National Institute for Health and Care Excellence

FINAL

Caesarean birth

[D] Techniques to close the uterus at caesarean birth

NICE guideline NG192

Evidence review

March 2021

Final

This evidence review was developed by the National Guideline Alliance which is a part of the Royal College of Obstetricians and Gynaecologists

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ISBN: 978-1-4731-4052-3

Contents _Toc61619091

Techniques to close the uterus

Review question

What is the efficacy of single layer closure of the uterus compared with double layer closure at caesarean birth?

Introduction

A caesarean birth is the most common surgical procedure in obstetrics and gynaecology. The uterus is incised to deliver the baby, and needs to be closed once the baby and placenta have been delivered.

Traditionally the uterus was closed in two layers, with a second set of stiches being used after the initial closure. However, the efficacy of double layer closure compared with single layer closure is uncertain, and it is not known if single layer closure increases the risk of wound dehiscence or uterine rupture.

This aim of this review is to determine if single layer closure is as effective and as safe as double layer closure.

Summary of the protocol

Please see Table 1 for a summary of the Population, Intervention, Comparison and Outcome (PICO) characteristics of this review.

Table 1: Summary of the protocol (PICO table)

Population	Women undergoing planned (elective) or unplanned (emergency/intrapartum) caesarean birth • pregnancy at or near term (≥ 34 weeks) • lower segment transverse uterine incision
Intervention	Single layer closure of the uterus
Comparison	Double layer closure of the uterus
Outcomes	**Critical outcomes:** • Need for blood transfusion (within 7 days of operation) • Additional surgical procedures (within 7 days of operation) • Uterine rupture in subsequent pregnancy **Important outcomes:** • Use of antibiotics (within 7 days of operation) • Morbidly adherent placenta/abnormal invasion of placenta in subsequent pregnancy • Peri-partum hysterectomy in subsequent pregnancy • Caesarean birth in subsequent pregnancy

For further details see the review protocol in appendix A.

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual (2014). Methods specific to this review question are described in the review protocol in appendix A.

Declarations of interest were recorded according to NICE's 2014 conflicts of interest policy until 31 March 2018. From 1 April 2018, declarations of interest were recorded according to NICE's 2018 conflicts of interest policy. Those interests declared until April 2018 were reclassified according to NICE's 2018 conflicts of interest policy (see Register of Interests).

Clinical evidence

Included studies

Fourteen publications were included in the review. These reported on 12 randomised controlled trials (RCTs) (Brocklehurst 2010, Chitra 2004, CORONIS 2013, Darj 1999, El-Gharib 2013, Hauth 1992, Nabhan 2008, Ohel 1996, Poonam 2006, Sood 2005, Xavier 2005, Yasmin 2011) and there were 2 longer term follow up studies of RCTs (Chapman 1997 which followed up Hauth 1992, and CORONIS 2016 which followed up CORONIS 2013).

Of the 12 RCTs included in this review, 6 directly compared single to double layer uterine closure (Brocklehurst 2010, CORONIS 2013, El-Gharib 2013, Hauth 1992, Sood 2005, Yasmin 2011), and 6 compared different caesarean birth techniques that included a comparison of single and double layer uterine closure along with variation in uterine incision, exteriorisation of the uterus (or not), peritoneal closure (or not), skin closure, and suture material (Chitra 2004, Darj 1999, Nabhan 2008, Ohel 1996, Poonam 2006, Xavier 2005).

The 2 follow up studies were of direct comparison of single or double layer uterine closure.

For simplicity, the follow up studies have been combined with the original trial for the analyses (GRADE tables and Forest plots): "CORONIS" includes the results of CORONIS 2013 and CORONIS 2016 and "Hauth/Chapman" includes the results of Hauth 1992 and Chapman 1997. In both cases the follow up publications reported long term outcomes in a subsequent pregnancy and no outcomes are double counted within a single analysis.

All outcomes were reported by at least 1 study. For short term outcomes (use of antibiotics, further operative procedures and blood transfusion), the timing of these was not specified in the publications. We therefore present the occurrence of these outcomes as reported in the studies.

Similarly, any use of antibiotics was not specifically reported as an outcome measure in the majority of trials. However, many trials reported closely related measures – including antibiotic use for wound infection, endometritis, or febrile morbidity. Where antibiotic use was not reported but infection was, this was used as a proxy for antibiotic use, as it was deemed unlikely that a recognised infection would be left untreated by antibiotics following caesarean birth. However, the results for different types of infection are reported separately, rather than pooled.

See the literature search strategy in appendix B and study selection flow chart in appendix C.

Excluded studies

Studies not included in this review with reasons for their exclusions are provided in appendix K.

Summary of clinical studies included in the evidence review

A summary of the studies that were included in this review are presented in Table 2.

Table 2: Summary of included studies

Study	Population	Intervention	Comparison	Outcomes	Comments
Brocklehurst 2010 UK and Italy RCT (2x2x2 factorial)	Women undergoing first CB • N=1483 single layer; • N=1496 double layer	Single layer uterine closure	Double layer uterine closure	• Blood transfusion • Antibiotics for febrile morbidity • Antibiotics for wound infection	
Chapman 1997 USA Retrospective (medical record search)	Women in subsequent pregnancy (after CB) • N=70 single layer • N=75 double layer	Single layer uterine closure	Double layer uterine closure	• Uterine dehiscence • Vaginal birth	Follow up to Hauth 1992 (RCT)
Chitra 2004 India RCT	Women undergoing elective or emergency first CB • N=100, Misgav-Ladach (single layer) • N=100, Pfannenstiel (double layer)	Misgav-Ladach (single layer)	Pfannenstiel (double layer)	• Blood transfusion	Compared different CB techniques
CORONIS 2013 UK (Argentina, Chile, Ghