 8, 52-56, 1986	No relevant outcome data presented
Ruiz-Bailen, M., Lopez-Martinez, A., Ramos-Cuadra, J. A., Diaz-Castellanos, M. A., Cardenas-Cruz, A., Rodriguez-Elvira, M., Montiel-Trujillo, A., Peripartum cardiomyopathy: A case series, Intensive Care Medicine, 27, 306-309, 2001	Study design does not meet inclusion criteria
Safirstein,J.G., Ro,A.S., Grandhi,S., Wang,L., Fett,J.D., Staniloae,C., Predictors of left ventricular recovery in a cohort of peripartum cardiomyopathy patients recruited via the internet, International Journal of Cardiology, 154, 27-31, 2012	No relevant prognostic tests were included
Stanic, Z., Roje, D., Vulic, M., Kopic, D., A ten-year study on peripartum cardiomyopathy in a	Conference abstract

Study	Reason for exclusion
clinical hospital centre split, Croatia, Journal of Perinatal Medicine, 45 (Supplement 2), 321, 2017	
Witlin,A.G., Mabie,W.C., Sibai,B.M., Peripartum cardiomyopathy: a longitudinal echocardiographic study, American Journal of Obstetrics and Gynecology, 177, 1129-1132, 1997	Population did not meet the inclusion criteria
Witlin,A.G., Mabie,W.C., Sibai,B.M., Peripartum cardiomyopathy: an ominous diagnosis, American Journal of Obstetrics and Gynecology, 176, 182-188, 1997	No relevant prognostic tests were included

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Clinical studies

Study	Reason for exclusion
Arany, Zolt, Elkayam, Uri, Peripartum Cardiomyopathy, Circulation, 133, 1397-409, 2016	Systematic review - references checked for inclusion
Arrigo, Mattia, Blet, Alice, Mebazaa, Alexandre, Bromocriptine for the treatment of peripartum cardiomyopathy: welcome on BOARD, European Heart Journal, 38, 2680-2682, 2017	Editorial paper
Biteker,M., Duran,N.E., Kaya,H., Gunduz,S., Tanboga,H.I., Gokdeniz,T., Kahveci,G., Akgun,T., Yildiz,M., Ozkan,M., Effect of levosimendan and predictors of recovery in patients with peripartum cardiomyopathy, a randomized clinical trial, Clinical Research in Cardiology, 100, 571-577, 2011	Intervention does not meet inclusion criteria
Blauwet, Lori A., Cooper, Leslie T., Diagnosis and management of peripartum cardiomyopathy, Heart (British Cardiac Society), 97, 1970-81, 2011	Narrative literature review
Carlin, Andrew J., Alfirevic, Zarko, Gyte, Gillian Ml, Interventions for treating peripartum cardiomyopathy to improve outcomes for women and babies, The Cochrane database of systematic reviews, CD008589, 2010	Systematic review - references checked for inclusion
Croix, G. R. S., Ibrahim, M., Chaparro, S., Use of bromocriptine in the management of peripartum cardiomyopathy: A systematic review, Circulation: Cardiovascular Quality and Outcomes, 10, 2017	A full text copy of the article could not be obtained
Desai, P., Peripartum Cardiomyopathy: A review, Journal of Obstetrics and Gynecology of India, 60, 25-32, 2010	Narrative literature review
Dodiyi-Manuel, S. T., Ezennaka, R. C., CURRENT MANAGEMENT OF PERIPARTUM CARDIOMYOPATHY: A REVIEW, Nigerian	A full text copy of the article could not be obtained

Study	Reason for exclusion
journal of medicine : journal of the National Association of Resident Doctors of Nigeria, 24, 363-9, 2015	
Ducloy-Bouthors, A. S., Gonzalez-Estevez, M., Constans, B., Turbelin, A., Barre-Drouard, C., Cardiovascular emergencies and cardiac arrest in a pregnant woman, Anaesthesia Critical Care and Pain Medicine, 35, S43-S50, 2016	Narrative literature review
Ersboll, Anne S., Damm, Peter, Gustafsson, Finn, Vejlstrup, Niels G., Johansen, Marianne, Peripartum cardiomyopathy: a systematic literature review, Acta Obstetricia et Gynecologica Scandinavica, 95, 1205-1219, 2016	Narrative literature review
Fett, James D., Cabergoline in the Treatment of Peripartum Cardiomyopathy, Revista brasileira de ginecologia e obstetricia : revista da Federacao Brasileira das Sociedades de Ginecologia e Obstetricia, 38, 423-4, 2016	Author's reply
Hilfiker-Kleiner, D., Haghikia, A., Berliner, D., Vogel-Claussen, J., Schwab, J., Franke, A., Schwarzkopf, M., Ehlermann, P., Pfister, R., Michels, G., Westenfeld, R., Stangl, V., Kindermann, I., Kuhl, U., Angermann, C. E., Schlitt, A., Fischer, D., Podewski, E., Bohm, M., Sliwa, K., Bauersachs, J., Bromocriptine for the treatment of peripartum cardiomyopathy: A multicentre randomized study, European Heart Journal, 38, 2671-2679, 2017	Comparison does not meet inclusion criteria
Horgan, Stephen J., Margey, Ronan, Brennan, Donal J., O'Herlihy, Colm, Mahon, Niall G., Natural history, management, and outcomes of peripartum cardiomyopathy: an Irish single-center cohort study, The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians, 26, 161-5, 2013	Population do not meet the inclusion criteria
Nanjappa, M. C., Math, R., Mahadevappa, M., Ravindranath, K. S., Jayadeva, S., Peri-partum cardiomyopathy-a clinical profile and its response to treatment with bromocryptine - A case control study, Indian Heart Journal, 65, S63-S64, 2013	Conference abstract
Sliwa,K., Skudicky,D., Candy,G., Bergemann,A., Hopley,M., Sareli,P., The addition of pentoxifylline to conventional therapy improves outcome in patients with peripartum cardiomyopathy, European Journal of Heart Failure, 4, 305-309, 2002	Intervention does not meet the inclusion criteria
Wu, V. C. C., Chen, T. H., Yeh, J. K., Wu, M., Lu, C. H., Chen, S. W., Wu, K. P. H., Cheng, C. W., Chang, C. H., Hung, K. C., Chern, M. S., Lin, F. C., Wen, M. S., Clinical outcomes of peripartum cardiomyopathy: A 15-year nationwide population-	Outcomes were not reported according to intervention and comparator groups

Study	Reason for exclusion
based study in Asia, Medicine (United States), 96, e8374, 2017	

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – anaesthesia

Clinical studies

Study	Reason for exclusion
Allyn, J., Guglielminotti, J., Omnes, S., Guezouli, L., Egan, M., Jondeau, G., Longrois, D., Montravers, P., Marfan's syndrome during pregnancy: anesthetic management of delivery in 16 consecutive patients, Anesthesia & Analgesia, 116, 392-8, 2013	Study design does not meet inclusion criteria - case series
Arendt,K.W., Fernandes,S.M., Khairy,P., Warnes,C.A., Rose,C.H., Landzberg,M.J., Craigo,P.A., Hebl,J.R., A case series of the anesthetic management of parturients with surgically repaired tetralogy of Fallot, Anesthesia and Analgesia, 113, 307-317, 2011	Population do not meet inclusion criteria - no women had general anaesthetic
Biswas, R. G., Bandyopadhyay, B. K., Sarkar, M., Sarkar, U. K., Goswami, A., Mukherjee, P., Perioperative management of pregnant patients with heart disease for caesarian section under anaesthesia, Journal of the Indian Medical Association, 101, 632, 634, 636-7 passim, 2003	Outcome data not reported by group
Bonnin,M., Mercier,F.J., Sitbon,O., Roger-Christoph,S., Jais,X., Humbert,M., Audibert,F., Frydman,R., Simonneau,G., Benhamou,D., Severe pulmonary hypertension during pregnancy: mode of delivery and anesthetic management of 15 consecutive cases, Anesthesiology, 102, 1133-1137, 2005	Outcome data not reported by group
Cauldwell, M., Von Klemperer, K., Uebing, A., Swan, L., Steer, P. J., Gatzoulis, M., Johnson, M. R., Why is post-partum haemorrhage more common in women with congenital heart disease?, International Journal of Cardiology, 218, 285-90, 2016	No relevant outcomes
Chohan, U., Afshan, G., Mone, A., Anaesthesia for caesarean section in patients with cardiac disease, JPMA - Journal of the Pakistan Medical Association, 56, 32-8, 2006	Narrative literature review
Curry, R. A., Fletcher, C., Gelson, E., Gatzoulis, M. A., Woolnough, M., Richards, N., Swan, L., Steer, P. J., Johnson, M. R., Pulmonary hypertension and pregnancy-a review of 12 pregnancies in nine women, BJOG: An	Outcome data not reported by group

Study	Reason for exclusion
International Journal of Obstetrics and Gynaecology., 2012	
Dob, D. P., Yentis, S. M., UK registry of high-risk obstetric anaesthesia: report on cardiorespiratory disease, International Journal of Obstetric Anesthesia, 10, 267-72, 2001	No outcome data reported by group
Gelson,E., Gatzoulis,M., Steer,P.J., Lupton,M., Johnson,M., Tetralogy of Fallot: maternal and neonatal outcomes, BJOG: An International Journal of Obstetrics and Gynaecology, 115, 398-402, 2008	Population do not meet inclusion criteria - unclear if women had general anaesthetic
Goldszmidt,E., MacArthur,A., Silversides,C., Colman,J., Sermer,M., Siu,S., Anesthetic management of a consecutive cohort of women with heart disease for labor and delivery, International Journal of Obstetric Anesthesia, #19, 266-272, 2010	No relevant outcomes reported
Hawes, R., Wilson, V., Newton, R., Ten Klooster, L., Kiely, D., Condliffe, R., Elliot, C., Gandhi, S., Safe delivery of parturients with pulmonary hypertension: 16 years' experience in a national specialist referral centre, Anaesthesia, 72, 56, 2017	Conference abstract
Hidano,G., Uezono,S., Terui,K., A retrospective survey of adverse maternal and neonatal outcomes for parturients with congenital heart disease, International Journal of Obstetric Anesthesia, 20, 229-235, 2011	Study design does not meet inclusion criteria - case series
Husodo, D. P., Hartono, R., Anesthesia management for sectio cesarian delivery in patient with mitral stenosis, Regional Anesthesia and Pain Medicine, 42, e129, 2017	Narrative literature review
Ioscovich, A. M., Goldszmidt, E., Fadeev, A. V., Grisaru-Granovsky, S., Halpern, S. H., Peripartum anesthetic management of patients with aortic valve stenosis: a retrospective study and literature review, International Journal of Obstetric Anesthesia, 18, 379-86, 2009	No relevant outcome data reported
Isogai, T., Matsui, H., Tanaka, H., Kohyama, A., Fushimi, K., Yasunaga, H., Clinical features and peripartum outcomes in pregnant women with cardiac disease: a nationwide retrospective cohort study in Japan, Heart and Vessels, 1-13, 2018	Outcome data were not reported by group
Ituk, U. S., Habib, A. S., Polin, C. M., Allen, T. K., Anesthetic management and outcomes of parturients with dilated cardiomyopathy in an academic centre, Canadian Journal of Anaesthesia, 62, 278-88, 2015	Study design does not meet inclusion criteria - case series
Kevane, B., McKenna, P., Walsh, K., Donnelly, J. C., Flood, K., Cullen, M., Bowen, M., Thornton, P., Loughrey, J., Coulter-Smith, S., Ainle, F. N., Haemorrhagic and thrombotic complications in pregnant women with acquired and congenital	Intervention does not meet inclusion criteria - unclear which type of anaesthetic was used

Study	Reason for exclusion
cardiac disease, Journal of Perinatal Medicine, 43, 165-169, 2015	
Langesaeter,E., Dragsund,M., Rosseland,L.A., Regional anaesthesia for a Caesarean section in women with cardiac disease: a prospective study, Acta Anaesthesiologica Scandinavica, 54, 46-54, 2010	Study design does not meet inclusion criteria - case series
Maxwell, B. G., El-Sayed, Y. Y., Riley, E. T., Carvalho, B., Peripartum outcomes and anaesthetic management of parturients with moderate to complex congenital heart disease or pulmonary hypertension, Anaesthesia, 68, 52-9, 2013	No relevant outcomes reported
Meng, M. L., Landau, R., Viktorsdottir, O., Banayan, J., Grant, T., Bateman, B., Smiley, R., Reitman, E., Pulmonary hypertension in pregnancy a report of 49 cases at four tertiary north American sites, Obstetrics and Gynecology, 129, 511-520, 2017	Study design does not meet inclusion criteria - case series
Michaelson-Cohen,R., Elstein,D., Ioscovich,A., Armon,S., Schimmel,M.S., Butnaru,A., Samueloff,A., Grisaru-Granovsky,S., Severe heart disease complicating pregnancy does not preclude a favourable pregnancy outcome: 15 years' experience in a single centre, Journal of Obstetrics and Gynaecology, 31, 597-602, 2011	Intervention does not meet inclusion criteria - unclear if general anaesthetic was used
Monagle, J., Manikappa, S., Ingram, B., Malkoutzis, V., Pulmonary hypertension and pregnancy: the experience of a tertiary institution over 15 years, Annals of Cardiac Anaesthesia, 18, 153-60, 2015	Outcome data not reported by group
Oakley, C., Child, A., Jung, B., Presbitero, P., Tornos, P., Klein, W., Alonso Garcia, M. A., Blomstrom-Lundqvist, C., De Backer, G., Dargie, H., Deckers, J., Flather, M., Hradec, J., Mazzotta, G., Oto, A., Parkhomenko, A., Silber, S., Torbicki, A., Trappe, H. J., Dean, V., Poumeyrol-Jumeau, D., Expert consensus document on management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases During Pregnancy of the European Society of Cardiology, European Heart Journal, 24, 761-781, 2003	Consensus paper - no data included
Pippen, J., Koonce, J., Frischhertz, B., Markham, L., Thompson, J., Maternal and neonatal outcomes in women with congenital heart disease at a single academic center, Obstetrics and Gynecology, 129, 130S, 2017	Conference abstract
Rex, Steffen, Devroe, Sarah, Anesthesia for pregnant women with pulmonary hypertension, Current opinion in anaesthesiology, 29, 273-81, 2016	Narrative literature review
Ten Klooster, L., Wilson, V., Selby, K., Newton, R., Gandhi, S., Bonnet, T., Fletcher, J.,	Conference abstract

Study	Reason for exclusion
Armstrong, I., Martin, L., Hamilton, N., Mills, G., Thompson, R., Charalampopoulos, A., Sabroe, I., Elliot, C., Condliffe, R., Kiely, D., Managing pregnancy in pulmonary hypertension using a multi-professional approach: A 16-year experience in a specialist referral centre, Thorax, 72, A179-A180, 2017	
Thaman,R., Varnava,A., Hamid,M.S., Firoozi,S., Sachdev,B., Condon,M., Gimeno,J.R., Murphy,R., Elliott,P.M., McKenna,W.J., Pregnancy related complications in women with hypertrophic cardiomyopathy, Heart, 89, 752-756, 2003	Intervention does not meet inclusion criteria - no women with regional anaesthesia
Tiouririne, M., de Souza, D. G., Beers, K. T., Yemen, T. A., Anesthetic Management of Parturients With a Fontan Circulation: A Review of Published Case Reports, Seminars in Cardiothoracic & Vascular Anesthesia, 19, 203-9, 2015	Outcome data not reported by group
Vause, S., Clarke, B., Tower, C. L., Hay, C., Knight, M., Pregnancy outcomes in women with mechanical prosthetic heart valves: a prospective descriptive population based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system, BJOG: An International Journal of Obstetrics & Gynaecology, 26, 26, 2016	No outcome data reported by group
Warrick, C. M., Hart, J. E., Lynch, A. M., Hawkins, J. A., Bucklin, B. A., Prevalence and descriptive analysis of congenital heart disease in parturients: obstetric, neonatal, and anesthetic outcomes, Journal of Clinical Anesthesia, 27, 492-8, 2015	No outcome data reported by group

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

Clinical studies

Study	Reason for exclusion
Allyn, J., Guglielminotti, J., Omnes, S., Guezouli, L., Egan, M., Jondeau, G., Longrois, D., Montravers, P., Marfan's syndrome during pregnancy: anesthetic management of delivery in 16 consecutive patients, Anesthesia & Analgesia, 116, 392-8, 2013	No relevant comparison
Bauce, B., Daliento, L., Frigo, G., Russo, G., Nava, A., Pregnancy in women with arrhythmogenic right ventricular cardiomyopathy/dysplasia, European Journal of	No relevant outcome data reported - no data on analgesia during labour or birth

Study	Reason for exclusion
Obstetrics, Gynecology, & Reproductive Biology, 127, 186-9, 2006	
Bonnin,M., Mercier,F.J., Sitbon,O., Roger-Christoph,S., Jais,X., Humbert,M., Audibert,F., Frydman,R., Simonneau,G., Benhamou,D., Severe pulmonary hypertension during pregnancy: mode of delivery and anesthetic management of 15 consecutive cases, Anesthesiology, 102, 1133-1137, 2005	No relevant comparison
Dob, D. P., Yentis, S. M., UK registry of high-risk obstetric anaesthesia: report on cardiorespiratory disease, International Journal of Obstetric Anesthesia, 10, 267-72, 2001	No relevant outcome data reported
Dresner,M., Pinder,A., Anaesthesia for caesarean section in women with complex cardiac disease: 34 cases using the Braun Spinocath spinal catheter, International Journal of Obstetric Anesthesia, 18, 131-136, 2009	No relevant comparison
Goldszmidt,E., MacArthur,A., Silversides,C., Colman,J., Sermer,M., Siu,S., Anesthetic management of a consecutive cohort of women with heart disease for labor and delivery, International Journal of Obstetric Anesthesia, #19, 266-272, 2010	No relevant outcome data reported
Haider, S., Sikander, R. I., Us Samad, B., Memon, I., Epidural tramadol and bupivacaine in obstetric patients with concurrent cardiac diseases, Anaesthesia, Pain and Intensive Care, 13, 15-18, 2009	No relevant comparison
Ioscovich, A. M., Goldszmidt, E., Fadeev, A. V., Grisaru-Granovsky, S., Halpern, S. H., Peripartum anesthetic management of patients with aortic valve stenosis: a retrospective study and literature review, International Journal of Obstetric Anesthesia, 18, 379-86, 2009	No relevant comparison
Isogai, T., Matsui, H., Tanaka, H., Kohyama, A., Fushimi, K., Yasunaga, H., Clinical features and peripartum outcomes in pregnant women with cardiac disease: a nationwide retrospective cohort study in Japan, Heart and Vessels, 1-13, 2018	The intervention does not meet the inclusion criteria
Maki, J., Hiramatu, Y., Masuyama, H., Akagi, T., The perinatal outcomes of pregnant women with heart disease in Okayama University Hospital and towards the future, Journal of Obstetrics and Gynaecology Research, 43, 59-60, 2017	Conference abstract
Maxwell, B. G., El-Sayed, Y. Y., Riley, E. T., Carvalho, B., Peripartum outcomes and anaesthetic management of parturients with moderate to complex congenital heart disease	No relevant comparison outcome data reported

Study	Reason for exclusion
or pulmonary hypertension, Anaesthesia, 68, 52-9, 2013	
Pippen, J., Koonce, J., Frischhertz, B., Markham, L., Thompson, J., Maternal and neonatal outcomes in women with congenital heart disease at a single academic center, Obstetrics and Gynecology, 129, 130S, 2017	Conference abstract
Rex, Steffen, Devroe, Sarah, Anesthesia for pregnant women with pulmonary hypertension, Current opinion in anaesthesiology, 29, 273-81, 2016	Narrative literature review
Ten Klooster, L., Wilson, V., Selby, K., Newton, R., Gandhi, S., Bonnet, T., Fletcher, J., Armstrong, I., Martin, L., Hamilton, N., Mills, G., Thompson, R., Charalampopoulos, A., Sabroe, I., Elliot, C., Condliffe, R., Kiely, D., Managing pregnancy in pulmonary hypertension using a multi-professional approach: A 16-year experience in a specialist referral centre, Thorax, 72, A179-A180, 2017	Study design does not meet the inclusion criteria - only 12 cases reported
Vriend, J. W. J., Drenthen, W., Pieper, P. G., Roos-Hesselink, J. W., Zwinderman, A. H., Van Veldhuisen, D. J., Mulder, B. J. M., Outcome of pregnancy in patients after repair of aortic coarctation, European Heart Journal, 26, 2173-2178, 2005	No relevant comparison
Warrick, C. M., Hart, J. E., Lynch, A. M., Hawkins, J. A., Bucklin, B. A., Prevalence and descriptive analysis of congenital heart disease in parturients: obstetric, neonatal, and anesthetic outcomes, Journal of Clinical Anesthesia, 27, 492-8, 2015	No relevant comparison

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of the third stage of labour

Clinical studies

Study	Reason for exclusion
Centre for Reviews and Dissemination, Carbetocin for the prevention of postpartum hemorrhage: a systematic review (Structured abstract), Database of Abstracts of Reviews of Effects, 2015	Population do not meet the inclusion criteria - women do not have underlying cardiac conditions

Study	Reason for exclusion
Leung,S.W., Ng,P.S., Wong,W.Y., Cheung,T.H., A randomised trial of carbetocin versus syntometrine in the management of the third stage of labour, BJOG: An International Journal of Obstetrics and Gynaecology, 113, 1459-1464, 2006	Population do not meet the inclusion criteria - women with pre-existing cardiac disease were excluded from the study
Maged, A. M., Hassan, A. M., Shehata, N. A., Carbetocin versus oxytocin for prevention of postpartum hemorrhage after vaginal delivery in high risk women, Journal of Maternal-Fetal & Neonatal Medicine, 29, 532-6, 2016	Population do not meet the inclusion criteria - women with pre-existing cardiac disease were excluded from the study
Modi, V., Goel, J. K., Kashyap, A., Arya, S. B., Kar, J., Goel, R., Active management of third stage of labor: A comparison of various uterotonic, Journal of SAFOG, 6, 151-155, 2014	Population do not meet the inclusion criteria - women with pre-existing cardiac disease were excluded from the study
Nizard, J., Nithart, A., Isnard, R., Iung, B., Macron, S., Vauthier-Brouzes, D., Dommergues, M., Management of pregnancy in women with mechanical heart valves:A 12-year retrospective French study in two centers, Journal of Obstetrics and Gynaecology Research, 41, 55-56, 2015	Conference abstract
Samimi, M., Imani-Harsini, A., Abedzadeh-Kalahroudi, M., Carbetocin vs. syntometrine in prevention of postpartum hemorrhage: A double blind randomized control trial, Iranian Red Crescent Medical Journal, 15, 817-822, 2013	Population do not meet the inclusion criteria - women with pre-existing cardiac disease were excluded from the study
Tharakan,T., Jha,J., Randomized double blind prospective trial of active management of the third stage of labor, Archives of Medical Science, 4, 79-82, 2008	Population do not meet the inclusion criteria - women with pre-existing cardiac disease were excluded from the study

Economic studies

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling..

1

Appendix E – Clinical evidence tables

Intrapartum care for women with cardiac disease – stratification of risk

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Full citation Balci, A., Sollie-Szarynska, K. M., Van Der Bijl, A. G. L., Ruys, T. P. E., Mulder, B. J. M., Roos-Hesselink, J. W., Van Dijk, A. P. J., Wajon, E. M. C. J., Vliegen, H. W., Drenthen, W., Hillege, H. L., Aarnoudse, J. G., Van Veldhuisen, D. J., Pieper, P. G., Prospective validation and assessment of cardiovascular and offspring risk models for pregnant women with congenital heart disease,	**Sample size** n=213 pregnancies in 203 women **Characteristics** None of the included women had uncorrected cyanotic congenital disease or SpO2 <90%, severe pulmonary hypertension or Eisenmenger syndrome, impaired glucose tolerance or	**Tests** CARdiac disease in PREGnancy (CARPREG) risk tool: For each CARPREG predictor present, a predictor-specific number of points is assigned for maternal cardiovascular risk or offspring risk Risk points for mother 1 point each for: i) prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia); ii) New York Heart Association (NYHA) functional class III/IV or cyanosis (oxygen saturation [SpO2] <90%); iii) left heart obstruction (mitral valve	**Methods** Maternal cardiovascular and offspring risks were scored by two investigators (blinded to pregnancy outcomes) according to aforementioned risk assessment models	**Results** Risk of maternal cardiovascular events CARPREG: number of observed cardiovascular events/pregnancies at risk (% of total) 0 point - 16/178 (83.6%) 1 point - 4/30 (14.1%) ≥1 points - 2/5 (2.3%) ZAHARA I: number of observed cardiovascular events/pregnancies at risk (% of total) <0.5 - 4/92 (43.2) 0.5-1.5 - 6/69 (32.4) 1.51-2.5 - 5/27 (12.7) 2.51 - 3.5 - 1/7 (3.3) >3.51 - 6/18 (8.5) Total number of predictors (TP): number of observed cardiovascular events/pregnancies at risk (% of total) 0: 3/76 (34.7) 1: 9/80 (39.4) 2: 5/35 (14.6)	**Limitations** Quality In Prognostic Studies (QUIPS) checklist 1. **Study participation** i) Source of target population: clearly described ii)Method used to identify population: described iii) Recruitment period: clearly described iv) Place of recruitment: clearly described v) Inclusion and exclusion criteria: described vi) Adequate study participation: not described vii) Baseline characteristics:

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Heart, 100, 1373-1381, 2014 **Ref Id** 561997 **Country/ies where the study was carried out** Netherlands **Study type** Prospective cohort study **Aim of the study** To validate CARPREG and ZAHARA I risk scores and to evaluate different risk assessment tools to identify the optimal assessment strategy for estimating the risk of cardiovascular and offspring events of pregnancy in women with	hypertensive disorder of pregnancy Age (mean±SD) in years: 28.7±4.4 Nulliparous: 137/213 (63.8%) NYHA class: I: 161/213 (75.6%) II: 51/213 (23.9%) III: 1/213 (0.5%) **Inclusion Criteria** Pregnant women with structural congenital heart disease (≥18 years) with ≤20 weeks of gestation were eligible	area <2 cm2 or aortic valve area <1.5 cm 2 or peak left ventricular outflow tract (LVOT) gradient >30 mmHg (echocardiography); iv) reduced systemic ventricular systolic function (ejection fraction [EF] <40%) 0 point - 5% maternal cardiovascular event 1 point - 27% ≥ 1 point - 75% Risk points for offspring 0.75 point for left heart obstruction (mitral valve area <2 cm2 or aortic valve area <1.5 cm2 or peak LVOT gradient >30 mmHg (echocardiography) 1 point each for i) NYHA functional class III/IV or cyanosis (SpO2<90%); ii) smoking; iii) heparin/warfarin during pregnancy 3 points for multiple gestation		3: 3/18 (9.4) 4: 0/2 (1.4) 5: 2/2 (0.5) WHO: number of observed cardiovascular events/pregnancies at risk (% of total) 1: 0/44 (20.7) 2: 8/118 (55.4) 3: 12/49 (23) 4: 2/2 (0.9) Disease complexity (DC): number of observed cardiovascular events/pregnancies at risk (% of total) Simple: 2/61 (28.6) Moderate: 17/141 (66.2) Complex: 3/11 (5.2) Receiver operator curve (ROC) (area under the curve [AUC], 95% confidence interval [CI], p value): Composite ROC; 0.8, 0.71-0.90, <0.0001 (composite ROC: optimal combination of risk assessment models of WHO class, total number of cardiovascular predictors and disease complexity) WHO Class: 0.77, 0.67-0.87, <0.0001 ZAHARA I: 0.71, 0.59 - 0.83, 0.001 TP: 0.67 (0.55-0.79), 0.01 DC: 0.64, 0.52-0.75, 0.035 CARPREG: 0.57, 0.43 - 0.70, 0.32 Risk of offspring complications	clearly described **Rating - LOW** 2. **Study attrition** i) Proportion of baseline sample available for analysis: adequate ii) Attempts to collect information on participants who dropped out: not described iii) Reasons and potential impact of subjects loss to follow-up: described iv) Outcome and prognostic factor information on those lost to follow-up: not described **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
congenital heart disease **Study dates** March 2008 to August 2011 **Source of funding** Netherlands Heart Foundation	**Exclusion Criteria** Women with known illicit drug or alcohol abuse Miscarriages or termination before 20 weeks of gestation	The higher the scores, the higher the risks of offspring complications Zwangerschap bij Aangeboren HARtAfwijkingen pregnancy in CHD (ZAHARA I) risk tool: for each ZAHARA predictor present, a predictor specific number of points is assigned to the pregnancy Risk points for mother 0.75 point each for i) NYHA functional class III/IV; ii) systemic atrioventricular valve regurgitation (moderate/severe); iii) pulmonary atrioventricular valve regurgitation (moderate/severe) 1 point for cyanotic congenital heart disease (corrected and uncorrected) 1.5 point each for i) prior arrhythmia; ii) cyanotic congenital		CARPREG - number of observed cardiovascular events/pregnancies at risk (% of total) 0 points - 45/147 (67.7%) 0.75 points - 16/46 (21.2%) 1.0 points - 8/10 (4.6%) 1.75 points - 5/7 (3.2%) >2.0 points - 7/7 (3.2%) Expected ZAHARA I risk - number of observed cardiovascular events/pregnancies at risk (% of total) 20% - 22/96 (44.2) 33.3% - 27/76 (38.7) >46.7% - 17/22 (17.1) Total number of predictors: number of observed cardiovascular events/pregnancies at risk (% of total) 1: 24/86 (39.6) 2: 30/81 (37.3) 3: 18/37(17.1) 4: 6/9 (4.1) 5: 2/3(0.5) 6: 2/1 (5) WHO: number of observed cardiovascular events/pregnancies at risk (% of total) 1: 33/103 (53.1) 2: 22/44 (22.7) 3: 2/3 (1.5) 4: 5/55 (55)	Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate v) Method used for missing data: not described **Rating - LOW** 4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: not described

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		heart disease (corrected and uncorrected) 2.5 points for left heart obstruction (peak LVOT gradient > 50 mmHg or aortic valve area <1.0 cm2) 4.25 points for mechanical valve prosthesis <0.5 point - 2.9% maternal cardiovascular complications 0.5 to 1.5 points - 7.5% 1.51 - 2.5 points - 17.5% 2.51 - 3.5 points - 43.1% >3.51 points - 70% Risk points for offspring 0.5 point for smoking during pregnancy 0.75 point each for i) cardiac medication before pregnancy; ii) cyanotic congenital disease (corrected and uncorrected) 1.75 points for twin or multiple gestation 2.5 points for		DC: number of observed cardiovascular events/pregnancies at risk (% of total) Simple: 21/58 (29.9) Moderate: 36/106 (54.6) Complex: 9/21 (10.8)	iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding measurement: not described v) Method used for missing data: not described vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: clearly described ii) Model development strategy: yes iii) Reporting results: no selective reporting **Rating - LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		mechanical valve prosthesis <0.5 points - 19.9% risk of offspring complication 0.5 to 0.99 points - 33.3% 1 - 1.49 points - 46.7% ≥1.50 points - 59.6% Total number of non-overlapping predictors of maternal cardiovascular events and offspring events (TPo) of ZAHARA I and CARPREG and Khairy et al.study (maternal risk: severe pulmonary regurgitation or subpulmonary ventricular dysfunction and smoking history and offspring risk: subaortic ventricular outflow tract gradient > 30 mmHg) were also assessed. Modified WHO classification: Class 1 = uncomplicated, small or mild pulmonary stenosis			**Other information** None

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		(or) successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage) Class II = (if otherwise well and uncomplicated), unoperated atrial or ventricular septal defect, repaired tetralogy of Fallot Class 2 - 3 (depending on individual) = native or tissue valvular heart disease not considered WHO 1 or 4; repaired coarctation; Marfan syndrome without aortic dilatation, bicuspid valve with aorta <45 mm; bicuspid aortic valve with aorta 45-50 mm Class 3 = mechanical valve; systemic RV; Fontan circulation; unrepaired cyanotic congenital heart disease; other complex congenital heart			

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		disease; Marfan syndrome with aorta 40-45 mm; bicuspid aortic valve with aorta 45 -50 mm Class 4 = (contra-indicated) pulmonary hypertension/Eisenmenger syndrome; systemic ventricular EF <30% or systemic ventricular dysfunction with NYHA class III-IV; severe mitral stenosis, severe symptomatic aortic stenosis, Marfan syndrome with aorta >45 mm; bicuspid aortic valve with aorta >45 mm; native severe coarctation Risk scores: Class I: no detectable increased risk of maternal mortality and no/mild increase in morbidity Class II: small increased risk of maternal mortality or moderate increase in morbidity			

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		Class III: significantly increased risk of maternal mortality or severe morbidity Class IV: extremely high risk of maternal mortality or severe morbidity, pregnancy is contraindicated. Disease complexity (DC): Simple congenital heart disease: isolated aortic or mitral valve disease, small atrial septal defect, mild pulmonic stenosis, repaired atrial or ventricular septal defect Moderate complex congenital heart disease: atrioventricular septal defect, coarctation, Ebstein's anomaly, tetralogy of Fallot Complex congenital heart disease: cyanotic congenital heart disease, transposition of great arteries, Fontan procedure, truncus			

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		arteriosu Outcomes definition: "Primary cardiovascular events were: cardiovascular mortality, clinically significant (needing treatment) arrhythmia, clinically significant (needing treatment) heart failure, thromboembolic events (e.g., pulmonary embolism, valve thrombosis or deep venous thrombosis), vascular events (e.g., stroke, myocardial infarction or dissection), need for urgent or invasive cardiovascular intervention up to 6 months postpartum, and endocarditis. Secondary cardiac events were: NYHA class deterioration ≥2 points compared to baseline. Offspring events were: fetal death, neonatal death, premature birth			

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
		(delivery <37 weeks gestation), small for gestational age birth weight (<10th percentile), respiratory distress syndrome, infections leading to hospital admission, neonatal intensive care unit admission, cerebral intraventricular haemorrhage, occurrence of congenital heart disease and occurrence of other congenital disease."			
Full citation Tanous, D., Siu, S. C., Mason, J., Greutmann, M., Wald, R. M., Parker, J. D., Sermer, M., Colman, J. M., Silversides, C. K., B-type natriuretic peptide in pregnant women with heart	**Sample size** n=66 3 women with spontaneous abortion were included in baseline characteristic analyses but excluded from outcome analyses	**Tests** CARPREG scores as described in Balci et al. (2014) studies were used (a total of 4 points) BNP	**Methods** BNP measurement: in the first and third trimester and after delivery (>6 weeks after delivery), where possible. Peripheral venous samples were collected into a tube with ethylenediaminetetraacetic acid and placed on ice	**Results** CARPREG scores (total number of women with the score): percentage of women with cardiac events: 0 (41)= 2% 1 (20) = 30% >1 (2) = 50% CARPREG / BNP≤100 pg/ml / BNP>100 pg/ml 0 / 0% / 8%	**Limitations** Quality In Prognostic Studies (QUIPS) checklist 1. **Study participation** i) Source of target population: clearly described ii)Method used to identify population: described iii) Recruitment period: clearly

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>disease, Journal of the American College of Cardiology, 56, 1247-1253, 2010

Ref Id
562906

Country/ies where the study was carried out
Canada

Study type
Prospective cohort study

Aim of the study
To evaluate B-type brain natriuretic peptide (BNP) response in pregnant women with heart disease and to examine the association between BNP levels and adverse maternal cardiac events during pregnancy</td>
<td>Characteristics
Age (mean±SD) years: 31±5

Median gestational age at enrolment (weeks): 13

Nulliparous: 42%

New York Heart Association class:
I: 82%
II: 15%
III: 3%

Inclusion Criteria
All pregnant women with structural congenital or acquired heart disease followed</td>
<td></td>
<td>immediately. The sample was spinned at 1800g for 10 min at 4'C and the plasma was kept at -80'C. Within 2 months, BNP was measured with a chemiluminescense immunoassay kit on i2000 Architect platform. BNP > 100 pg/ml was used to define a value suggestive of heart failure.
Maternal cardiac events were defined as any of the following: sustained symptomatic tachyarrhythmia or bradyarrhythmia requiring treatment, stoke, cardiac arrest or cardiac death, pulmonary oedema (documented on chest radiograph or by crackles heard over more than 1/3 of posterior lung fields), a decline in New York Heart Association (NYHA) functional</td>
<td>
<table>
<tr><td>1</td><td>0%</td><td>60%, p=0.03</td></tr>
</table>
<table>
<tr><td>Maternal risk factors</td><td>Women with cardiac events (n=8)</td><td>Women without cardiac events (n=55)</td></tr>
<tr><td>Cardiac event before pregnancy</td><td>5 (63%)</td><td>6 (11%)</td></tr>
<tr><td>NYHA>2</td><td>1 (13%)</td><td>1 (2%)</td></tr>
<tr><td>LVEF <55%</td><td>4 (50%)</td><td>11 (20%)</td></tr>
<tr><td>Left heart obstruction</td><td>2 (25%)</td><td>9 (16%)</td></tr>
<tr><td>LVEF on initial echo (%)</td><td>54±4</td><td>62±7</td></tr>
<tr><td>BNP max (pg/ml), median (IQR)</td><td>354 (229 – 805)</td><td>73 (43-131)</td></tr>
<tr><td>Maximum BNP >100 pg/ml</td><td>8 (100%)</td><td>16 (19%)</td></tr>
<tr><td>Initial BNP >100 pg/ml</td><td>4 (50%)</td><td>2 (4%)</td></tr>
</table>
IQR = interquartile range; LVEF = left ventricular ejection fraction
BNP levels were not associated with adverse fetal and/or neonatal events (p=0.77)
</td>
<td>described
iv) Place of recruitment: clearly described
v) Inclusion and exclusion criteria: described
vi) Adequate study participation: not described
vii) Baseline characteristics: clearly described
Rating - LOW
2. Study attrition
i) Proportion of baseline sample available for analysis: yes
ii) Attempts to collect information on participants who dropped out: not applicable (no drop out)
iii) Reasons and potential impact of subjects loss to follow-up: not applicable (no drop out)
iv) Outcome and prognostic factor</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates November 2006 to June 2008 **Source of funding** Grants from the Heart and Stroke Foundation of Canada and Canadian institute of Health Research Donation from Mrs Josephine Rogers Dr Siu was supported by The Ramsay Gunton Professorship in Cardiology of the Schulich School of Medicine and Dentistry	during pregnancy **Exclusion Criteria** Women with cardiac arrhythmias and structurally normal hearts Women presenting late or at time of labour or delivery		class (≥2 classes) compared with baseline or need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery.		information on those lost to follow-up: not applicable (no drop out) **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate v) Method used for missing data: not described **Rating - LOW** 4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: not described iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding measurement: not described v) Method used for missing data: not described vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: not described ii) Model development strategy: no iii) Reporting results: no selective reporting **Rating - HIGH** (as this is a descriptive study and the study did not analyse for predictive accuracy of the tool) Note: Only the prognostic component of the study was assessed. **Other information** None
Full citation Pijuan-Domenech, A., Galian, L., Goya,	**Sample size** n=179 pregnancies	**Tests** CARPREG risk assessment was done before pregnancy or at	**Methods** Any cardiac failure necessitating treatment or admission	**Results** Primary cardiac complications = 21 (11.7%) Secondary cardiac complications = 3 (1.7%)	**Limitations** Quality In Prognostic Studies (QUIPS) checklist

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
M., Casellas, M., Merced, C., Ferreira-Gonzalez, I., Marsal-Mora, J. R., Dos-Subira, L., Subirana-Domenech, M. T., Pedrosa, V., Baro-Marine, F., Manrique, S., Casaldaliga-Ferrer, J., Tornos, P., Cabero, L., Garcia-Dorado, D., Cardiac complications during pregnancy are better predicted with the modified WHO risk score, International Journal of Cardiology, 195, 149-54, 2015 **Ref Id** 574348 **Country/ies where the study was carried out** Spain **Study type**	in 164 women **Characteristics** All except one patient can be categorised in one of the four modified WHO levels. Subgroup 2-3 was considered as group 2, group 3 and a separate group 2-3 Mean age = 32 years NYHA class 1 prior to pregnancy = 84.7% Congenital heart disease = 123 (68.7%), acquired valvulopathies = 28 (15.7%)	the first visit prospectively whereas modified WHO risk assessment was performed retrospectively. Modified CARPREG proposed by Khairy et al (*) (OR) ZAHARA RS (ZRS) (**) were calcuated for women with congenital heart disease	and bedrest, any sustained tachycardia which required treatment, any thrombo-embolic complication, any myocardial infarction and/or any cerebrovascular accident and death from any cause was considered as primary cardiac complications A decrease in NYHA class in comparison with baseline or need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery was considered as secondary cardiac event	Maternal death = 0 Heart failure = 71%; heart failure requiring urgent cardiac surgery due to endocarditis or valvuloplasty = 3 (12.5%) Sustained arrhythmia = 14% Postpartum percutaneous coarctation = 10% Stroke = 5% Area under the curve (AUC) mWHO = 0.763 (0.651 to 0.874) CARPREG = 0.672 (0.547 to 0.797)	1. **Study participation** i) Source of target population: clearly described ii)Method used to identify population: described iii) Recruitment period: clearly described iv) Place of recruitment: clearly described v) Inclusion and exclusion criteria: not described exclusion criteria vi) Adequate study participation: not described vii) Baseline characteristics: clearly described **Rating - LOW** 2. **Study attrition** i) Proportion of baseline sample available for analysis: adequate ii) Attempts to collect information on participants who dropped out: not

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Prospective cohort study **Aim of the study** To evaluate the predictability of risk scores for cardiac complications among pregnant women with heart disease **Study dates** January 2007 to 2012 **Source of funding** Not reported	**Inclusion Criteria** Pregnant women attending cardiac and obstetric teaching hospital due to heart disease **Exclusion Criteria** Not reported				applicable (no drop out) iii) Reasons and potential impact of subjects loss to follow-up: not applicable (no drop out) iv) Outcome and prognostic factor information on those lost to follow-up: not applicable (no drop out) **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					v) Method used for missing data: not described **Rating - LOW** 4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: not described iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding measurement: not

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					described v) Method used for missing data: not described vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: clearly described ii) Model development strategy: yes iii) Reporting results: no selective reporting **Rating - LOW** **Other information** None
Full citation	**Sample size** n=730	**Tests**	**Methods**	**Results** Predicting maternal cardiac events	**Limitations**

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Fu, Q., Lin, J., Predictive accuracy of three clinical risk assessment systems for cardiac complications among Chinese pregnant women with congenital heart disease, International Journal of Gynaecology and Obstetrics, 134, 140-144, 2016
Ref Id
740832
Country/ies where the study was carried out
China
Study type
Retrospective cohort study
Aim of the study
To examine the predictive accuracy of three risk assessment systems among pregnant women</td>
<td>Characteristics
18-35 years of age = 700 (95.9%)
Nulliparous = 566 (77.5%)
New York Heart Association (NYHA) class I-II = 723 (99%)
Prior surgical interventions = 307 (42.1%)
Prior cardiac event or sustained arrhythmia = 11 (1.5%)

Inclusion Criteria
Pregnant women with heart disease who were a minimum of 20 weeks of gestation</td>
<td>CARPREG risk score

(1 point for the presence of each: prior cardiac event - heart failure, transient ischaemic attack, stroke before pregnancy) or arrhythmia, baseline New York Heart Association (NYHA) II or more or cyanosis or left ventricular outflow obstruction (mitral valve <2 cm2, aortic valve <1.5 cm2 or peak left ventricular outflow tract (LVOT) gradient >30 mmHg by echocardiography) and decreased ventricular systolic function (ejection fraction [EF] <40%))
Predicted risk - 0 point = 5%; 1 point =27%; >1 point = 75%
ZAHARA risk score

1.5 points - history of cardiac arrhythmia, cardiac medication before pregnancy</td>
<td>Primary cardiac events = heart failure, sustained arrhythmia requiring treatment, thromboembolic complications, myocardial infarction and/or cerebrovascular accidents and death
Secondary cardiac events = decline in NYHA class (≥2) compared with baseline and the need for urgent invasive cardiac procedures either during pregnancy or within 6 months of birth
Neonatal asphyxia = 5-minute APGAR score <7
Fetal death = >/= 20 weeks
Neonatal death = within 28 days of birth</td>
<td>
<table>
<tr><th></th><th>AUC (95% confidence interval [CI])</th><th>p value</th></tr>
<tr><td>mWHO</td><td>0.71(0.67-0.76)</td><td><0.001</td></tr>
<tr><td>CARPERG</td><td>0.63(0.57-0.71)</td><td>=0.001</td></tr>
<tr><td>ZAHARA</td><td>0.68(0.60-0.75)</td><td><0.001</td></tr>
</table>
Odds ratio (OR (95% CI)
Cardiac events before pregnancy = 21.5 (5.18, 89.18)
Oxygen saturation (SpO2) <90% = 2.74 (1.07, 7)
NYHA class >II = 15.79 (2.50, 99.78)
LVOT = 3.83 (1.19, 12.31)
</td>
<td><u>Quality In Prognostic Studies (QUIPS) checklist</u>
1. Study participation
i) Source of target population: clearly described
ii)Method used to identify population: described
iii) Recruitment period: clearly described
iv) Place of recruitment: clearly described
v) Inclusion and exclusion criteria: described
vi) Adequate study participation: Yes
vii) Baseline characteristics: clearly described
Rating - LOW
2. Study attrition
i) Proportion of baseline sample available for analysis: adequate
ii) Attempts to collect information on</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
with congenital heart disease **Study dates** 1 January 1993 to 31 December 2014 **Source of funding** National Science and Technology pillar program during Twelfth Five-year Plan Period	**Exclusion Criteria** Pregnant women <20 weeks of pregnancy Women undergoing induced abortion voluntarily	0.75 point - NYHA class II or higher prior to pregnancy 2.5 points - left ventricular outflow obstruction WHO risk			participants who dropped out: not described iii) Reasons and potential impact of subjects loss to follow-up: described iv) Outcome and prognostic factor information on those lost to follow-up: not described **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate v) Method used for missing data: not

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					described **Rating - LOW** 4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: no ii) Definition of confounding factor: no iii) Valid and reliable measurement of confounders: no iv) Method and setting of confounding measurement: no v) Method used for missing data: not

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					described vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: clearly described ii) Model development strategy: yes iii) Reporting results; no selective reporting **Rating - LOW** **Other information** None
Full citation Lu, C. W., Shih, J. C., Chen, S. Y., Chiu, H. H., Wang, J. K.,	**Sample size** n=268 out of 190 women	**Tests** ZAHARA risk score modified WHO (mWHO) risk score CARPREG risk score	**Methods** Cardiac events = cardiac death/cardiac arrest/stroke/symptomatic sustained	**Results** Number of women with cardiac complications = 18/268 (6.7%) Number of women with obstetric events = 10 (3.7%)	**Limitations** Quality In Prognostic Studies (QUIPS) checklist

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Chen, C. A., Chiu, S. N., Lin, M. T., Lee, C. N., Wu, M. H., Comparison of 3 Risk Estimation Methods for Predicting Cardiac Outcomes in Pregnant Women With Congenital Heart Disease, Circulation journal : official journal of the Japanese Circulation Society, 79, 1609-1617, 2015 **Ref Id** 740877 **Country/ies where the study was carried out** Taiwan **Study type** Retrospective cohort study **Aim of the study** To examine the predictive efficacy of cardiac risk assessment tools (WHO,	Characteristics Nullip = 125 (65.8%) **Inclusion Criteria** Women with congenital heart diseases who gave birth after 20 weeks of gestation **Exclusion Criteria** Not reported		arrhythmias requiring treatment, pulmonary oedema, a fall in 2 New York Heart Association (NYHA) functional classes, necessitating urgent invasive cardiac interventions during pregnancy or within 6 weeks postpartum Obstetric events = preeclampsia (sustained systolic blood pressure [SBP] ≥140 mmHg, or diastolic blood pressure [DBP] ≥90 mmHg), profound postpartum haemorrhage (defined as an estimated blood loss ≥500 mL for vaginal delivery or ≥1 L for caesarean delivery), non-cardiac death Fetal and neonatal events = preterm birth (before 37 weeks of gestation), small gestational age (SGA [<10th percentile]),	Number of women with fetal/neonatal events = 53 (19.8%) Maternal death = 2 Neonatal or fetal death = 5 Predicting risk of maternal cardiac events Risk assessment / AUC (95% CI) CARPREG / 0.732 (0.589, 0.876) ZAHARA / 0.737 (0.611, 0.864) WHO / 0.827 (0.745, 0.909) AUC = area under the curve; CI = confidence interval Predicting maternal cardiac events: NYHA class >II or cyanosis: odds ratio (OR) (95% CI) = 17.88 (1.06, 301.2; p=0.045) adjusting for great congenital heart disease complexity, caesarean section, previous arrhythmia, NYHA class >II or cyanosis, Moderate/severe systemic atrioventricular valve regurgitation, moderate/severe pulmonary atrioventricular valve regurgitation, pulmonary hypertension) Predicting fetal/neonatal outcomes: Maternal smoking: OR (95% CI) = 6.94 (2.24, 21.53); p=0.0008	1. **Study participation** i) Source of target population: clearly described ii)Method used to identify population: described iii) Recruitment period: clearly described iv) Place of recruitment: clearly described v) Inclusion and exclusion criteria: described vi) Adequate study participation: not described vii) Baseline characteristics: clearly described **Rating - LOW** 2. **Study attrition** i) Proportion of baseline sample available for analysis: adequate ii) Attempts to collect information on participants who dropped out: not described

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
CARPREG and ZAHARA) among women with cardiac conditions **Study dates** 1985 to 2011 **Source of funding** National Taiwan University Hospital			respiratory distress syndrome, cerebral intraventricular bleeding, fetal death after 20 weeks of gestation, neonatal death (within the first month after birth), or the presence of congenital heart disease		iii) Reasons and potential impact of subjects loss to follow-up: described iv) Outcome and prognostic factor information on those lost to follow-up: not described **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate v) Method used for missing data: not described **Rating - LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: no iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding measurement: not described v) Method used for missing data: not described

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>vi) Appropriate accounting for confounding: yes
Rating - LOW (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk)
6. Statistical analysis and reporting
i) Presentation of analytical strategy: clearly described
ii) Model development strategy: yes
iii) Reporting results: no selective reporting
Rating - LOW

Other information
None</td></tr>
<tr><td>Full citation
Billebeau, G., Etienne, M., Cheikh-Khelifa, R., Vauthier-</td><td>Sample size
n=43 pregnancies in 36 women</td><td>Tests
WHO cardiac risk assessment tool</td><td>Methods
Data were summarised by descriptive statistics</td><td>Results<table><tr><td></td><td>DCM (n=10)</td><td>HCM (n=28)</td><td>TIC (n=1)</td><td>ARVC (n=3)</td><td>LVNC (n=1)</td></tr></table></td><td>Limitations

<u>Quality In Prognostic Studies (QUIPS) checklist</u></td></tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Brouzes, D., Gandjbakhch, E., Isnard, R., Nizard, J., Komajda, M., Dommergues, M., Charron, P., Pregnancy in women with a cardiomyopathy: Outcomes and predictors from a retrospective cohort, Archives of Cardiovascular Diseases, 111, 199-209, 2018 **Ref Id** 826165 **Country/ies where the study was carried out** France **Study type** Retrospective cohort study **Aim of the study** To examine the maternal and neonatal risks among women with different kinds of cardio-myopathies	**Characteristics** Average age in years = 30.5 Cardiomyopathy types(n):DCM (10), HCM(28), ARVC (3), TIC(1), LVNC (1) NYHA class >1 = 22% DCM; mean LVEF before pregnancy = 35.9±9% HCM; mean wall thickness = 18.2±5 mm and 7 had severe outflow tract obstruction (> 30 mmHg) **Inclusion Criteria**	CARPREG risk assessment tool were used to predict Maternal cardiovascular complications - new onset or worsening of heart failure (including acute pulmonary oedema), ventricular arrhythmia (sustained or non-sustained ventricular tachycardia), thromboembolic events, cardiogenic shock, cerebrovascular accident, sudden cardiac death, worsening of LVEF and cardiovascular death Fetal and neonatal events - premature birth <37 weeks, low birth weight as birth weight below the 10th centile of the neonatal weight curves, from Audi-pog Sentinel Network data, Apgar score <7, hypoglycaemia, hypocalcaemia, fetal death (after 20 weeks of gestation) or neonatal death (before 28 days)	Continuous variables were analysed for normal distribution by the Agostino-Pearson test (normal distribution mean SD otherwise median interquartile range). Discrete variables are presented as numbers and percentages and proportions compared by the χ2 test	<table><tr><td>Cardiac death*</td><td>2</td><td>1</td><td>0</td><td>1</td><td>0</td></tr><tr><td>Acute heart failure</td><td>3</td><td>2</td><td>1</td><td>0</td><td>0</td></tr><tr><td>PPCDI</td><td>0</td><td>3</td><td>0</td><td>0</td><td>0</td></tr><tr><td>CARPREG I**</td><td>2</td><td>9</td><td>0</td><td>2</td><td>0</td></tr><tr><td>CARPREG II**</td><td>2</td><td>9</td><td>1</td><td>1</td><td>1</td></tr><tr><td>CARPREG III**</td><td>4</td><td>8</td><td>0</td><td>1</td><td>0</td></tr><tr><td>Live birth</td><td>10</td><td>25</td><td>1</td><td>3</td><td>1</td></tr><tr><td>Emergency CS due to CV cause</td><td>4</td><td>1</td><td>0</td><td>0</td><td>0</td></tr></table> ARVC = arrhythmogenic right ventricular cardiomyopathy; CS = caesarean section; CV = cardiovascular; DCM = dilated cardiomyopathy; HCM = hypertrophic cardiomyopathy; LVNC = left ventricular non-compaction; PPCDI=post-partum cardiac device implementation; TIC = tachycardia-induced cardiomyopathy * All 3 deaths occurred among women without any knowledge of cardiac condition or poor compliance with treatment/follow-up ** Missing data so values do not add up to the total value. This was analysed to predict maternal cardiovascular events ++ Missing data. This was analysed to predict fetal or neonatal events	1. **Study participation** i) Source of target population: clearly described ii)Method used to identify population: described iii) Recruitment period: clearly described iv) Place of recruitment: clearly described v) Inclusion and exclusion criteria: described vi) Adequate study participation: not described vii) Baseline characteristics: clearly described **Rating - LOW** 2. **Study attrition** i) Proportion of baseline sample available for analysis: adequate ii) Attempts to collect information on participants who dropped out: not described

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Study dates March 1997 to August 2013 **Source of funding** None	Women with a cardiomyopathy (DCM, HCM, TIC, LVNC, ARVC) Dilated cardiomyopathy (DCM) was identified if there was a dilated ventricle resulting in decreased left ventricular ejection fraction in the absence of coronary, valvular, congenital or any systemic diseases known to cause impaired myocardial dysfunction Hypertrophic cardiomyopat	Obstetric complications - pregnancy-induced hyper-tension, gestational diabetes, intrahepatic cholestasis of pregnancy and postpartum haemorrhage		Maternal cardiovascular complications according to risk factors: Previous cardiac event = 7/10 New York Heart Association (NYHA) class III/IV = 2/3 Left ventricular outflow tract obstruction (LVOTO) = 2/7 Left ventricular ejection fraction (LVEF) ≤40% = 2/5 None = 4/13 DCM; LVEF ≤40% = 2/5 HCM; with LVOTO = 2/7; without LVOTO = 4/12 ZAHARA I risk: 0-0.5 = 6/14 0.51 - 1.5 = 4/8 1.51 - 2.5 = 0/2 2.51 - 3.5 = 2/5 >3.5 = 3/9 WHO risk: 4 = 4/13 2/3 = 6/16 2 = 1/3	iii) Reasons and potential impact of subjects loss to follow-up: described iv) Outcome and prognostic factor information on those lost to follow-up: not described **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for analysis: adequate v) Method used for missing data: not described **Rating - LOW**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	hy (HCM) was defined as a ventricular wall thickness of more than or equal to 15 mm in ≥ 1 wall of LV which was not solely due to loading conditions. Tachycardia-induced cardiomyopathy (TIC) was identified if there was a history of supraventricular arrhymia resulting from previous event of acute heart failure and systolic function. LVNC=Left ventricular			Fetal or neonatal complications according to risk factors: NYHA III/IV = 2/3 Anticoagulation = 3/3 LVOTO = 6/7	4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: no iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding measurement: not described v) Method used for missing data: not described

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	non-compaction ARVC=Arrhythmogenic right ventricular cardiomyopathy **Exclusion Criteria** Peripartum cardiomyopathy (PPCM) - defined as heart failure due to left ventricular systolic dysfunction in near term (usually last month) or in the months after delivery after exclusion of other possible causes				vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: not described ii) Model development strategy: not described iii) Reporting results: no selective reporting **Rating - HIGH** (as this is a descriptive study and did not analyse for the predictive accuracy of the tool) **Other information** None

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Full citation
Martins, Luciana Carvalho, Freire, Claudia Maria Vilas, Capurucu, Carolina Andrade Braganca, Nunes, Maria do Carmo Pereira, Rezende, Cezar Alencar de Lima, Risk Prediction of Cardiovascular Complications in Pregnant Women With Heart Disease, Arquivos brasileiros de cardiologia, 106, 289-96, 2016
Ref Id
826201
Country/ies where the study was carried out
Brazil
Study type
Retrospective cohort study
Aim of the study
To identify the predictors of cardiovascular</td>
<td>Sample size
n=132

Characteristics
Mean age = 27.59±7.17
Congenital heart disease = 18
Rheumatic heart disease = 82
Arrhythmias = 15
Mitral valve prolapse = 6
Cardiomyopathies and other cardiac diseases =11
Smoking = 20 (smoked mean cigarettes of 8.63)
NYHA class III = 4
LVEF <40% = 2

Inclusion Criteria</td>
<td>Tests
Predictors of maternal cardiovascular complications = "age; parity; number of visits to the high-risk prenatal care (HRPC); HRPC beginning on the third trimester; maternal smoking; previous cardiac complications and previous surgical or clinical heart treatments; need to begin or change cardiac medication during pregnancy for patients who changed, at the most, one functional class during follow-up, or dose adjustment to abide by a follow-up protocol; valve prosthesis; New York Heart Association (NYHA) functional class ≥ III at the beginning of HRPC; left ventricular (LV) systolic dysfunction; associated preeclampsia or systemic arterial</td>
<td>Methods
Cardiovascular complications - "death due to heart disease; heart failure with acute pulmonary edema (documented on chest X-ray or bilateral pulmonary rales on posterior chest auscultation on physical examination); acute myocardial infarction; sustained symptomatic tachyarrhythmia or bradyarrhythmia requiring treatment; worsening of at least 2 NYHA functional classes as compared to baseline; and need for emergency invasive procedures during pregnancy."</td>
<td>Results
CARPREG to predict cardiovascular complications
0 = 15.2 %
1 = 16.4 %
>1 = 42.1 %

<table>
<tr><th></th><th>%</th><th>Odds ratio (OR)</th><th>95% confidence interval (CI)</th></tr>
<tr><td>LHO</td><td>60.9</td><td>3.04</td><td>1.35-6.86</td></tr>
<tr><td>EF< 40%</td><td>18.5</td><td>2.38</td><td>1.34-5.42</td></tr>
<tr><td>NYHA class III*</td><td>25</td><td>3.89</td><td>1.23-7.69</td></tr>
<tr><td>NYHA class III*(multivariate)</td><td>-</td><td></td><td>0.032-0.134</td></tr>
<tr><td>Maternal smoking</td><td>29.4</td><td>1.86</td><td>0.59-5.86</td></tr>
</table>

EF = ejection fraction; LHO = Left heart obstruction; NYHA = New York Heart Association
* class III on first antenatal visit
Variable for multivariate model if the variable</td>
<td>Limitations

<u>Quality In Prognostic Studies (QUIPS) checklist</u>
1. Study participation
i) Source of target population: clearly described
ii)Method used to identify population: described
iii) Recruitment period: clearly described
iv) Place of recruitment: clearly described
v) Inclusion and exclusion criteria: described
vi) Adequate study participation: not described
vii) Baseline characteristics: clearly described
Rating - LOW
2. Study attrition
i) Proportion of baseline sample available for</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
and neonatal complications among women with heart disease **Study dates** January 2005 to July 2010 **Source of funding** None	Pregnant women with heart conditions from prenatal until delivery and postpartum **Exclusion Criteria** Miscarriage (fetal loss before 20th week) Delivery at other institutions Twin pregnancies Peripartum cardiomyopathy (PPCM) developed in the puerperium period	hypertension (SAH); left heart obstruction (LHO); and calculated CARPREG risk score" and "gestational age at the beginning of prenatal care and number of consultations; cardiac complications during pregnancy; invasive procedures required during prenatal care; NYHA functional classification; comorbidities; delivery type; hospital length of stay; and obstetric complications" and "gestational age at the time of delivery and birth weight" LHO = "mitral stenosis with valve area <2.0 cm2; aortic stenosis with valve area <1.5 cm2; and LV outflow tract gradient >30 mmHg"		is p<0.2 on univariate analysis (LHO, previous cardiac complications, EF >60%, NYHA class III)	analysis: adequate ii) Attempts to collect information on participants who dropped out: not described iii) Reasons and potential impact of subjects loss to follow-up: described iv) Outcome and prognostic factor information on those lost to follow-up: not described **Rating - LOW** 3. **Prognostic factor measurement** i) Definition of prognostic factor (PF): clearly described ii) Valid and reliable measurement of risk factor: adequately valid and reliable iii) Method and Setting of prognostic factor measurement: same for all participants iv) Proportion of data on PF available for

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					analysis: adequate v) Method used for missing data: not described **Rating - LOW** 4. **Outcome measurement** i) Definition of outcome: clearly described ii) Valid and reliable measurement of outcome: probably valid and reliable iii) Method and setting of outcome measurement: the same for all study participants **Rating - LOW** 5. **Study confounding** i) Important confounders measured: yes ii) Definition of confounding factor: not described iii) Valid and reliable measurement of confounders: yes iv) Method and setting of confounding

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					measurement: not described v) Method used for missing data: not described vi) Appropriate accounting for confounding: yes **Rating - LOW** (the risk assessment protocol considered all relevant cardiovascular risk factors to stratify the risk which was justified as low risk) 6. **Statistical analysis and reporting** i) Presentation of analytical strategy: not described ii) Model development strategy: no iii) Reporting results: no selective reporting **Rating - HIGH** (as this is a descriptive study and did not analyse for the predictive accuracy of the tool)

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Other information None

ARVC: arrhymogenic right ventricular cardiomyopathy; AUC: area under curve; BNP: brain natriuretic peptide; CARPREG: CARdiac disease in PREGnancy; CHD: congenital heart disease; CI: confidence interval; CS: caesarean section; CV: cardiovascular; DC: disease complexity; DCM: dilated cardiomyopathy; EF: ejection fraction; HCM: hypertrophic cardiomyopathy; HRPC: high risk prenatal care; LHO: left heart obstruction; LVEF: left ventricular ejection fraction; LVNC: left ventricular non-compaction; LVOT/LVOTO: left ventricular outflow obstruction; mWHO: modified World Health Organization criteria; N: total number of participants; NYHA: New York Heart Association; PPCDI: post-partum cardiac device implementation; PPCM: peripartum cardiomyopathy; ROC: receiver operator curve; SD: standard deviation; SpO2: measure of oxygen saturation in the blood; TIC: tachycardia-induced cardiomyopathy; TP: total number of predictors; WHO: World Health Organization; ZAHARA I: Zwangerschap bij Aangeboren HARtAfwijkingen pregnancy in congenital heart disease risk tool

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Khamoushi,A.J., Kashfi,F., Hosseini,S., Ghavidel,A.R.A., Samiei,N., Haddadzadeh, M., Anti-coagulation during pregnancy in women with mechanical heart valves: A prospective study, International Journal of Fertility and	**Sample size** N=49 pregnancies in 44 women with mechanical prosthetic heart valves **Characteristics** • Age at time of pregnancy (mean±SD): 29.8 ± 5.3 years [Group A: 30.28 ± 5.2 vs	**Interventions** • Group A (n=38) received warfarin throughout their pregnancy, the international normalised ratio (INR) was checked routinely and kept between 2.0 to 3.5 as needed • Group B n=11 received intravenous (IV) injections of unfractionated heparin (UFH) during the first	**Details** All women were visited during the first trimester of their pregnancies. Patients' clinical and socioeconomic conditions determined their anticoagulant regimens. When the patient refused the recommended anticoagulation therapy, an alternative regimen was started. All patients underwent periodic transthoracic echocardiography (TTE) in addition to transoesophageal echocardiography (TEE) when needed during the	**Results** <u>Group A versus Group B</u> • Prosthetic valve dysfunction in third trimester or after delivery Group A = 3/38 (7.9%) Group B = 1/11 (9.2%); p = 0.65 • No complications Group A = 33 Group B = 5 • Prosthetic valve dysfunction in first trimester Group A = 1 Group B = 5 • Maternal death Group A = 1 Group B = 0 • Live births (caesarean section (CS) + vaginal birth)	**Limitations** <u>Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies</u> Selection: 1) Representativeness of the exposed cohort: a) truly representative 2) Selection of the non exposed cohort: a) taken

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Sterility, 5, 47-51, 2011 **Ref Id** 285564 **Country/ies where the study was carried out** Iran **Study type** Prospective cohort study **Aim of the study** To investigate the effect of anticoagulants on pregnancy outcomes and their potential risks in pregnant women with mechanical heart valves **Study dates** 2002 and 2007	Group B: 28.09 ± 3.9) • Mitral valve replacement pregnancies: 36/49 (74%) [Group A: 28 (73.7%) versus Group B: 8 (72.7%)] • Aortic valve replacement pregnancies: 8/49 (16%) [Group A = 5 (13.2%) vs Group B = 3 (27.3%)] • Aortic and mitral valve replacement pregnancies: 5/49 (10%) [Group A = 5 (13.2%) Group B = 0] • None of the pregnancies were twins • Five women became pregnant	trimester (6th-12th week), after which they received warfarin until the 36th week of gestation followed by heparin for the last two weeks of pregnancy. The activated partial thromboplastin time (aPTT) was maintained at twice the control level • Both groups received heparin at the time of delivery	follow-up period. Pediatricians examined all newborns. Statistical analysis was performed using SPSS version 13 software. Continuous variables were described as mean ± standard deviation (SD). Student's t-test compared continuous variables. The Mann-Whitney rank-sum test compared medians when the normality test failed. Noncontinuous variables were compared by either the chi-square test or Fisher's exact test, as appropriate. A p value less than 0.05 was statistically significant.	Group A = 22 Group B = 7 • CS Group A = 15 Group B = 5 • Intrauterine fetal death (IUFD) Group A = 1 Group B = 1 • Abortion Total (spontaneous + therapeutic) Group A = 15 Group B = 3 • Spontaneous birth Group A = 9 Group B = 3 <u>Group A sub-analysis: warfarin ≤5mg (n=29) vs. warfarin >5mg (n=9)</u> • Abortion ≤5 mg = 8 >5 mg = 7 • Live birth ≤5 mg = 20 >5 mg = 2 • Maternal death ≤5 mg = 1 >5 mg = 0	from the same community as the exposed group 3) Ascertainment of exposure: d) no description 4) Demonstration that outcome of interest was not present at start of study: a) yes Comparability: 1) Comparability of cohorts on the basis of the design and the analysis: c) unclear Outcome: 1) Assessment of outcome: d) no description 2) Was follow-up long enough for outcomes to occur: c) yes for the reported outcomes

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>Source of funding
Heart Valve Research Center of Tehran University, Shaheed Rajaei Heart Hospital</td><td>twice during the study period

Inclusion criteria
• Pregnant women in their first trimester referred to Department of Cardiac Surgery, Rajaee Heart Hospital, Tehran, Iran

Exclusion criteria
• Pregnant women referred during their second or third trimesters</td><td></td><td></td><td></td><td>3) Adequacy of follow up of cohorts: a) complete follow up

Overall score: 5/9

Other information
None</td></tr>
<tr><td>Full citation
Soma-Pillay, P., Nene, Z., Mathivha, T. M., Macdonald, A.</td><td>Sample size
N=62

Characteristics
• Setting - combined</td><td>Interventions
Management protocol: Until 12 weeks gestation, twice daily subcutaneous unfractionated heparin</td><td>Details
Near miss = a woman with acute organ failure resulting in death if not treated properly</td><td>Results<table><tr><td></td><td>Group 1 n = 28</td><td>Group 2 n = 21</td><td>Group 3 n = 13</td></tr><tr><td>Average INR</td><td>2.5</td><td>2.8</td><td>2.7</td></tr></table></td><td>Limitations
Quality Assessment: Newcastle-Ottawa Assessment</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
P., The effect of warfarin dosage on maternal and fetal outcomes in pregnant women with prosthetic heart valves, Obstetric Medicine, 4, 24-7, 2011 **Ref Id** 588884 **Country/ies where the study was carried out** South Africa Study type Prospective observational study **Aim of the study** To examine the effects of warfarin on pregnancy outcomes among women	cardiac-obstetric unit • Mean age (range) = 23 (14 to 41)years • Nullip = 17(27%) • Mean gestation at booking = 16 weeks • Mitral: 51/62 (82%) • Aortic: 2/62 (3%) • Double: 9/62 (15%) Note - Most implantations were due to childhood rheumatic heart disease "41(66%) was booked after first trimester and were exposed to warfarin during this period." • No maternal death and cases of	(UFH) (titrated against prothrombin time [PTT] between 70 to 90 seconds). From week 12 to 36, warfarin was given (international normalised ratio [INR] 2.5 to 3.5) Week 36 onwards, warfarin was stopped and converted to twice daily subcutaneous UFH; elective CS was performed at 38 weeks with morning heparin being withheld on the day of CS. Then, woman was transferred to prebooked cardiac intensive care unit (ICU) post-delivery. Six hours after birth, subcutaneous heparin was resumed and warfarin was restarted the morning after birth unless there is any bleeding complication (INR between 2.5 and 3) Daily warfarin doses 1. Group 1 = 5 mg or less 2. Group 2 = 5.1 to 7.4 mg	Live baby = babies above 500g born alive Miscarriage = fetal loss <500g Stillbirth = fetus >500g born dead * weight was used as gestational age was uncertain warfarin embryology = if the mother took warfarin in first trimester and the baby was born with midline hypoplasia	Live birth: 19 (68); 13 (62); 6 (46) Birthweight in kg: 2.9 ± 0.84; 2.78 ± 0.83; 2.7 ± 1.22 Pregnancy loss: 9 (32); 8 (38); 6 (46) Miscarriages: 8 (29); 5 (24); 1 (7.7) Stillbirths: 1 (3.6); 3 (14); 5 (38.5) INR = international normalised ratio mean ± SD; n (%)	Scale for Cohort Studies Selection: 1) Representativeness of the exposed cohort: a) truly representative 2) Selection of the non exposed cohort: a) taken from the same community as the exposed group 3) Ascertainment of exposure: d) no description 4) Demonstration that outcome of interest was not present at start of study: a) yes Comparability: 1) Comparability of cohorts on the basis of the design and the

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
with prosthetic heart valves **Study dates** January 2005 to August 2009 **Source of funding** Not reported	valve thrombosis • Maternal near miss: 6/62(9.7%) • Heart failure: 4/62 (7%) • Post-CS bleeding problems: 2/62 (7%) • Warfarin embryopath: 5/62 (12%) (average warfarin dosage was ranged from 3.5 to 7.5 mg with average INR of 2.3 to 3.1 with highest INR of 3.2 to 6.1) **Inclusion criteria** • Women with mechanical heart valve being managed in a combined cardiac-	3. Group 3 = 7.5 mg or more			analysis: c) unclear Outcome: 1) Assessment of outcome: b) record linkage 2) Was follow-up long enough for outcomes to occur: c) yes for the reported outcomes 3) Adequacy of follow up of cohorts: a) complete follow up Overall score: 5/9 **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	obstetric unit within the study period **Exclusion criteria** Not reported				
Full citation Xu, Z., Fan, J., Luo, X., Zhang, W. B., Ma, J., Lin, Y. B., Ma, S. H., Chen, X., Wang, Z. P., Ou, J. S., Zhang, X., Anticoagulation Regimens During Pregnancy in Patients With Mechanical Heart Valves: A Systematic Review and Meta-analysis, Canadian Journal of Cardiology, 32, 1248.e1-1248.e9, 2016	**Sample size** N = 2113 pregnancies from 51 studies **Characteristics** • Vitamin K antagonist (VKA) low dose regimen = 11 studies • VKA high dose regimen = 7 studies • Heparin (H)/VKA regimen= 13 studies • Low molecular weight heparin (LMWH) regimen= 12 studies	**Interventions** Group 1: A regimen of a VKA throughout pregnancy Group 2: A H/VKA regimen, which includes use of VKAs except for adjusted doses of UFH or LMWH during 6-12 weeks of pregnancy Group 3: An LMWH regimen of adjusted LMWH doses throughout pregnancy Group 4: A UFH regimen of adjusted doses of UFH throughout pregnancy	**Details** The study was performed according to the Meta-analysis of Observational Studies in Epidemiology (MOOSE) guidelines. Electronic searches to June 2015 of: - Medline, EMBASE, Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and the Database of Abstracts of Review of Effectiveness for the following MeSH and search terms: “heart valve prosthesis,” “pregnancy” “anticoagulants,” “antithrombins” “coumarins” “warfarin” “heparin low-molecular-weight” “thromboembolism” and “hemorrhage”	**Results** • Maternal major thrombotic event (fatal thromboembolism, prosthetic valve thrombosis requiring thrombolysis or emergency surgery, documented evidence of central nervous system embolization, documented evidence of peripheral limb and visceral embolization requiring surgery, and any other related events requiring hospitalization), Number of pregnancies (%) [95% confidence interval]: 1. VKA regimen: 39/1398 (2.79) [2.01-3.84] 2. Low-dose subgroup: 4/351 (1.14) [0.37-3.09] 3. H/VKA regimen: 25/337 (7.42) [4.95-10.90] 4. LMWH regimen: 5/113 (4.42) [1.64-10.52] 5. UFH regimen: 20/67 (29.85) [19.60-42.43] • Maternal major antenatal haemorrhagic event (major haemorrhagic events in the antenatal period, including death	**Limitations** **ROBIS Checklist** (for systematic review) DOMAIN 1: STUDY ELIGIBILITY CRITERIA 1.1 Did the review adhere to pre-defined objectives and eligibility criteria? Probably yes 1.2 Were the eligibility criteria appropriate for the review question? Yes 1.3 Were eligibility criteria unambiguous?

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Ref Id 588934 **Country/ies where the study was carried out** China **Study type** Systematic review of cohort studies and case series (N ≥6 women) **Aim of the study** To evaluate the effectiveness and safety of 4 anticoagulation regimens in women with mechanical heart valves. **Study dates** 2015-2016	• UFH regimen = 8 studies **Inclusion criteria** • the study designs were case series (6 pregnancies or more), cohort studies or randomized control trials of pregnancies in women with MPHVs • the anticoagulation regimens were clearly specified and did not change during the whole pregnancy • at least 1 outcome of interest was reported		- Conference articles (from the ISI Web of Knowledge Platform of ISI Proceedings) - Unpublished theses and dissertations (from ProQuest Digital Dissertations) Manual search of secondary sources, including the references of initially identified articles and recent review articles Two investigators independently screened the titles and abstracts. Authors were contacted for clarification if any uncertain issues arose. Any disagreements were further discussed between the investigators. Standardised data extraction was performed for each eligible study	due to haemorrhage, intracranial bleeding or documented cardiac tamponade requiring intervention, haemorrhage requiring transfusion, and any other related events requiring inpatient treatment), Number (%) of pregnancies [95% confidence interval]: 1. VKA regimen: 5/1027 (0.49) [0.18-1.21] 1. Low-dose subgroup: 3/442 (0.68) [0.18-2.14] 2. H/VKA regimen: 2/329 (0.61) [0.11-2.42] 3. LMWH regimen: 4/98 (4.08) [1.31-10.71] 4. UFH regimen: 6/114 (5.26) [2.15-11.57] • Maternal death: any maternal antenatal death from any cause, Number (%) of pregnancies [95% confidence interval]: 1. VKA regimen: 12/1353 (0.89) [0.48-1.60] 1. Low-dose subgroup: 1/325 (0.31) [0.02-1.97] 2. H/VKA regimen: 3/348 (0.86) [0.22-2.70] 3. LMWH regimen: 2/113 (1.77) [0.31-6.88] 4. UFH regimen: 1/114 (0.88) [0.05-5.51] • Fetal wastage: spontaneous abortion, therapeutic abortion, stillbirth and neonatal death, Number (%) of	Probably yes 1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Probably yes 1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Yes Concerns regarding specification of study eligibility criteria LOW DOMAIN 2: IDENTIFICATION AND

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Supported by Medical Scientific Research Foundation of Guangdong Province, PR. China(Grant No. B2013103); Scientific Research Fund of Chinese Preventive Medicine Association (Grant No.20131909); the Project of the Natural Science Foundation of Guangdong Province, PR. China (Grant No. 2015A030310055) and the National Clinical Key	**Exclusion criteria** • the study was not written in English • the study did not follow all pregnancies until completion • the anticoagulation regimen was not consistent with standards of care and the data from patient subgroups whose regimens were in line with the standards could not be extracted • the data had already been included and cited in any previously			pregnancies [95% confidence interval]: 1. VKA regimen: 325/999 (32.53) [29.65-35.55] 2. Low-dose subgroup: 85/442 (19.23) [15.73-23.28] 3. H/VKA regimen: 77/340 (22.65) [18.38-27.55] 4. LMWH regimen: 12/98 (12.24) [6.76-20.78] 5. UFH regimen: 37/69 (53.62) [41.28-65.55]	SELECTION OF STUDIES 2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? Yes 2.2 Were methods additional to database searching used to identify relevant reports? Yes 2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? Yes 2.4 Were restrictions based on date, publication format, or language appropriate? Yes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Specialty Fund of China.	selected studies • the anticoagulation intensity was not consistent with standards of care (international normalized ratio [INR], 2.0-4.5; active partial thromboplastin time, 2-3 times the normal value; or peak anti-Xa level, 0.5-1.2 IU/mL)				2.5 Were efforts made to minimise error in selection of studies? Yes Concerns regarding methods used to identify and/or select studies LOW DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL 3.1 Were efforts made to minimise error in data collection? Yes 3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Yes 3.3 Were all

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					relevant study results collected for use in the synthesis? Yes 3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Yes 3.5 Were efforts made to minimise error in risk of bias assessment? Yes Concerns regarding methods used to collect data and appraise studies LOW DOMAIN 4: SYNTHESIS AND FINDINGS 4.1 Did the synthesis include all studies that it should? Probably yes 4.2 Were all pre-

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					defined analyses reported or departures explained? Yes 4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? Yes 4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? Yes 4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? No 4.6 Were biases in primary studies minimal or addressed in the

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>synthesis? Yes
Concerns regarding the synthesis and findings LOW

Other information
None</td></tr>
<tr><td>Full citation
Ayad, Sherif W., Hassanein, Mahmoud M., Mohamed, Elsayed A., Gohar, Ahmed M., Maternal and Fetal Outcomes in Pregnant Women with a Prosthetic Mechanical Heart Valve, Clinical Medicine Insights. Cardiology, 10, 11-7, 2016

Ref Id</td><td>Sample size
N=100

Characteristics
Not reported in details

Inclusion criteria
Women with mechanical heart valves

Exclusion criteria
Not reported</td><td>Interventions
Anticoagulant treatment in late trimester -
Group 1: >5 mg of oral warfarin (n = 65)
Group 2: ≤5 mg of warfarin (n = 33)
Group 3: LMWH (enoxaparin sodium) (n = 2)

Note - First trimester anticoagulants included oral warfarin = 17 (>5 mg =9 and ≤ 5mg = 8), subcutaneous heparin calcium = 28, subcutaneous LMWH (enoxaparin sodium) = 53, IV UFH = 2. The protocol of anticoagulant therapy was not</td><td>Details
Not reported</td><td>Results<table><tr><td></td><td>≤5 mg (n = 33)</td><td>>5 mg (n = 65)</td></tr><tr><td>Live birth</td><td>23</td><td>27</td></tr><tr><td>Warfarin embryopathy</td><td>0</td><td>0</td></tr><tr><td>Congenital anomaly</td><td>1</td><td>1</td></tr></table></td><td>Limitations
Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies:

Selection:
1) Representativeness of the exposed cohort
a) truly representative

2) Selection of the non exposed cohort
a) taken from the</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
741569 **Country/ies where the study was carried out** Egypt **Study type** Prospective observational study **Aim of the study** To examine the pregnancy outcomes of pregnant with prosthetic heart valves on anticoagulant therapy **Study dates** Not reported **Source of funding** None		reported in details. It was assumed that these stated anticoagulants which were used during first trimester and were switched to warfarin in late trimester			same community as the exposed group 3) Ascertainment of exposure d) no description 4) Demonstration that outcome of interest was not present at start of study a) yes Comparability: 1) Comparability of cohorts on the basis of the design and the analysis c) unclear Outcome: 1) Assessment of outcome d) no description 2) Was follow-up long enough for outcomes to occur c) yes for the reported

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td>outcomes

3) Adequacy of follow up of cohort
a) complete follow up

Overall score: 5/9

Other information
None</td></tr>
<tr><td>Full citation
Khader, Khalid Abd Aziz Mohamad, Saad, Ahmed Samy, Abdelshafy, Mohammed, Pregnancy Outcome in Women with Mechanical Prosthetic Heart Valves Treated with Unfractionated Heparin (UFH) or Enoxaparin,</td><td>Sample size
N=40

Characteristics
• Mean age: 26.5 years
• Mean weight: 71.5 kg
• Mean pregnancies: 2
• Mitral valve replacement (MVR): 65%
• Aortic valve replacement (AVR): 23%</td><td>Interventions
• UFH - Before 6 weeks gestation, warfarin was replaced with UFH (15.000 IU/12 hours) and continued until 12 hours before birth and resumed 4-6 hours after birth if there was no complication. Activated partial thromboplastin time (aPTT) was kept at double the control</td><td>Details
Not reported</td><td>Results
<table><tr><th></th><th>UFH (n)</th><th>LMWH (n)</th></tr><tr><td>Maternal death</td><td>0</td><td>0</td></tr><tr><td>Full term live birth</td><td>11</td><td>10</td></tr><tr><td>Live birth</td><td>17</td><td>14</td></tr><tr><td>Abortion</td><td>3</td><td>5</td></tr><tr><td>Thrombotic complication</td><td>0</td><td>1</td></tr><tr><td>Antepartum haemorrhage</td><td>2</td><td>2</td></tr><tr><td>Postpartum haemorrhage</td><td>2</td><td>3</td></tr></table></td><td>Limitations
Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies:

Selection:
1) Representativeness of the exposed cohort:
a) truly representative</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Journal of obstetrics and gynaecology of India, 66, 321-6, 2016 **Ref Id** 741588 **Country/ies where the study was carried out** Egypt **Study type** Prospective non-randomised controlled trial **Aim of the study** To compare the maternal and neonatal outcomes between unfractionated heparin (UFH) and enoxaparin among pregnant	• MVR + AVR: 13% **Inclusion criteria** • Pregnant women with prosthetic heart valves attending in high-risk pregnancy units **Exclusion criteria** Not reported	level throughout heparin treatment. • LMWH - Before 6 weeks gestation, warfarin was replaced with enoxaparin (1 mg/kg twice daily [bd]) until 36 weeks gestation when it was switched to UFH (15.000 IU/12 hours) until 12 hours before birth and restarted 4-6 hours after birth unless any complication. Antifactor Xa level was maintained at 0.7-1.2 IU/ml / 4 hour post dose throughout enoxaparin treatment.		Vaginal birth: 10 | 9 Caesarean section: 7 | 5	2) Selection of the non exposed cohort: a) taken from the same community as the exposed group 3) Ascertainment of exposure: d) no description 4) Demonstration that outcome of interest was not present at start of study: a) yes Comparability: 1) Comparability of cohorts on the basis of the design and the analysis: c) study controlled for age weight total pregnancies before and site of cardiac valve lesions Outcome: 1) Assessment of outcome:

<table>
<tr><th>Study details</th><th>Participants</th><th>Interventions</th><th>Methods</th><th>Outcomes and Results</th><th>Comments</th></tr>
<tr><td>women with mechanical heart valves

Study dates
May 2012 to March 2014

Source of funding
Not reported</td><td></td><td></td><td></td><td></td><td>b) record linkage

2) Was follow-up long enough for outcomes to occur: a) yes for the reported outcomes

3) Adequacy of follow up of cohorts: a) complete follow up

Overall score: 6/9

Other information
None</td></tr>
<tr><td>Full citation
Vause, S., Clarke, B., Tower, C. L., Hay, C. R. M., Knight, M., Pregnancy outcomes in women with mechanical prosthetic</td><td>Sample size
N = 53

Characteristics
• 210 hospitals with consultant-led maternity units were included</td><td>Interventions
Group 1: Warfarin throughout pregnancy (n= 3, 5%)
Group 2: Low molecular weight heparin (LMWH) throughout pregnancy (n= 41, 71%)
Group 3: First trimester LMWH with subsequent warfarin until early third</td><td>Details
• Poor maternal outcome = maternal death or serious morbidity, admission to intensive care for > 1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident, or bleeding</td><td>Results<table><tr><td></td><td>*</td><td>**</td><td>***</td><td>****</td></tr><tr><td>I</td><td>1 (33)</td><td>1 (33)</td><td>1 (33)</td><td>0</td></tr><tr><td>II</td><td>10 (24)</td><td>13 (32)</td><td>10 (24)</td><td>8 (20)</td></tr><tr><td>III</td><td>2 (22)</td><td>1 (11)</td><td>1 (11)</td><td>5 (56)</td></tr><tr><td>IV</td><td>1 (20)</td><td>0</td><td>1 (20)</td><td>3 (60)</td></tr></table></td><td>Limitations
Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies
Selection:</td></tr>
</table>

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
heart valves: a prospective descriptive population based study using the United Kingdom Obstetric Surveillance System (UKOSS) data collection system, BJOG: An International Journal of Obstetrics and Gynaecology, 124, 1411-1419, 2017 **Ref Id** 741604 **Country/ies where the study was carried out** UK **Study type** Prospective population-	<u>Characteristics of women:</u> • Median age (range) in years: 31 (18-47) • White British: 38 (66%) • Asian: 7 (12%) • Black: 9(15%) • Other: 4 (7%) • BMI ≥25: 23 (40%) • Nullip: 25 (43%) • Smoking during pregnancy: 13 (22%) • Heart valve replacement for (congenital heart disease: 29 (50%), for rheumatic heart disease: 14 (24%), endocarditis: 9 (16%),	trimester, converting to heparin before birth (n= 9, 16%) Group 4: Other (n= 5, 9%) Note - Of women presenting before 7 weeks gestation (n=33), 3 (9%) had used pre-pregnancy LMWH and 21 (64%) switched to LMWH before 7 weeks; 2 women used warfarin throughout pregnancy and one woman who had termination did not convert to LMWH. At 10 weeks of gestation, 25/30(83%) women on LMWH needed a higher dose than that recommended by BNF. At 20 weeks gestation, 25/28 (89%) needed higher dose.	requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma • Poor fetal outcome = any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of < 7 at 5 minutes or admission to the neonatal unit	n (%) * Poor maternal outcome, poor fetal outcome ** Poor maternal outcome, good fetal outcome *** Good maternal outcome, poor fetal outcome **** Good maternal outcome, good fetal outcome	1) Representativeness of the exposed cohort a) truly representative 2) Selection of the non exposed cohort a) taken from the same community as the exposed group 3) Ascertainment of exposure a) secure record 4) Demonstration that outcome of interest was not present at start of study a) yes Comparability: 1) Comparability of cohorts on the basis of the design and the analysis c) unclear

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
based observational study **Aim of the study** To examine the maternal and fetal outcomes of women with mechanical prosthetic heart valves with different anticoagulation therapy during pregnancy **Study dates** 1 February 2013 to 31 January 2015 **Source of funding** Wellbeing of women	aortopathy: 3 (5%, unknown: 3 (5%)) • Warfarin: 49 (84%) • Low molecular weight heparin 4(7%) • Dabigatran: 1(2%) • No anticoagulation: 4(7%) • 57 women had prosthetic heart valve replacement before pregnancy whereas one woman had valve implant during 2nd trimester (for unexpected aortic dissection). • 33 (58%) women				Outcome: 1) Assessment of outcome b) record linkage 2) Was follow-up long enough for outcomes to occur c) yes for the reported outcomes 3) Adequacy of follow up of cohorts a) complete follow up Overall score: 7/9 **Other information** None

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	presented before 7 weeks of gestation 28 women had pre-pregnancy counselling. • Termination of pregnancy: 4 (7%) • Miscarriage: 5 (9%) • Still birth: 1 (2%) • Live birth: 45 (78%) • Neonatal death: 0 • Unknown: 1 (2%) • Maternal death with fetus undelivered: 5 (9%) (1 cardiovascular accident and 4 thrombosed valve/dysfunction)				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Serious maternal morbidity = 24 (41%) (4 cardiovascular accident, 5 thrombosed valve, 1 primary postpartum haemorrhage, 6 secondary postpartum haemorrhage, 6 wound haematoma, 4 intraabdominal bleed, 1 vaginal haematoma) • Mode of birth (spontaneous vaginal delivery: 18 (39%), instrumental vaginal birth: 3 (6%), LSCS in labour: 1 (2%), LSCS before labour: 24 (51%),				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	unknown: 1 (2%)) • Onset of labour (induced: 17 (37%), spontaneous: 5 (11%), Unknown: 1 (2%)) <u>Characteristics of live birth babies (n = 45):</u> • <37 weeks of gestation (preterm): 11 (24%) • Birthweight <10th percentile for sex and gestation: 14 (31%) • APGAR < 7 at 5 minutes: 5 (11%) • Neonatal intensive care unit (NICU) admission = 14 (31%)				

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	Inclusion criteria "a case was defined as any women in the UK with artificial mechanical prosthetic heart valve who became pregnant in 2-year period between 1 February 2013 and 31 January 2015, irrespective of pregnancy outcomes Data were prospectively collected from consultant-led maternity unit (as such women were not cared in any other setting in UK)" **Exclusion criteria** Not reported				

1 *BMI: body mass index; BNF: British National Formulatory; CS: caesarean section; INR: international normalised ratio; LMWH: low-molecular-weight heparin; LSCS: lower*
2 *segment caesarean section; N: number of participants; SD: standard deviation; UFH: unfractionated heparin*

Intrapartum care for women with cardiac disease – mode of birth

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Ruys, T. P., Roos-Hesselink, J. W., Pijuan-Domenech, A., Vasario, E., Gaisin, I. R., Iung, B., Freeman, L. J., Gordon, E. P., Pieper, P. G., Hall, R., Boersma, E., Johnson, M. R., Ropac investigators, Is a planned caesarean section in women with cardiac disease beneficial?, Heart, 101, 530-6, 2015 **Ref Id** 392538 **Country/ies where the study was carried out** Registry data from 28 countries **Study type** Retrospective cohort study	**Sample size** N=1262 births **Characteristics** • Age in years, median: 30, SD:5.6, range: 16-53 Planned VB n=869; Planned CS (any reason) n=393; Planned cardiac CS n=173 Age (SD): 30 (5.4); 30 (6.0); 30 (5.8) Congenital heart disease: 69; 57; 49 Valvular heart disease: 25; 29; 35 Cardiomyopathy: 5.1; 10; 13 Ischaemic heart disease: 1.4; 3.1; 3.5 NYHA class 1: 76; 61; 45 NYHA class 2: 21; 31; 43	**Interventions** Comparison 1: Planned CS for cardiac reasons vs. planned VB Comparison 2. Planned CS for either cardiac or obstetric reasons vs. planned VB	**Details** Data were prospectively gathered from 2008 except for women who were pregnant during 2007 for whom data was retrospectively reviewed. To evaluate pregnancy outcome by mode of birth the following data were gathered: place of delivery, planned mode of delivery, performed mode of delivery, reason for CS, start of labour, rupture of membranes, complications during delivery and NYHA classification	**Results** 1262 pregnancies with mode of birth data: planned CS for cardiac reasons n=172 and planned VB n=869 <u>Planned CS for cardiac reasons vs. planned VB:</u> • Maternal mortality: planned CS for cardiac reasons n= 8/172* vs. planned VB n=5/869* • Maternal morbidity: Postpartum heart failure: planned CS for cardiac reasons n = 17/172* vs. planned VB n=34/869* • Postpartum haemorrhage: planned CS for cardiac reasons n = 13/172* vs. planned VB n=42/869*	**Limitations** Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies Selection: High risk of bias 1) Representativeness of the exposed cohort b) somewhat representative of the average female cardiac disease population; however the population studied was heterogeneous with a multitude of different underlying cardiac diagnoses, and there was no stratified analysis by severity of disease or by cardiac condition 2) Selection of the non exposed cohort b) drawn from a different source (in the planned vaginal birth

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study To determine the relationship between mode of delivery and pregnancy outcome in women with pre-existing heart disease **Study dates** 2007 - 1 June 2011 **Source of funding** The Registry is part of the EurObservational Research Programme sponsored by: Abbott Vascular, Amgen, Bayer Pharma, Bristol Myers Squibb, Boehringer Ingelheim, Boston Scientific, Daiichi Sankyo, Menarini, Merck & Co. (MSD), Novartis, Pfizer, and Servier	<table><tr><td>NYHA class 3</td><td>1.4</td><td>6.1</td><td>11</td></tr><tr><td>NYHA class 4</td><td>0.4</td><td>0.5</td><td>1.2</td></tr><tr><td>Pre-eclampsia</td><td>2.3</td><td>5.9</td><td>3.5</td></tr><tr><td>Anticoagulation</td><td>9.1</td><td>14.5</td><td>25</td></tr></table> P values for the comparison planned caesarean section (CS) (any reason) vs. planned vaginal birth: Type of heart disease: <0.001 NYHA class: <0.001 Pre-eclampsia: 0.001 Anticoagulation: 0.004 **Inclusion criteria** • Women enrolled in the European Registry on Pregnancy and Heart Disease (including women with structural [valvular, congenital or cardiomyopathy] heart disease or ischaemic heart disease presenting with pregnancy) between January 2007 and June 2011 with available data on mode of birth **Exclusion criteria**		Endpoints were: maternal mortality, postpartum heart failure, postpartum haemorrhage, perinatal and neonatal mortality, gestation length, premature labour and birth weight Statistical analysis: Patients stratified into World Health Organization (WHO) risk classification for pregnancy in women with cardiac disease and matched with propensity scoring to study performed mode of delivery and adverse outcome (maximal difference of 0.3	• Perinatal mortality: planned CS for cardiac reasons n=4/172* vs. planned VB n=14/869* • Neonatal mortality: planned CS for cardiac reasons n=0/172* vs. planned VB n=4/869* • Emergency CS (for either cardiac or obstetric reasons): planned CS for cardiac reasons n=30/172 ** vs. planned VB: n=143/869 * Numerators calculated by the NGA technical team based on percentages and denominators given in the paper ** Numerator calculated by the NGA technical team - as follows: 172-142=30 (172 is the number of planned elective CS for	group there was a higher percentage of women with NYHA class 1 and a lower percentage with NYHA class 2,3 and 4 as opposed to the planned cardiac CS group, although the paper did not mention if the difference was statistically significant. The paper showed that there was a statistically significant difference in NYHA class and type of heart disease between the planned vaginal birth group and the planned CS group) 3) Ascertainment of exposure a) registry data 4) Demonstration that outcome of interest was not present at start of study a) yes Comparability: High risk of bias

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• Non-structural heart disease		points on range of -1 to 1)	cardiac reasons; 142 is the number of performed elective CS for cardiac reasons) <u>Planned CS (for either cardiac or obstetric reasons) vs. planned VB</u>: • Emergency CS for cardiac reasons: planned CS (for either cardiac or obstetric reasons): n = 25/393 vs. planned VB: n = 13***/869 Please note: • Emergency CS in women with planned VB: n=143/869 (Emergency CS for obstetric reasons n=130***; Emergency CS for cardiac reasons n=13***) • Emergency CS in women with planned CS: n=53/393 (Emergency CS for obstetric reasons	1) Comparability of cohorts on the basis of the design or analysis Study does not control for any important factors Outcome: Low risk of bias 1) Assessment of outcome b) record linkage 2) Was follow-up long enough for outcomes to occur a) yes, outcomes were intrapartum/postpartum events 3) Adequacy of follow up of cohorts a) complete follow up - all subjects accounted for: yes Overall risk of bias: High **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
				n=28; Emergency CS for cardiac reasons n=25) • Heart failure n=13 • Arrhythmia n=5 • Acute coronary syndrome n=1 • Ischaemic cerebral event n=1 • Unknown n=5 *** Calculated by the NGA team - as follows: 38-25=13 (38 is the total number of emergency CS for cardiac reasons; 25 is the number of emergency CS for cardiac reasons after planned elective CS)	Outcomes are presented in several ways in the paper: 1. All elective CS vs. all emergency CS 2. Elective CS for cardiac reasons vs. emergency CS for cardiac reasons 3. Elective CS for obstetric reasons vs. emergency CS for obstetric reasons 4. Emergency CS from planned VB group vs. elective CS 5. Matched analysis of performed VB vs. performed CS

1 *CS: caesarean section; N: total number of participants; NGA: National Guideline Alliance; NYHA: New York Heart Association; SD: standard deviation; VB: vaginal birth*

Intrapartum care for women with cardiac disease – fluid management

3 No clinical evidence was identified for this review and so there are no evidence tables.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

<table>
<tr><th>Bibliographic details</th><th>Participants</th><th>Tests</th><th>Methods</th><th>Outcomes and results</th><th>Comments</th></tr>
<tr>
<td>Full citation
Fett,J.D., Validation of a self-test for early diagnosis of heart failure in peripartum cardiomyopathy, Critical Pathways in Cardiology: A Journal of Evidence-Based Medicine, 10, 44-45, 2011

Ref Id
195283

Country/ies where the study was carried out
USA

Study type
Case-control study

Aim of the study
To validate self-test questionnaires of common heart failure symptoms to identify women with peripartum cardiomyopathy (PPCM)

Study dates
2003 to 2010</td>
<td>Sample size
N=57

Characteristics
Women with PPCM:
• Mean age: 31 years
• Diagnosis before birth: 6/47(13%)
• Left ventricular ejection fraction (LVEF) (median and range): 0.22 (0.07 - 0.40)
Note - PPCM =idiopathic first onset heart failure during last month of pregnancy up to 6 months postpartum with LVEF ≤45%

Inclusion Criteria
• PPCM were recruited from 2 PPCM networks - A Mother's Heart and Facebook PPCM groups</td>
<td>Tests
Self-test questionnaires which include orthopnoea, dyspnoea, unexplained cough, swelling lower extremities, excessive weight gain during last month of pregnancy and palpitation</td>
<td>Methods
53 PPCM women took part in survey (6 who did not meet diagnostic criteria were excluded)</td>
<td>Results
<table>
<tr><th></th><th>PPCM (n=47)</th><th>No PPCM (n=10)</th></tr>
<tr><td>Orthopnoea</td><td>45</td><td>0</td></tr>
<tr><td>Dyspnoea</td><td>47</td><td>2</td></tr>
<tr><td>Cough</td><td>34</td><td>1</td></tr>
<tr><td>Oedema</td><td>45</td><td>7</td></tr>
<tr><td>Excess weight gain</td><td>39</td><td>3</td></tr>
<tr><td>Palpitations</td><td>36</td><td>0</td></tr>
</table></td>
<td>Limitations
<u>Quality assessment by QUADAS 2</u>

Patient selection
<u>A. Risk of Bias:</u>
1. Was a consecutive or random sample of patients enrolled? Unclear
2. Was a case-control design avoided? No
3. Did the study avoid inappropriate exclusions? Probably yes
4. Could the selection of patients have introduced bias? Unclear risk
<u>B. Concerns regarding applicability</u>:
1. Are there concerns that the included patients and setting do not match the review question? LOW concern

Index Test</td>
</tr>
</table>

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Source of funding None	• Non-PPCM were earlier pregnancy in PPCM women, or their friends or relatives **Exclusion Criteria** Not reported				A. Risk of Bias 1. Were the index test results interpreted without knowledge of the results of the reference standard? Unclear risk 2. If a threshold was used, was it pre-specified? Not applicable 3. Could the conduct or interpretation of the index test have introduced bias? High risk B. Concerns regarding applicability 1. Are there concerns that the index test, its conduct, or interpretation differ from the review question? HIGH concern as this is a case-control study and the symptoms (index test) were assessed by questionnaire checklists ***Reference***

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					Standard A. Risk of Bias *Target condition and reference standard(s)* 1. Is the reference standards likely to correctly classify the target condition? Probably yes 2. Were the reference standard results interpreted without knowledge of the results of the index tests? Yes 3. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk B. Concerns regarding applicability 1. Are there concerns that the target condition as defined by the reference standard does not match the question? LOW concern ***Flow and Timing***

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					A. Risk of Bias 1. Was there an appropriate interval between index test and reference standard? Not applicable 2. Did all patients receive the same reference standard? Probably yes 3. Were all patients included in the analysis? Probably yes 4. Could the patient flow have introduced bias? Low risk **Other information** None
Full citation Haghikia, A., Podewski, E., Libhaber, E., Labidi, S., Fischer, D., Roentgen, P., Tsikas, D., Jordan, J., Lichtinghagen, R., von Kaisenberg, C. S., Struman, I., Bovy, N., Sliwa, K., Bauersachs, J., Hilfiker-Kleiner, D.,	**Sample size** N=115; 113 PPCM vs. 19 healthy postpartum controls **Characteristics** • Mean age: 32 years	**Tests** NT-proBNP	**Methods** Not reported	**Results** NT-proBNP in PPCM (n=69) vs. in control (n=19) median (range) (pg/ml) PPCM = 3315 (875 - 26082) Control = 61 (24 - 531)	**Limitations** Quality assessment by QUADAS 2 **Patient selection** A. Risk of Bias: 1. Was a consecutive or random sample of patients enrolled? Probably yes

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
Phenotyping and outcome on contemporary management in a German cohort of patients with peripartum cardiomyopathy, Basic Research in Cardiology, 108, 366, 2013 **Ref Id** 391719 **Country/ies where the study was carried out** Germany **Study type** Case-control study **Aim of the study** To examine the epidemiology and treatment in cohort of women with peripartum cardiomyopathy (PPCM) **Study dates** 2004 to 2012 **Source of funding** Not reported	• C-section: 68% in PPCM vs. 26% in controls **Inclusion Criteria** • PPCM: Diagnosis criteria for PPCM included left ventricular ejection fraction (LVEF) of ≤45% and absence of previously known cardiomyopathy • Control: Healthy postpartum women with confirmed normal cardiac function by echocardiography, left ventricular ejection fraction (LVEF) >55% in the first postpartum week **Exclusion Criteria** Not reported				2. Was a case-control design avoided? No 3. Did the study avoid inappropriate exclusions? Yes 4. Could the selection of patients have introduced bias? Low risk <u>B. Concerns regarding applicability</u>: 1. Are there concerns that the included patients and setting do not match the review question? LOW concern **Index Test** <u>A. Risk of Bias</u> 1. Were the index test results interpreted without knowledge of the results of the reference standard? Unclear risk 2. If a threshold was used, was it pre-specified? Not applicable 3. Could the conduct

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					or interpretation of the index test have introduced bias? Unclear risk B. Concerns regarding applicability 1. Are there concerns that the index test, its conduct, or interpretation differ from the review question? MODERATE concern as this is a case-control study **Reference Standard** A. Risk of Bias *Target condition and reference standard(s)* 1. Is the reference standards likely to correctly classify the target condition? Yes 2. Were the reference standard results interpreted without knowledge of the results of the index tests? No 3. Could the reference standard, its conduct, or its interpretation

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					have introduced bias? Low risk B. Concerns regarding applicability 1. Are there concerns that the target condition as defined by the reference standard does not match the question? LOW concern **Flow and Timing** A. Risk of Bias 1. Was there an appropriate interval between index test and reference standard? Not applicable 2. Did all patients receive the same reference standard? Probably yes Were all patients included in the analysis? Yes 3. Could the patient flow have introduced bias? Low risk **Other information**

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					None
Full citation Karaye, K. M., Lindmark, K., Henein, M. Y., Electrocardiographic predictors of peripartum cardiomyopathy, Cardiovascular Journal of Africa, 27, 66-70, 2016 **Ref Id** 562401 **Country/ies where the study was carried out** South Africa **Study type** Case-control study **Aim of the study** To evaluate electrocardiographic predictors of peripartum cardiomyopathy (PPCM) **Study dates** Not reported **Source of funding** Funds from Umea University, Sweden	**Sample size** N=131; n=54 PPCM and n=77 controls Characteristics • Mean age: 27 years • Body mass index (BMI) = 22 kg/m2 • K+ (mmol/L): 3.9±0.8 in PPCM vs. 4.6±0.7 in controls (p<0.001) • Na+ (mmol/L): 136.9±5.9 in PPCM vs. 139.6±4.4 (p<0.009) • Creatinine (umol/L): 93.2±67.1 in PPCM vs. 74.7±19.3 (p=0.045) **Inclusion Criteria** • PPCM: onset of symptoms near end of pregnancy and	**Tests** ECG - considered abnormal if T-wave inversion with or without ST-segment depression (using digital electrocardiograph)	**Methods** Not reported	**Results** • All PPCM or controls had sinus rhythm. • Tachycardia control: 17/77 (22%) • Heart rate (beats per minute [bpm]), mean ±SD: PPCM: 111±16 Control : 90±16 • ECG heart rate (bpm) (odds ratio [OR], 95% confidence interval [CI]): Univariate (continuous): 1.078 (1.048, 1.109) Univariate (normal heart rate): 0.103 (0.044, 0.241) Multivariate (heart rate, QRS, QTc, ST-T wave abnormalities): 1.073 (1.036, 1.112) Multivariate (heart rate, ST-T wave abnormalities, serum potassium (K+): 1.066 (1.029, 1.104) Multivariate (heart rate, ST-T wave abnormalities, serum sodium (Na+): 13.415 (4.203, 42.825)	**Limitations** <u>Quality assessment by QUADAS 2</u> ***Patient selection*** <u>A. Risk of Bias:</u> 1. Was a consecutive or random sample of patients enrolled? Yes 2. Was a case-control design avoided? No Did the study avoid inappropriate exclusions? Yes 3. Could the selection of patients have introduced bias? Low risk <u>B. Concerns regarding applicability</u>: 1. Are there concerns that the included patients and setting do not match the review question? LOW concern ***Index Test***

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	within 9 months postpartum, ≥18 years, PPCM diagnosed by Heart Failure Association of the European Society of Cardiology working group and left ventricular ejection fraction (LVEF) <50% • Control: no history of cardiac disease or systemic hypertension, non-specific electrocardiography (ECG) changes (flat T waves in lead III or aVF and inverted T waves in aVR, V1 or V2) **Exclusion Criteria** • PPCM: onset of symptoms in early pregnancy or after first 5 months of postpartum,				A. Risk of Bias 1. Were the index test results interpreted without knowledge of the results of the reference standard? Unclear 2. If a threshold was used, was it pre-specified? Yes 3. Could the conduct or interpretation of the index test have introduced bias? Low risk B. Concerns regarding applicability 1. Are there concerns that the index test, its conduct, or interpretation differ from the review question? MODERATE concern as this is a case-control study ***Reference Standard*** A. Risk of Bias *Target condition and reference standard(s)* 1. Is the reference

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
	symptoms due to other diagnosis other than PPCM • Control: came to hospital to have their children immunised, known or found clinically to have any cardiac disease				standards likely to correctly classify the target condition? Yes 2. Were the reference standard results interpreted without knowledge of the results of the index tests? Probably yes 3. Could the reference standard, its conduct, or its interpretation have introduced bias? Low risk <u>B. Concerns regarding applicability</u> 1. Are there concerns that the target condition as defined by the reference standard does not match the question? LOW concern ***Flow and Timing*** <u>A. Risk of Bias</u> 1. Was there an appropriate interval between index test and reference standard? Not applicable 2. Did all patients

Bibliographic details	Participants	Tests	Methods	Outcomes and results	Comments
					receive the same reference standard? No as echocardiogram was not performed in the control group 3. Were all patients included in the analysis? Yes 4. Could the patient flow have introduced bias? High risk **Other information** None

1 *bpm: beats per minute; C-section: caesarean section; ECG: electrocardiogram; K+: potassium level; LVEF: left ventricular ejection fraction; N: total number of participants; Na+:*
2 *sodium level; NT-proBNP: N-terminal pro-brain natriuretic peptide; PPCM: peripartum cardiomyopathy; SD: standard deviation*

Intrapartum care for women with cardiac disease – management of cardiomyopathy

4

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Sliwa, K., Blauwet, L., Tibazarwa, K., Libhaber, E., Smedema, J. P., Becker, A., McMurray, J., Yamac, H., Labidi, S., Struhman, I., Hilfiker-Kleiner, D., Evaluation of bromocriptine in the treatment of acute severe	**Sample size** N=20 **Characteristics** • Age (mean±SD) in years= 26±8.3 years • Parity median (range)= 2 (1-6) • New York Heart Association	**Interventions** Symptoms and signs were recorded during first presentation at the cardiac unit at baseline and after a follow-up period of 6 months. Clinical assessment, echocardiography and blood analysis were performed at	**Details** Randomisation was done with a computerised generated randomisation list within 24 hours of diagnosis. Patients receiving bromocriptine had	**Results** • Number of mothers survived at 6 months follow-up: 9 in PPCM-Bromocriptine (PPCM-Br) vs. 6 in PPCM-	**Limitations** Cochrane Collaboration's tool for assessing risk of bias Selection bias i) Random sequence allocation -

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
peripartum cardiomyopathy: A proof-of-concept pilot study, Circulation, 121, 1465-1473, 2010 **Ref Id** 573782 **Country/ies where the study was carried out** South Africa **Study type** Randomised controlled trial **Aim of the study** To assess the efficacy of bromocriptine on the recovery of left ventricular (LV) function, symptom status and other clinical measures in patients' presenting within the first month postpartum with new-onset symptomatic peripartum cardiomyopathy (PPCM) and an LV ejection fraction (LVEF) <35%	(NYHA) class II: NYHA class III/IV= 5:5 **Inclusion criteria** • Patients presenting with symptoms of congestive cardiac failure in the last month of pregnancy or during the first month postpartum, no other identifiable cause for heart failure and LVEF <35% by transthoracic echocardiography. **Exclusion criteria** • Systolic blood pressure >160 or <95 mmHg or diastolic blood pressure >105 mmHg • Clinical conditions other than cardiomyopathy that could increase plasma levels of inflammatory markers such as	baseline and at 6 months. Cardiac magnetic resonance imaging (MRI) was obtained 4 to 6 weeks after diagnosis in patients receiving bromocriptine. 1.5-T MRI scanner was used. All patients received standard treatment with the diuretic frusemide and the angiotensin-converting enzyme (ACE) inhibitor enalapril. Patients with an LVEF < 25% or LV thrombus received anticoagulation therapy with wafarin for 6 months. Carvedilol was added after resolution of overt heart failure. Enalapril and carvedilol doses were titrated in the first 4 weeks as tolerated and remained unchanged for the 6-month study period. Frusemide dose was decreased based on clinical judgement. Bromocriptine: The intervention group received bromocriptine in addition to standard treatment.	cardiac MRI at 4 to 6 weeks after diagnosis to detect possible mural thrombi NYHA class was evaluated by a physician blinded to treatment allocation and laboratory results. The combined end point of poor outcome was defined as death, NYHA functional class III/IV or LVEF < 35% at 6 months as previously described.	Standard (PPCM-Std) • Poor outcome (number out of surviving patients): LVEF<35% = 0/9 in PPCM-Br vs. 2/6 in PPCM-Std • NYHA functional class III/IV at 6 months: 0% PPCM-Br vs. 50% in PPCM-Std • Death within 6 months: 1/10 in PPCM-Br vs 4/10 in PPCM-Std • No adverse effects including thromboembolism were reported in either group • Neonatal mortality: 0 in both groups • No significant differences in growth curves between the children of the PPCM-Br patients	appropriate randomisation method (computer generated randomisation list) ii) Allocation concealment - Unclear LEVEL - UNCLEAR Performance bias Blinding of participants and personnel - Unclear LEVEL - HIGH Detection bias Blinding of outcome assessments - Yes LEVEL - LOW Attrition bias Incomplete outcome data - Sample size did not mention LEVEL

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates Not reported **Source of funding** Medical Research Council of South Africa and the University of the Witwatersrand; the Leducq Foundation	sepsis, human immunodeficiency virus (HIV) positivity • Significant liver disease (transaminase levels > 2 times the upper limit of normal) • History of peptic ulcer disease • History of psychiatric disorders • Impaired renal function (urea and/or creatinine >1.5 times the upper limit of normal) • Any clinical condition that precluded inclusion in the study such as ischaemic heart disease or malignancy	Bromocriptine was given 2.5 mg twice daily (bd) for 2 weeks followed by 2.5 mg once daily (od) for 6 weeks.		and those of the PPCM-Std patients at 3 months of age	- UNCLEAR/LOW Reporting bias Selective reporting - The outcomes reported in method and result sessions were justified LEVEL - LOW Other bias Other sources of bias - Not reported LEVEL - LOW **Other information** None

1 *LV: left ventricle; LVEF: left ventricular ejection fraction; MRI: magnetic resonance imaging; N: total number of participants; NYHA: New York Heart Association; PPCM:*
2 *peripartum cardiomyopathy; PPCM-Br: women with peripartum cardiomyopathy who received bromocriptine; PPCM-Std: women with peripartum cardiomyopathy who received*
3 *standard treatment alone; SD: standard deviation*

Intrapartum care for women with cardiac disease – anaesthesia

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Bedard, E., Dimopoulos, K., Gatzoulis, M. A., Has there been any progress made on pregnancy outcomes among women with pulmonary arterial hypertension?, European Heart Journal, 30, 256-65, 2009 **Ref Id** 391198 **Country/ies where the study was carried out** UK **Study type** Systematic review of published case reports/case series. **Aim of the study** To assess the reported pregnancy outcomes for	**Sample size** 73 participants overall were identified from a total of 47 published articles. N = 53 Caesarean section n = 23 general anaesthetic n = 30 regional anaesthetic† † Of total study population, type of anaesthetic was not reported for 8 women, but it is unclear whether these women gave birth by caesarean section or vaginal delivery. Therefore presumed that the remaining 30 women had regional anaesthesia for caesarean section. **Characteristics** Not reported specifically for women who gave birth by caesarean section. Overall study population: n = 29 idiopathic pulmonary arterial hypertension	**Interventions** Women underwent either regional anaesthesia or general anaesthesia during the peripartum period† †anaesthesia was presumed to be for Caesarean section, although this is not explicitly stated in the article	**Details** Maternal death was assessed in relation to characteristics of the study population, in order to ascertain risk factors for maternal mortality.	**Results** **Maternal mortality** Risk of death in patients receiving general anaesthesia compared to regional anaesthesia: OR 4.37 (95% CI 1.28 to 16.5, p = 0.02)† The number of women who died in each group is not reported. † unclear whether comparator includes only women who gave birth by Caesarean section, or all women who received regional anaesthesia	**Limitations** ROBIS Checklist (for systematic review) DOMAIN 1: STUDY ELIGIBILITY CRITERIA 1.1 Did the review adhere to pre-defined objectives and eligibility criteria? No information 1.2 Were the eligibility criteria appropriate for the review question? Yes 1.3 Were eligibility criteria unambiguous? Probably yes 1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Probably yes 1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? No information Concerns regarding

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
women with pulmonary arterial hypertension **Study dates** Articles published between January 1997 and September 2007 were included **Source of funding** British Heart Foundation, European Society of Cardiology, Cardiology Institute of Quebec, Laval University, Cardiologists Association for the Province of Quebec	n = 29 congenital heart disease associated pulmonary arterial hypertension n = 15 other pulmonary arterial hypertension Maternal death n = 18 **Inclusion criteria** • Published reports of pregnancies in women with pulmonary arterial hypertension. • English language publication, or English language translation available. **Exclusion criteria** • Cases of pulmonary arterial hypertension related to chronic lung disease or acquired heart disease. • Reports of pregnancy which ended before 22 weeks				specification of study eligibility criteria LOW DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES 2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? No 2.2 Were methods additional to database searching used to identify relevant reports? No 2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? Yes 2.4 Were restrictions based on date, publication format, or language appropriate? Yes 2.5 Were efforts made to minimise error in selection of studies? No Concerns regarding methods used to identify and/or select studies HIGH Rationale for concern: Only MEDLINE database was used; No dual screening; No

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	(either by miscarriage or termination). For article selection: • Inadequate type of study (which does not include data on individual cases or case series) • Study with insufficient detail on relevant cases • Article not available				information on studies that were excluded or included DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL 3.1 Were efforts made to minimise error in data collection? Unclear 3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? No information 3.3 Were all relevant study results collected for use in the synthesis? No information 3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? No information 3.5 Were efforts made to minimise error in risk of bias assessment? No information Concerns regarding methods used to collect data and appraise studies HIGH Rationale for concern: High risk of bias from individual studies as no information on

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					whether dual screening and dual data collection were done and whether formal risk of bias assessment was made for each study. DOMAIN 4: SYNTHESIS AND FINDINGS 4.1 Did the synthesis include all studies that it should? Probably yes 4.2 Were all pre-defined analyses reported or departures explained? No information 4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? Yes 4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? No 4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? No 4.6 Were biases in primary studies minimal or addressed

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
					in the synthesis? No Concerns regarding the synthesis and findings HIGH Rationale for concern: Studies were case series that provided descriptive data only, are susceptible to selection bias and low internal validity.

1 *CI: confidence interval; N: total number of participants eligible for the review; OR: odds ratio*

Intrapartum care for women with cardiac disease – analgesia

3 No clinical evidence was identified for this review and so there are no evidence tables.

Intrapartum care for women with cardiac disease – management of the third stage of labour

5

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Cauldwell, M., Steer, P. J., Swan, L., Uebing, A., Gatzoulis, M. A., Johnson, M. R., The management of the third stage of labour in women	**Sample size** N=59 (Low dose infusion (Control/Ctrl) = 29 versus additional 2 IU (Intervention/ Iv)) = 30) **Characteristics**	**Interventions** The first 30 women who attended the clinic were given low-dose infusion (10 U of oxytocin diluted in 500 ml of normal saline given at a rate of 36 mL/hour for 4 hours (12mU/min)) while the next 30 women received an additional	**Details** Not stated	**Results** Two out of 62 women recruited were excluded for evidence of maternal sepsis. Estimated blood loss at delivery	**Limitations** Quality Assessment: Newcastle-Ottawa Assessment Scale for Cohort Studies Selection: 1) Representativeness of the exposed cohort: b)

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
with heart disease, Heart., 19, 2016 **Ref Id** 580433 **Country/ies where the study was carried out** UK **Study type** Prospective cohort study **Aim of the study** To examine the safety and efficacy of increased oxytocin doses in women with cardiac disease on cardiovascular side effects and postpartum haemorrhage **Study dates** September 2015 to June 2016 **Source of funding** Not reported	• Age (years) Iv: 33.1 (5.2) versus Ctrl: 30.2 (5.1) (p=0.03) • BMI at booking=26 • Nullipara = 33/59 (56%) • Spontaneous birth = 15/59 (25%) • Assisted birth = 20/59 (33%) • Elective caesarean section= 14/59 (23%) • Emergency caesarean section = 13/59 (21%) • Duration of 2nd stage Iv: 41 (44) vs Ctrl: 23 (41) (p=0.09) • Valvular heart disease = 20/59 (34%) • Complex congenital = 24/59 (41%) • Cardiomyopathy = 4/59 (7%) • Arrhymia = 6/59 (10%) • NYHA >1 = 1/59 (2%)	slow bolus injection of 2 IU of oxytocin over 10 min immediately after birth. Holter monitoring (Spacelabs) was performed for 12 hours at 30 minutes before oxytocin administration. The recordings were read by a cardiac physiologist blinded to treatment being given. Serum Troponin T was also examined 12 hours after oxytocin injection. Clinical signs of hypotension such as blood pressure and heart rate, were monitored every minute for first 10 min after commencing oxytocin and 10% change from the baseline was regarded as acceptable. The use of phenylephrine use during birth was also recorded.		(ml) Iv: 511±328 Ctrl: 830±444 Number of women requiring phenylephrine Iv: 5 Ctrl: 5 Number of women receiving additional uterotonic agents Iv: 1 Ctrl: 7 Number of women requiring blood transfusion Iv: 0 Ctrl: 1	somewhat representative of the women in labour with cardiac disease but the administration of oxytocin was not described in enough details 2) Selection of the non exposed cohort: a) same setting as intervention group 3) Ascertainment of exposure: a) prospective record 4) Demonstration that outcome of interest was not present at start of study: a) yes Comparability: 1) Comparability of cohorts on the basis of the design or analysis: no control of confounders Outcome: 1) Assessment of outcome: b) record linkage 2) Was follow-up long enough for outcomes to occur: a) yes

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
	• LMWH (therapeutic dose) = 2/59 (3%) **Inclusion criteria** • Women with underlying cardiac disease (congenital or acquired) **Exclusion criteria** • Delivered at other centre • Developed features of maternal sepsis in labour (temperature > 37.8 C on two occasions, or positive blood or urine cultures)				3) Adequacy of follow up of cohorts: a) complete follow up - all subjects accounted for: yes Overall score: 7/9 **Other information** None

BMI: body mass index; Ctrl: control group; Iv: intervention group; IU: international unit; LMWH: low-molecular-weight heparin; N: total number of participants; NYHA: New York Heart Association

Appendix F – Forest plots

Intrapartum care for women with cardiac disease – stratification of risk

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – mode of birth

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – fluid management

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – anaesthesia

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – analgesia

No meta-analysis was undertaken for this review and so there are no forest plots.

Intrapartum care for women with cardiac disease – management of the third stage of labour

No meta-analysis was undertaken for this review and so there are no forest plots.

Appendix G – GRADE tables

Intrapartum care for women with cardiac disease – stratification of risk

Table 18: Clinical evidence profile for predictive accuracy of different risk assessment tools, outcomes for the woman: cardiovascular events[11]

Number of studies	Design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	AUC (95% CI) or number of events/number of pregnancies at risk in each group (%)	Quality	Importance
CARPREG[a]									
1 (Balci 2014)	Prospective cohort study	213	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.57 (0.43 – 0.70)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Fu 2016)	Retrospective cohort study	730	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.63 (0.57-0.71)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Lu 2015)	Retrospective cohort study	268	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.73 (0.59-0.88)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Martins 2016)	Cohort study	132	Serious[3]	Not applicable	Serious[1]	Not assessed	0: (7/46)15.2% 1: (11/67)16.4% >1: (8/19) 42.1%	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Pijuan-Domenech 2015)	Prospective cohort study	179	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.67 (0.55-0.80)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*

[11] Sustained symptomatic tachyarrhythmia or bradyarrrhymia requiring treatment, cardiac arrest or cardiac death, pulmonary oedema, a decline in New York Heart Association (NYHA) functional class compared with baseline, need for urgent invasive cardiac procedures during pregnancy or within 6 months after delivery, any cardiac failure (new onset or worsening) necessitating treatment or admission and bedrest, any thrombo-embolic complication, any myocardial infarction and/or any cerebrovascular accident, death from any cause or worsening of left ventricular ejection fraction (LVEF)

Number of studies	Design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	AUC (95% CI) or number of events/number of pregnancies at risk in each group (%)	Quality	Importance
1 (Tanous 2010)	Prospective cohort study	66	Moderate risk of bias[3]	Not applicable	Serious[1]	Not assessed	0: (1/41)2% 1: (6/20)30% >1: (1/2)50%	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
Disease complexity[b]									
1 (Balci 2014)	Prospective cohort study	213	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.64 (0.52 – 0.75)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
Modified WHO criteria[c]									
1 (Balci 2014)	Prospective cohort study	213	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.77 (0.67 – 0.87)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Billebeau 2018)	Retrospective cohort study	43	Serious[3]	Not applicable	Serious[1]	Not assessed	2: 4/13 (33%) 2/3: 6/16 (37.5%) 4: 1/3 (30.8%)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Fu 2016)	Retrospective cohort study	730	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.71 (0.67-0.76)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Lu 2015)	Retrospective cohort study	268	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.83 (0.75-0.91)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Pijuan-Domenech 2015)	Prospecitve cohort study	179	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.76 (0.65-0.87)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*

Number of studies	Design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	AUC (95% CI) or number of events/number of pregnancies at risk in each group (%)	Quality	Importance
ZAHARA I[d]									
1 (Balci 2014)	Prospective cohort study	213	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.71 (0.59 – 0.83)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Billebeau 2018)	Retrospective cohort study	43	Serious[3]	Not applicable	Serious[1]	Not assessed	0-0.5: 6/14 (42.9%) 0.51-1.5: 4/8 (50%) 1.51-2.5: 0/2 (0%) 2.51-3.5: 2/5 (40%) >3.5: 3/9 (33%)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Fu 2016)	Retrospective cohort study	730	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.68 (0.60-0.75)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
1 (Lu 2015)	Retrospective cohort study	268	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.74 (0.61-0.86)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*
A total of all risk assessment protocol[e]									
1 (Balci 2014)	Prospective cohort study	213	No risk of bias	Not applicable	Serious[1]	Serious[2]	0.67 (0.55 – 0.79)	⊕⊖⊖⊖ VERY LOW	CRITICAL/IMPORTANCE*

AUC: area under receiver operating characteristic curve; CARPREG: CARdiac disease in PREGnancy; CHD: congenital heart disease; CI: confidence interval; DC: disease complexity; EF: ejection fraction; LVOT: left ventricular outflow tract; MID: minimal important difference; N: number of participants; TPo: total number of non-overlapping predictors of maternal cardiovascular events and offspring events (TPo); WHO: World Health Organziation; ZAHARA: Zwangerschap bij Aangeboren HARtAfwijkingen pregnancy in CHD (ZAHARA)

[1] The study used composite outcome

[2]The judgement of precision was based on the AUC value and its 95% CI. Thresholds for precision were set at 0.3 and 0.7. The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

[3]This was a descriptive study and analysis was not done for predictive accuracy of the tool

**The outcome of cardiovascular events consisted of critical and important outcomes for the woman*

[a]CARPREG: Risk points for woman include one point each for for i) prior cardiac event (heart failure, transient ischaemic attack, stroke, arrhythmia); ii) NYHA functional class III/IV or cyanosis (SpO2 <90%); iii) Left heart obstruction (mitral valve area <2 cm^2 or aortic valve area <1.5 cm^2 or peak LVOT gradient >30 mmHg (echocardiography); iv) Reduced systemic ventricular systolic function (EF <40%. The cardiovascular risks associated were 5%, 27% and 75% for 0 point, 1 point and ≥1 points respectively. The risk points for offspring were 0.75 point for left heart obstruction (mitral valve area <2 cm^2 or aortic valve area <1.5 cm^2 or peak LVOT gradient >30 mmHg (echocardiography)

1 point each for i) NYHA functional class III/IV or cyanosis (SpO2<90%); ii) smoking; iii) heparin/warfarin during pregnancy; 3 points for multiple gestation. The higher the scores, the higher the risks of offspring complications.

[b] DC: there were 3 types of DC: 1) Simple CHD: isolated aortic or mitral valve disease, small atrial septal defect, mild pulmonic stenosis, repaired atrial or ventricular septal defect, 2) Moderate complex CHD: atrioventricular septal defect, coarctation, Ebstein's anomaly, tetralogy of Fallot, 3) Complex CHD: cyanotic CHD, transposition of great arteries, Fontan procedure, truncus arteriosus

[c] Modified WHO classification: The cardiovascular risks associated were Class 1: no detectable increased risk of maternal mortality and no/mild increase in morbidity, Class 2: small increased risk of maternal mortality or moderate increase in morbidity, Class 3: significantly increased risk of maternal mortality or severe morbidity and Class 4: extremely high risk of maternal mortality or severe morbidity

[d] ZAHARA I: Risk points for woman include 0.75 point each for i) NYHA functional class III/IV; ii) systemic atrioventricular valve regurgitation (moderate/severe); iii) pulmonary atrioventricular valve regurgitation (moderate/severe), 1 point for cyanotic congential heart disease (corrected and uncorrected), 1.5 point each for i) prior arrhymia; ii) cyanotic congenital heart disease (corrected and uncorrected), 2.5 points for left heart obstruction (peak LVOT gradient > 50 mm Hg or aortic valve area <1.0 cm^2)and 4.25 points for mechanical valve prosthesis. The cardiovascular risks associated were 2.9%, 7.5%, 17.5%, 43.1% and 70% for <0.5 point, 0.5 to 1.5 points, 1.51 – 2.5 points, 2.51-3.5 points and >3.51 points respectively. Risk points for offspring include 0.75 points each for i) cardiac medication before pregnancy; ii) cyanotic congenital disease (corrected and uncorrected), 1.75 points for twin or multiple gestation and 2.5 points for mechanical valve prosthesis. The offspring complication risks associated were 19.9%, 33.3%, 46.7% and 59.6% for <0.5 points, 0.5 to 0.99 points, 1 – 1.49 points and ≥ 1.5 points were 19.9%, 33.3%, 46.7% and 59.6% respectively

[e] A total of all other risk factors including TPo of ZAHARA I and CARPREG and from Khairy et al study (maternal risk: severe pulmonary regurgitation or subpulmonary ventricular dysfunction and smoking history and offspring risk: subaortic ventricular outflow tract gradient >30 mmHg)

Note - AUC is a summary outcome of both sensitivity and specificity, and it does not allow us to make more detailed conclusions about the ability of the test to rule in or rule out the condition. AUC of 1 indicates a test with perfect discrimination and 0.5 indicates a test that performs at chance

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

Unfractionated heparin alone versus low-molecular-weight heparin±unfractionated heparin for women with mechanical heart valves

Table 19: Clinical evidence profile for unfractionated heparin alone versus low-molecular-weight heparin ± unfractionated heparin, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UFH	LMWH	Relative (95% CI)	Absolute	Quality	Importance
Mortality (all causes) - UFH alone versus LMWH alone												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	1/114 (0.88%)	2/113 (1.8%)	RR 0.5 (0.05 to 5.39)	9 fewer per 1000 (from 17 fewer to 78 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Mortality (all causes) - UFH alone versus LMWH followed by UFH												
1 (Khader 2016)	Observational studies	Serious[4]	Not applicable	No serious indirectness	Not estimable due to 0 events	None	0/20 (0%)	0/20 (0%)	Not estimable*	Not estimable*	⊕⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event - UFH alone versus LMWH alone												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	20/67 (29.9%)	5/113 (4.4%)	RR 6.75 (2.66 to 17.14)	254 more per 1000 (from 73 more to 714 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UFH	LMWH	Relative (95% CI)	Absolute		
Major morbidity: major thromboembolic event - UFH alone versus LMWH followed by UFH												
1 (Khader 2016)	Observational studies	Serious[4]	Not applicable	No serious indirectness	Very serious[3]	None	0/20 (0%)	1/20 (5%)	RR 0.33 (0.01 to 7.72)	34 fewer per 1000 (from 49 fewer to 336 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event - UFH alone versus LMWH alone												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	6/114 (5.3%)	4/98 (4.1%)	RR 1.29 (0.37 to 4.44)	12 more per 1000 (from 26 fewer to 140 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event - UFH alone versus LMWH followed by UFH												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	2/20 (10%)	2/20 (10%)	RR 1 (0.16 to 6.42)	0 fewer per 1000 (from 84 fewer to 542 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UFH	LMWH	Relative (95% CI)	Absolute	Quality	Importance
Major morbidity: postpartum haemorrhagic event - UFH alone versus LMWH followed by UFH												
1 (Khader 2016)	Observational studies	Serious[4]	Not applicable	No serious indirectness	Very serious[3]	None	2/20 (10%)	3/20 (15%)	RR 0.67 (0.12 to 3.57)	49 fewer per 1000 (from 132 fewer to 386 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio; LMWH: low-molecular-weight heparin; MID: minimal important difference; UFH: unfractionated heparin
[1] Xu et al. 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest
[2] This is a systematic review of observational studies
[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds
[4] Khader et al. 2016 - prospective cohort; study controlled for age, weight, totol pregnancies before and site of cardiac valve lesions
** 0 events in the control group*

Table 20: Clinical evidence profile for unfractionated heparin alone versus low-molecular-weight heparin ± unfractionated heparin, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UFH	LMWH	Relative (95% CI)	Absolute	Quality	Importance
Mortality - UFH alone versus LMWH alone												
1 (Khader 2016)	Observational studies	Serious[2]	Not applicable	Serious[3]	No serious imprecision	None	37/69 (53.6%)	12/98 (12.2%)	RR 4.38 (2.47 to 7.77)	414 more per 1000 (from 180 more to 829 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Mortality - UFH alone versus LMWH followed by UFH												
1 (Khader 2016)	Observational studies	Serious[2]	Not applicable	No serious indirectness	Very serious[1]	None	3/20 (15%)	6/20 (30%)	RR 0.5 (0.14 to 1.73)	150 fewer per 1000 (from 258 fewer to 219 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio; LMWH: low-molecular-weight heparin; MID = minimal important difference; UFH: unfractionated heparin

[1] *The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

[2] *Khader et al. 2016 - prospective cohort; study controlled for age, weight, totol pregnancies before and site of cardiac valve lesions*

[3] *This outcome comprised of abortion and was downgraded by one level*

Heparin followed by warfarin followed by heparin versus low-molecular-weight heparin for women with mechanical heart valves

Table 21: Clinical evidence profile for heparin followed by warfarin followed by heparin versus low-molecular-weight heparin, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin f/by warfarin f/by heparin**	**LMWH**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (all causes)												
1 (Xu 2016)	Observational studies	Serious[1]	Serious[2]	No serious indirectness	Very serious[3]	None	3/348 (0.86%)	2/113 (1.8%)	RR 0.49 (0.08 to 2.88)	9 fewer per 1000 (from 16 fewer to 33 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	25/337 (7.4%)	5/113 (4.4%)	RR 1.68 (0.66 to 4.28)	30 more per 1000 (from 15 fewer to 145 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Serious[4]	None	2/329 (0.61%)	4/98 (4.1%)	RR 0.15 (0.03 to 0.8)	35 fewer per 1000 (from 8 fewer to 40 fewer)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin f/by warfarin f/by heparin**	**LMWH**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Poor maternal outcome[a]												
1 (Vause 2017)	Observational studies	Serious[5]	Not applicable	Serious[6]	Very serious[3]	None	3/9 (33.3%)	23/41 (56.1 %)	RR 0.59 (0.23 to 1.56)	230 fewer per 1000 (from 432 fewer to 314 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL /IMPORTANCE*

CI: confidence interval; RR: risk ratio; LMWH: low-molecular weight heparin; MID = minimal important difference
[a] Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for >1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident or bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)
[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest
[2] This is a systematic review of observational studies
[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds
[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold
[5] Vause 2017 - prospective cohort; unclear comparability
[6] The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level
** This composite outcome consisted of critical and important outcomes for the woman*

Table 22: Clinical evidence profile for heparin followed by warfarin followed by heparin versus low-molecular-weight heparin, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin f/by warfarin f/by heparin**	**LMWH**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	Serious[4]	None	77/340 (22.6%)	12/98 (12.2 %)	RR 1.85 (1.05 to 3.25)	104 more per 1000 (from 6 more to 276 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Poor fetal outcome[a]												
1 (Vause 2017)	Observational studies	Serious[5]	Not applicable	Serious[6]	Very serious[7]	None	3/9 (33.3%)	20/41 (48.8 %)	RR 0.68 (0.26 to 1.81)	156 fewer per 1000 (from 361 fewer to 395 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL /IMPORTANCE*

CI: confidence interval; RR: risk ratio; LMWH: low-molecular-weight heparin; MID: minimal important difference

[a] *Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit*

[1] *Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest*

[2] *This is a systematic review of observational studies*

[3] *This outcome comprised of abortion and downgraded by one level*

[4] *The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold*

[5] *Vause 2017 - prospective cohort; unclear comparability*

[6] *The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level*

[7] *The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

* *This composite outcome consisted of critical and important outcomes for the baby*

1 **Low-dose warfarin (≤5 mg/day) versus high-dose warfarin (>5 mg/day) for women with mechanical heart valves**

2 **Table 23: Clinical evidence profile for low-dose warfarin (≤5 mg/day) versus high-dose warfarin (>5 mg/day), outcomes for the woman**

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Low-dose warfarin**	**High-dose warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (all causes)												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	1/325 (0.31%)	3/348 (0.86 %)	RR 0.36 (0.04 to 3.41)	6 fewer per 1000 (from 8 fewer to 21 more)	⊕⊖ ⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	4/351 (1.1%)	25/337 (7.4%)	RR 0.15 (0.05 to 0.44)	63 fewer per 1000 (from 42 fewer to 70 fewer)	⊕⊖ ⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	3/442 (0.68%)	2/329 (0.61 %)	RR 1.12 (0.19 to 6.64)	1 more per 1000 (from 5 fewer to 34 more)	⊕⊖ ⊖⊖ VERY LOW	CRITICAL

3 *CI: confidence interval; MID: minimal important difference; RR: risk ratio*
4 *[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest*
5 *[2] This is a systematic review of observational studies*
6 *[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

1 **Table 24: Clinical evidence profile for low-dose warfarin (≤5 mg/day) versus high-dose warfarin (>5 mg/day), outcomes for the baby**

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Low-dose warfarin**	**High-dose warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality - warfarin throughout pregnancy												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	Serious[4]	None	85/442 (19.2%)	77/329 (23.4%)	RR 0.82 (0.63 to 1.08)	42 fewer per 1000 (from 87 fewer to 19 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Mortality - warfarin throughout pregnancy												
1 (Ayad 2016)	Observational studies	Very serious[5]	Not applicable	No serious indirectness	Serious[4]	None	10/33 (30.3%)	38/65 (58.5%)	RR 0.52 (0.3 to 0.9)	281 fewer per 1000 (from 58 fewer to 409 fewer)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Low-dose warfarin	High-dose warfarin	Relative (95% CI)	Absolute		
Mortality - warfarin followed by UFH at 36 weeks gestation: Pregnancy loss												
1 (Soma-Pillay 2011)	Observational studies	Very serious [6]	Not applicable	Serious[7]	Very serious[8]	None	9/28 (32.1%)	15/34 (44.1 %)	RR 0.73 (0.38 to 1.41)	119 fewer per 1000 (from 274 fewer to 181 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio; UFH: unfractionated heparin
[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest
[2] This is a systematic review of observational studies
[3] This outcome comprised of abortion and downgraded by one level
[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold
[5] Ayad 2016 - prospective cohort; unclear exposure; unclear comparability
[6] Soma-Pillay 2011 - prospective cohort; unclear exposure; unclear comparability
[7] The outcome comprised of miscarriage and stillbirth. As miscarriage was not outcome of interest for this review, the evidence was downgraded by one level
[8] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds

1 **Low-molecular-weight heparin versus warfarin for women with mechanical heart valves**

2 **Table 25: Clinical evidence profile for for low-molecular-weight heparin versus warfarin, outcomes for the woman**

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**LMWH**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (all causes)												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	2/113 (1.8%)	1/394 (0.25 %)	RR 6.97 (0.64 to 76.21)	15 more per 1000 (from 1 fewer to 191 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Serious[4]	None	5/113 (4.4%)	5/424 (1.2%)	RR 3.75 (1.11 to 12.74)	32 more per 1000 (from 1 more to 138 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	4/98 (4.1%)	3/539 (0.56 %)	RR 7.33 (1.67 to 32.26)	35 more per 1000 (from 4 more to 174 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LMWH	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Poor maternal outcome[a]												
1 (Vause 2017)	Observational studies	Serious[5]	Not applicable	Serious[6]	Very serious[3]	None	23/41 (56.1%)	2/3 (66.7 %)	RR 0.84 (0.36 to 1.96)	107 fewer per 1000 (from 427 fewer to 640 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL /IMPORTANCE*

CI: confidence interval; RR: risk ratio; LMWH: low-molecular-weight heparin
[a]Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for >1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident or bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)
[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest
[2] This is a systematic review of observational studies
[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds
[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold
[5] Vause 2017 - prospective cohort; unclear comparability
[6] The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level
** This composite outcome consisted of critical and important outcomes for the woman.*

Table 26: Clinical evidence profile for low-molecular-weight heparin versus warfarin, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	LMWH	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	No serious imprecision	None	12/98 (12.2%)	147/539 (27.3%)	RR 0.45 (0.26 to 0.78)	150 fewer per 1000 (from 60 fewer to 202 fewer)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Poor fetal outcome[a]												
1 (Vause 2017)	Observational studies	Serious[4]	Not applicable	Serious[5]	Very serious[3]	None	20/41 (48.8%)	2/3 (66.7%)	RR 0.73 (0.31 to 1.73)	180 fewer per 1000 (from 460 fewer to 487 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL /IMPORTANCE*

CI: confidence interval; RR: risk ratio; LMWH: low-molecular-weight heparin

[a]*Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit*

[1] *Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest*

[2] *This is a systematic review of observational studies*

[3] *This outcome comprised of abortion and downgraded by one level*

[4] *Vause 2017 - prospective cohort; unclear comparability*

[5]*The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level*

[6]*The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

** This composite outcome consisted of critical and important outcomes for the baby*

Unfractionated heparin versus warfarin for women with mechanical heart valves

Table 27: Clinical evidence profile for unfractionated heparin versus warfarin, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**UFH**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (all causes)												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	1/114 (0.88%)	1/394 (0.25 %)	RR 3.46 (0.22 to 54.82)	6 more per 1000 (from 2 fewer to 137 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	20/67 (29.9%)	5/424 (1.2%)	RR 25.31 (9.83 to 65.16)	287 more per 1000 (from 104 more to 757 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	UFH	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Major morbidity: major antenatal haemorrhagic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	6/114 (5.3%)	3/539 (0.56 %)	RR 9.46 (2.4 to 37.25)	47 more per 1000 (from 8 more to 202 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

1 *CI: confidence interval; MID = minimal important difference; RR: risk ratio; UFH: unfractionated heparin*
2 *[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest*
3 *[2] This is a systematic review of observational studies*
4 *[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

Table 28: Clinical evidence profile for unfractionated heparin versus warfarin, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**UFH**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	No serious imprecision	None	37/69 (53.6%)	147/539 (27.3%)	RR 1.97 (1.52 to 2.55)	265 more per 1000 (from 142 more to 423 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio; UFH: unfractionated heparin

[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest

[2] This is a systematic review of observational studies

[3]This outcome comprised of abortion and downgraded by one level

Heparin (unspecified) versus warfarin for women with mechanical heart valves

Table 29: Clinical evidence profile for heparin (unspecified) versus warfarin, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (all causes) – heparin (unspecified) versus warfarin												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	3/227 (1.3%)	1/394 (0.25 %)	RR 5.21 (0.54 to 49.76)	11 more per 1000 (from 1 fewer to 124 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event – heparin (unspecified) versus warfarin												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	25/180 (13.9%)	5/424 (1.2%)	RR 11.78 (4.58 to 30.28)	127 more per 1000 (from 42 more to 345 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Major morbidity: major antenatal haemorrhagic event – heparin (unspecified) versus warfarin												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	10/212 (4.7%)	3/539 (0.56 %)	RR 8.47 (2.36 to 30.49)	42 more per 1000 (from 8 more to 164 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL

1 *CI: confidence interval; RR: risk ratio*
2 *[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest*
3 *[2] This is a systematic review of observational studies*
4 *[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds*

Table 30: Clinical evidence profile for heparin (unspecified) versus warfarin, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Heparin**	**Warfarin**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality: heparin (unspecified) versus warfarin												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	Serious[4]	None	49/167 (29.3%)	147/539 (27.3%)	RR 1.08 (0.82 to 1.41)	22 more per 1000 (from 49 fewer to 112 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; RR: risk ratio

[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest

[2] This is a systematic review of observational studies

[3] This outcome comprised of abortion and downgraded by one level

[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

Heparin followed by warfarin followed by heparin versus warfarin for women with mechanical heart valves

Table 31: Clinical evidence profile for heparin followed by warfarin followed by heparin versus warfarin, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Heparin f/by warfarin f/by heparin	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Mortality (all causes)												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	3/348 (0.86%)	1/394 (0.25 %)	RR 3.4 (0.35 to 32.5)	6 more per 1000 (from 2 fewer to 80 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major thromboembolic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	No serious imprecision	None	25/337 (7.4%)	5/424 (1.2%)	RR 6.29 (2.43 to 16.26)	62 more per 1000 (from 17 more to 180 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: major antenatal haemorrhagic event												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	No serious indirectness	Very serious[3]	None	2/329 (0.61%)	3/539 (0.56 %)	RR 1.09 (0.18 to 6.5)	1 more per 1000 (from 5 fewer to 31 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Heparin f/by warfarin f/by heparin	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Poor maternal outcome[a]												
1 (Vause 2017)	Observational studies	Serious[4]	Not applicable	Serious[5]	Very serious[3]	None	3/9 (33.3%)	2/3 (66.7 %)	RR 0.5 (0.15 to 1.7)	333 fewer per 1000 (from 567 fewer to 467 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL /IMPORTANCE*
Prosthetic valve dysfunction: third trimester or after birth												
1 (Khamoushi 2011)	Observational studies	Very serious [6]	Not applicable	No serious indirectness	Very serious[3]	None	1/11 (9.1%)	3/38 (7.9%)	RR 1.15 (0.13 to 10)	12 more per 1000 (from 69 fewer to 711 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; MID = minimal important difference; RR: risk ratio
[a] Poor maternal outcome: maternal death or serious morbidity – admission to intensive care for >1 day, valve thrombosis, valve dysfunction resulting in heart failure, cerebrovascular accident or bleeding requiring transfusion or return to theatre (primary postpartum haemorrhage, secondary postpartum haemorrhage, intraabdominal bleeding, vaginal haematoma, wound haematoma)
[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest
[2] This is a systematic review of observational studies
[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds
[4] Vause 2017 - prospective cohort; unclear comparability
[5] The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level
[6] Khamoushi 2011 - prospective cohort; unclear exposure; unclear comparability
** This composite outcome consisted of critical and important outcomes for the woman*

Table 32: Clinical evidence profile for heparin followed by warfarin followed by heparin versus warfarin alone, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Heparin f/by warfarin f/by heparin	Warfarin	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1 (Xu 2016)	Observational studies	Serious[1]	Very serious[2]	Serious[3]	Serious[4]	None	77/340 (22.6%)	147/539 (27.3%)	RR 0.83 (0.65 to 1.06)	46 fewer per 1000 (from 95 fewer to 16 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Poor fetal outcomes[a]												
1 (Vause 2017)	Observational studies	Serious[5]	Not applicable	Serious[6]	Very serious[7]	None	3/9 (33.3%)	2/3 (66.7%)	RR 0.5 (0.15 to 1.7)	333 fewer per 1000 (from 567 fewer to 467 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL/ IMPORTANCE*

CI: confidence interval; MID = minimal important difference; RR: risk ratio

[a] Poor fetal outcome: any pregnancy loss (miscarriage or termination of pregnancy), stillbirth, neonatal death, fetal abnormality, Apgar score of <7 at 5 minutes or admission to the neonatal unit

** This composite outcome consisted of critical and important outcomes for the baby.*

[1] Xu 2016 - systematic review of cohort and case series; unclear prior study design; unclear conflict of interest

[2] This is a systematic review of observational studies

[3] This outcome comprised of abortion and downgraded by one level

[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold
This was downgraded by 1 or 2 levels if 95% RR crosses 1 or 2 thresholds of MID, i.e., 0.8-1.25, respectively.

[5] Vause 2017 - prospective cohort; unclear comparability

[6] The composite outcome included the outcomes outside of this review's interest and thus, downgraded by one level.

[7] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds

Intrapartum care for women with cardiac disease – mode of birth

Planned caesarean section for cardiac reasons versus planned vaginal birth

Table 33: Clinical evidence profile for planned caesarean section for cardiac reasons versus planned vaginal birth, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Planned caesarean section for cardiac reasons	Planned vaginal birth	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	No serious imprecision	None	8/172 (4.7%)	5/869 (0.58%)	RR 8.08 (2.68 to 24.41)	41 more per 1000 (from 10 more to 135 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: postpartum heart failure												
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	No serious imprecision	None	17/172 (9.9%)	34/869 (3.9%)	RR 2.53 (1.44 to 4.42)	60 more per 1000 (from 17 more to 134 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: postpartum haemorrhage												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Planned caesarean section for cardiac reasons	Planned vaginal birth	Relative (95% CI)	Absolute	Quality	Importance
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	Serious[2]	None	13/172 (7.6%)	42/869 (4.8%)	RR 1.56 (0.86 to 2.85)	27 more per 1000 (from 7 fewer to 89 more)	⊕⊖⊖⊖ VERY LOW	CRITICAL
Emergency caesarean section (for either obstetric or cardiac reasons)												
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	Very serious[3]	None	30/172 (17.4%)	143/869 (16.5%)	RR 1.06 (0.74 to 1.52)	10 more per 1000 (from 43 fewer to 86 more)	⊕⊖⊖⊖ VERY LOW	IMPORTANT

1 *CI: confidence interval; MID: minimal important difference; RR: relative risk*
2 *[1] Evidence was downgraded by 2 levels due to selection and comparability bias*
3 *[2] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold*
4 *[3] The quality of the evidence was downgraded by 2 level because the 95% CI crosses 2 default MID thresholds*

Table 34: Clinical evidence profile for planned caesarean section for cardiac reasons versus planned vaginal birth, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Planned caesarean section for cardiac reasons	Planned vaginal birth	Relative (95% CI)	Absolute	Quality	Importance
Mortality												
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	Very serious[2]	None	4/172 (2.3%)	18/869 (2.1%)	RR 1.12 (0.38 to 3.28)	2 more per 1000 (from 13 fewer to 47 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; MID: minimal important difference; RR: relative risk

[1] Evidence was downgraded by 2 levels due to selection and comparability bias

[2] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds

Planned caesarean section (for obstetric or cardiac reasons) versus planned vaginal birth

Table 35: Clinical evidence profile for planned caesarean section (for obstetric or cardiac reasons) versus planned vaginal birth, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Planned caesarean section for any reason	Planned vaginal birth	Relative (95% CI)	Absolute	Quality	Importance
Emergency caesarean section (for cardiac reasons)												
1 (Ruys 2015)	Observational studies	Very serious [1]	Not applicable	No serious indirectness	No serious imprecision	None	25/393 (6.4%)	13/869 (1.5%)	RR 4.25 (2.2 to 8.22)	49 more per 1000 (from 18 more to 108 more)	⊕⊖⊖⊖ VERY LOW	IMPORTANT

CI: confidence interval; RR: relative risk

[1] *Evidence was downgraded by 2 levels due to selection and comparability bias*

Intrapartum care for women with cardiac disease – fluid management

No clinical evidence was identified for this review and so there are no GRADE tables.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Table 36: Clinical evidence profile for diagnostic index tests for peripartum cardiomyopathy defined by echocardiogram plus expert clinical interpretation (by a cardiologist)

Number of studies	Design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect				Quality	Importance
							Sensitivity % (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR- (95% CI)		
BNP: NTproBNP (pg/ml)												
1 (Haghikia 2011)	Prospective case-control study	88[1]	Serious[2]	Not applicable	No serious indirectness	Not assessed	Median (range) PPCM: 3315 (875-26082) Control: 61 (24-531); p<0.001				⊕⊖⊖⊖ VERY LOW	NR
Orthopnoea												
1 (Fett 2011)	Retrospective case-control study	57	Very serious[3]	Not applicable	No serious indirectness	No serious imprecison	96 (85-99)	100 (69 to 100)	20.8 (2.8 to 8891050)	0.04 (0.01 to 0.17)	⊕⊖⊖⊖ VERY LOW	NR
Pulmonary oedema: unexplained cough												
1 (Fett 2011)	Retrospective case-control study	57	Very serious[3]	Not applicable	No serious indirectness	Serious[4]	72 (58 to 84)	90 (56 to 100)	7.23 (1.12 to 46.8)	0.31 (0.19 to 0.51)	⊕⊖⊖⊖ VERY LOW	NR
Tachycardia: heart rate ≥100 beats per minute												

Number of studies	Design	N	Risk of bias	Inconsistency	Indirectness	Imprecision	Effect				Quality	Importance
							Sensitivity % (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR- (95% CI)		
1 (Karaye 2016)	Prospective case-control study	131	Very serious[5]	Not applicable	No serious indirectness	No serious imprecision	67 (53 to 79)	78 (67 to 87)	3.02 (1.91 to 4.8)	0.43 (0.29 to 0.64)	⊕⊖⊖⊖ VERY LOW	NR
Tachycardia: palpitation (sensation of irregular heart beats)												
1 (Fett 2011)	Retrospective case-control study	56	Very serious[3]	Not applicable	No serious indirectness	Serious[4]	77 (62 to 88)	100 (63 to 100)	16.73 (2.02 to 8891050)	0.23 (0.14 to 0.39)	⊕⊖⊖⊖ VERY LOW	NR
Systemic oedema: ankle oedema												
1 (Fett 2011)	Retrospective case-control study	57	Very serious[3]	Not applicable	No serious indirectness	No serious imprecision	96 (86 to 100)	30 (7 to 65)	1.37 (0.91 to 2.06)	0.14 (0.03 to 0.74)	⊕⊖⊖⊖ VERY LOW	NR
Systemic oedema: weight gain in last month of pregnancy (>2 pounds per week)												
1 (Fett 2011)	Retrospective case-control study	57	Very serious[3]	Not applicable	No serious indirectness	Serious[4]	69 (83 to 92)	70 (35 to 93)	2.77 (1.06 to 7.19)	0.24 (0.11 to 0.51)	⊕⊖⊖⊖ VERY LOW	NR

CI: confidence interval; LR: likelihood ratio; LR+: positive likelihood ratio; LR-: negative likelihood ratio; N: number of participants; NGA = National Guideliens Alliance; NR: not relevant; NTproBNP: N-terminal prohormone of brain natriuretic peptide; PPCM: peripartum cardiomyopathy

[1] The number of participants is different from summary table because the BNP value was not available for some participants

[2] Haghikia 2016 – case-control study, unclear on whether index test results were interpreted without knowledge of results of reference standard

[3] Fett 2011 – case-control study, unclear about consecutive sample collection, the controls were not taken from the same setting as cases and unable to justify the comparable

baseline characters between cases and controls, unclear on whether index test results were interpreted without knowledge of results of reference standard, questionnaires checklist was used as the test

[4] The judgement of precision was based on the confidence interval of test sensitivity as this was considered to be the primary measure of interest. A range of 0-20% of differences in 95% confidence interval of sensitivity was considered not imprecise, 20-40% serious imprecisions and >40% very serious imprecision. The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

[5] Karaye 2016 – case-control study, echocardiogram of control group was not performed

Note - point estimates of sensitivity, specificity and likelihood ratios and confidence intervals were calculated by the NGA technical team using https://www.medcalc.org/calc/diagnostic_test.php

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Table 37: Clinical evidence profile for bromocriptine plus standard treatment versus standard treatment alone, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bromocriptine plus standard treatment**	**Standard treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (6 months follow-up)												
1 (Sliwa 2010)	Randomised trials	Serious[1]	Not applicable	No serious indirectness	Very serious[2]	None	1/10 (10%)	4/10 (40%)	RR 0.25 (0.03 to 1.86)	300 fewer per 1000 (from 388 fewer to 344 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bromocriptine plus standard treatment**	**Standard treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Recovery of ventricular function measured by LVEF: LVEF < 35% (follow-up 6 months)												
1 (Sliwa 2010)	Randomised trials	Serious[1]	Not applicable	No serious indirectness	Very serious[2]	None	0/9 (0%)	2/6 (33.3%)	RR 0.14 (0.01 to 2.49)	287 fewer per 1000 (from 330 fewer to 497 more)	⨁⊖⊖⊖ VERY LOW	CRITICAL
Major morbidity: NYHA III/IV class (follow-up 6 months)												
1 (Sliwa 2010)	Randomised trials	Serious[1]	Not applicable	No serious indirectness	Very serious[2]	None	1/9 (11.1%)	3/6 (50%)	RR 0.22 (0.03 to 1.66)	390 fewer per 1000 (from 485 fewer to 330 more)	⨁⊖⊖⊖ VERY LOW	IMPORTANT
Major morbidity: adverse events including thromboembolism (follow-up 6 months)												
1 (Sliwa 2010)	Randomised trials	Serious[1]	Not applicable	No serious indirectness	Not estimable due to 0 events	None	0/10 (0%)	0/10 (0%)	Not estimable*	Not estimable*	⨁⨁⨁⊖ MODERATE	IMPORTANT

CI: confidence interval; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association functional classification; RR: risk ratio
[1] No allocation concealment and the participants and some of the care providers were not blinded
[2] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds
** There are 0 events in the control group*

Table 38: Clinical evidence profile for bromocriptine plus standard treatment versus standard treatment alone, outcomes for the baby

Quality assessment							No of patients		Effect			
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Bromocriptine plus standard treatment**	**Standard treatment**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality (follow-up 6 months)												
1 (Sliwa 2010)	Randomised trials	Serious[1]	Not applicable	No serious indirectness	Not estimable due to 0 events	None	0/10 (0%)	0/10 (0%)	Not estimable*	Not estimable*	⨁⨁⨁⊖ MODERATE	CRITICAL

CI: confidence interval; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association functional classification; RR: risk ratio
[1] No allocation concealment and participants and some of the care providers were not blinded
** There are 0 events in the control group*

Intrapartum care for women with cardiac disease – anaesthesia

Table 39: Clinical evidence profile for regional anaesthesia versus general anaesthesia in women with pulmonary arterial hypertension, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Regional anaesthetic	General anaesthetic	Relative (95% CI)	Absolute	Quality	Importance
Mortality of the woman												
1 (Bédard 2009)	Systematic review of case reports/ case series	Very serious [1,2]	Not applicable	No serious indirectness	Serious[3]	None	30	23	OR 4.37 (95% CI 1.28 to 16.5)	Not calculable (number of events in each group not reported)	⨁⊖⊖⊖ VERY LOW	CRITICAL

CI: confidence interval; OR: odds ratio
[1] Very serious risk of publication bias in included studies
[2] Analysis does not account for confounders
[3] The 95% CI did not cross the null effect but it is wide.

Intrapartum care for women with cardiac disease – analgesia

No clinical evidence was identified for this review and so there are no GRADE tables.

Intrapartum care for women with cardiac disease – management of the third stage of labour

Table 40: Clinical evidence profile for bolus oxytocin plus standard oxytocin infusion versus standard oxytocin infusion alone, outcomes for the woman

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bolus oxytocin on-top	Standard oxytocin alone	Relative (95% CI)	Absolute	Quality	Importance
PPH: estimated blood loss at birth (ml)												
1 (Cauldwell 2016)	Observational studies	Serious[1]	Not applicable	No serious indirectness	Serious[2]	None	30	29	-	MD 319 lower (518.72 to 119.28 lower)	⊕⊖⊖⊖ VERY LOW	IMPORTANT
PPH: phenylephrine required												
1 (Cauldwell 2016)	Observational studies	Serious[1]	Not applicable	No serious indirectness	Very serious[3]	None	5/30 (16.7%)	5/29 (17.2%)	RR 0.97 (0.31 to 2.99)	5 fewer per 1000 (from 119 fewer to 343 more)	⊕⊖⊖⊖ VERY LOW	IMPORTANT
PPH: blood transfusion required												

Quality assessment							No of patients		Effect			
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Bolus oxytocin on-top	Standard oxytocin alone	Relative (95% CI)	Absolute	Quality	Importance
1 (Cauldwell 2016)	Observational studies	Serious[1]	Not applicable	No serious indirectness	Very serious[3]	None	0/30 (0%)	1/29 (3.4%)	RR 0.32 (0.01 to 7.61)	23 fewer per 1000 (from 34 fewer to 228 more)	⊕⊖⊖⊖ VERY LOW	IMPORTANT
PPH: additional uterotonic agents received												
1 (Cauldwell 2016)	Observational studies	Serious[1]	Not applicable	No serious indirectness	Serious[4]	None	1/30 (3.3%)	7/29 (24.1%)	RR 0.14 (0.02 to 1.05)	208 fewer per 1000 (from 237 fewer to 12 more)	⊕⊖⊖⊖ VERY LOW	IMPORTANT

CI: confidence interval; MD: mean difference; MID = minimal important difference; PPH: postpartum haemorrhage; RR: risk ratio

[1] No controlling for potential confounders

[2] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold (+/- 222 ml)

[3] The quality of the evidence was downgraded by 2 levels because the 95% CI crosses 2 default MID thresholds

[4] The quality of the evidence was downgraded by 1 level because the 95% CI crosses 1 default MID threshold

Appendix H – Economic evidence study selection

Intrapartum care for women with cardiac disease – management of the third stage of labour

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – mode of birth

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – fluid management

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – anaesthesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of the third stage of labour

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix I – Economic evidence tables

Intrapartum care for women with cardiac disease – stratification of risk

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – mode of birth

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – fluid management

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – anaesthesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix J – Health economic evidence profiles

Intrapartum care for women with cardiac disease – stratification of risk

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – mode of birth

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – fluid management

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – anaesthesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of the third stage of labour

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix K – Health economic analysis

Intrapartum care for women with cardiac disease – stratification of risk

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – mode of birth

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling

Intrapartum care for women with cardiac disease – fluid management

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of cardiomyopathy

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – anaesthesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – analgesia

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Intrapartum care for women with cardiac disease – management of the third stage of labour

See Supplement 2 (Health economics) for details of economic evidence reviews and health economic modelling.

Appendix L – Research recommendations

Intrapartum care for women with cardiac disease – stratification of risk

No research recommendations were made for this review.

Intrapartum care for women with cardiac disease – management of anticoagulation for valvular disease

No research recommendations were made for this review.

Intrapartum care for women with cardiac disease – mode of birth

No research recommendations were made for this review.

Intrapartum care for women with cardiac disease – fluid management

Is point of care, focused echocardiography superior to standard care (clinical evaluation, JVP/CVP) for prediction of fluid responsiveness in peripartum women with cardiac disease?

Why this is important

Fluid management decisions in the intrapartum period in women with heart disease are a frequent source of dispute between obstetricians, anaesthetists and physicians. Assessment of intravascular fluid volume and likely response to fluid transfusion is a common clinical problem which is more complex in the setting of pregnancy in women with cardiac disease. A state of hypovolaemia may result in cardiovascular failure but fluid overload can lead to pulmonary oedema.

Point of care, focused echocardiography and lung ultrasound by appropriately trained physicians or practitioners may be able to inform fluid management decisions in this patient population but it has not been evaluated.

Research recommendation rationale

Research question	Is point of care, focused echocardiography superior to standard care (clinical evaluation, JVP/CVP) for prediction of fluid responsiveness in peripartum women with cardiac disease?
Importance to 'patients' or the population	Some cardiac conditions are made worse by changes in the circulating volume. This can lead to pulmonary oedema or circulatory collapse and result in severe maternal morbidity. Echocardiography and lung ultrasound are well tolerated investigations which can provide evidence to support fluid management decisions.
Relevance to NICE guidance	The committee found little evidence on which to base recommendations for what is an important clinical dilemma. The

Research question	Is point of care, focused echocardiography superior to standard care (clinical evaluation, JVP/CVP) for prediction of fluid responsiveness in peripartum women with cardiac disease?
	recommendations made in this area are based on clinical consensus and good practice. The indications for a focussed ECHO examination to answer a limited range of clinical questions is becoming standard practice in a variety of settings and needs to be evaluated in the peripartum period.
Relevance to NHS	Morbidity from both fluid overload (resulting in pulmonary oedema) and dehydration (acute kidney injury) is associated with significant health care costs. Optimising fluid management for women with cardiac disease should reduce maternal morbidity in the peripartum period. Point of care echocardiography, by appropriately trained physicians or practitioners is finding increasing applications in acute medical settings.
National priorities	Supporting the aim of NHSE to reduce maternal morbidity and mortality
Current evidence base	While there is some evidence to support the use of cardiac echocardiography and lung ultrasound to guide fluid management in the intensive care setting, there are no data in peripartum women with heart disease.
Equality	NA

CVP: central venous pressure; ECHO: echocardiogram; JVP: jugular venous pressure; NA: not applicable; NHSE: NHS England; NICE: National Institute for Health and Care Excellence

Research recommendation PICO

Criterion	Explanation
Population	Peri-partum women with cardiac disease (WHO2 / NYHA II or worse)
Intervention	Focused echocardiography examination and lung ultrasound by appropriately trained physicians or practitioners
Comparison	Standard care (either estimation of JVP/CVP [common method] or other measures of cardiac output or volume status used in routine clinical practice)
Outcomes	• Pulmonary oedema • Occurrence of severe maternal morbidity

Criterion	Explanation
Population	Peri-partum women with cardiac disease (WHO2 / NYHA II or worse)
Study design	RCT
Timeframe	Up to 6 weeks post partum

CVP: central venous pressure; JVP: jugular venous pressure; NYHA: New York Heart Association; RCT: randomised controlled trial; WHO: World Health Organization

Intrapartum care for women with cardiac disease – diagnosis of cardiomyopathy

Can near patient BNP testing diagnose cardiomyopathy?

Why this is important

Cardiomyopathy is one of the differential diagnoses of shortness of breath during the intrapartum period. Rapid diagnosis is essential to provide a woman with appropriate care. A near patient test which does not involve specialist equipment or skills but could assist in differentiating breathlessness of cardiac origin from other causes of shortness of breath would be useful. BNP (brain natriuretic peptide) is a biomarker for cardiac failure, however, its use in the peripartum period has not been studied.

Research recommendation rationale

Research question	Can near patient BNP testing diagnose cardiomyopathy?
Importance to 'patients' or the population	Several conditions can cause breathlessness in the peripartum period. If an early distinction can be made between cardiac and respiratory causes of breathlessness then, unnecessary investigations can be avoided and appropriate treatment can be initiated more quickly.
Relevance to NICE guidance	The committee considered that while a careful history and clinical examination are the first steps towards accurate diagnosis the availability of a simple bedside test to highlight cardiac causes of breathlessness would be useful.
Relevance to NHS	Access to echocardiography (especially out of hours) is limited in many NHS hospitals. CT scanning (including pulmonary angiography) is not without risk. An accurate near patient test for cardiomyopathy could reduce unnecessary investigation and streamline treatment decisions.
National priorities	Supportive of NHSE's aim to reduce maternal morbidity and mortality
Current evidence base	While there are well established data on the normal range, diagnostic and prognostic uses of BNP in the non pregnant population,

Research question	Can near patient BNP testing diagnose cardiomyopathy?
	there is little evidence regarding its use in peripartum women
Equality	NA

BNP: brain natriuretic peptide; CT: computed tomography; NA: not applicable; NHSE: NHS England; NICE: National Institute for Health and Care Excellence

Research recommendation PIRO

Criterion	Explanation
Population	Intrapartum women with suspected cardiomyopathy
Index test	Near patient BNP testing (b-type natriuretic peptide or NT-proBNP)
Reference	Diagnosis of cardiomyopathy or confirmation of normal cardiac function by echocardiography
Outcome	• Sensitivity and specificity
Study design	Prospective cohort study
Timeframe	Up to 6 months post partum

BNP: brain natriuretic peptide; NT-proBNP: N-terminal pro brain natriuretic peptide

Intrapartum care for women with cardiac disease – management of cardiomyopathy

Is there a role for bromocriptine in the management of peripartum cardiomyopathy?

Why this is important

PPCM is a rare but important cause of maternal morbidity and mortality. It presents between the last month of pregnancy and the first 6 months after birth. The cause is unknown, but animal studies suggest an association with the breakdown products of prolactin. Prolactin is a hormone released, in increasing amounts, towards the end of pregnancy and during lactation. Bromocriptine inhibits prolactin production and has been hypothesised to improve the outcome of PPCM. However, many women recover spontaneously from PPCM and the committee found no good trial evidence to confirm that bromocriptine is effective in improving recovery rates from PPCM. In addition, bromocriptine has important side effects in preventing breast feeding and increasing the risk of depression. The committee discussed that if bromocriptine is found to have a beneficial effect on the recovery of PPCM, early introduction of bromocriptine in women with suspected PPCM will help reliably differentiate PPCM from other causes of heart failure.

Research recommendation rationale

Research question	Is there a role for Bromocriptine in the management of peripartum cardiomyopathy?
Importance to 'patients' or the population	Current treatment recommendations are based on small case series, and the beneficial effects of bromocriptine are

Research question	Is there a role for Bromocriptine in the management of peripartum cardiomyopathy?
	unproven, Its use has to be balanced against its side effects of preventing breast feeding and increasing the risk of mental health problems
Relevance to NICE guidance	The committee found insufficient evidence to recommend the use of bromocriptine in women with suspected PPCM. A strong evidence based recommendation would be useful for clinicians in this situation
Relevance to NHS	The number of women with PPCM is not high, but the condition carries a high risk of severe morbidity and death and has a long term impact on NHS resources
National priorities	Supportive of NHSE's aim to reduce maternal morbidity and mortality
Current evidence base	Current evidence is inadequate to support a recommendation of the routine use of bromocriptine in women with suspected PPCM. The committee is aware that there is variation in practice around the country
Equality	NA

1 *NA: not applicable; NICE: National Institute for Health and Care Excellence; NHSE: NHS England; PPCM:*
2 *peripartum cardiomyopath*

Research recommendation PICO

Criterion	Explanation
Population	Women presenting with suspected PPCM
Intervention	Bromocriptine and standard heart failure treatment
Comparison	Standard heart failure treatment alone
Outcomes	• Recovery of ventricular function on echocardiography and MRI
Study design	RCT
Timeframe	Up to 1 year post partum

4 *MRI: magnetic resonance imaging; PPCM: peripartum cardiomyopathy; RCT: randomised controlled trial*

Intrapartum care for women with cardiac disease – anaesthesia

6 No research recommendations were made for this review.

Intrapartum care for women with cardiac disease – analgesia

8 No research recommendations were made for this review.

Intrapartum care for women with cardiac disease – management of the third stage of labour

What is the optimum uterotonic regime for the prevention of postpartum haemorrhage (PPH) in women with heart disease?

Why this is important

After a baby has been born the placenta (afterbirth) detaches from the wall of the womb and the womb contracts to expel the placenta and membranes. This process is often assisted by the use of drugs (uterotonics) that accelerate this process and promote sustained contraction of the uterus.

Medical management of the third stage of labour reduces the risk of postpartum haemorrhage which may be particularly dangerous for women with heart disease. At the same time, the drugs used can have unwanted effects on a woman's heart and circulation.

There is no evidence about the choice of uterotonic agent, dose and mode of administration for women with heart disease.

Research recommendation rationale

Research question	What is the optimum uterotonic regime for the prevention of PPH in women with cardiac disease?
Importance to 'patients' or the population	Medical management of the third stage of labour is a key part of obstetric care. Preventing post partum haemorrhage in women with heart disease is particularly important since many are intolerant of hypovolaemia. However the drugs used can cause severe morbidity to women with cardiac conditions.
Relevance to NICE guidance	In section 2.9 the committee was only able to base their recommendations on best practice and theoretical considerations of the impact of uterotonic drugs on the physiology of women with cardiac conditions. Clinical trial evidence was lacking. A strong, evidence based recommendation would be useful for clinicians faced with this situation.
Relevance to NHS	The number of peripartum women with severe cardiac disease is not high but severe maternal morbidity and the death of a new woman are devastating outcomes with long term impacts on the NHS.
National priorities	Reduce maternal morbidity and mortality
Current evidence base	The committee was aware of a variety of clinical practice around the UK in this area and found the current evidence base to be inadequate to make a strong recommendation. The need to avoid ergometrine in women with cardiac disease

Research question	What is the optimum uterotonic regime for the prevention of PPH in women with cardiac disease?
	is widely recognised but the optimal posology of alternative agents has not been studied.
Equality	NA

PPH: postpartum haemorrhage; NA: not applicable; NICE: National Institute for Health and Care Excellence

Research recommendation PICO

Criterion	Explanation
Population	Peripartum women with cardiac conditions
Intervention	Low dose, slow infusion of syntocinon
Comparison	• Bolus Syntocinon IV • Bolus Syntocinon IM • Carbocetin • Carboprost
Outcomes	• Maternal morbidity (PPH, myocardial ischaemia, requirement for circulatory or inotropic support, requirement for respiratory support)
Study design	RCT
Timeframe	Up to 6 weeks post partum

IM: intramuscular; IV: intravenous; PPH: postpartum haemorrhage; RCT: randomised controlled trial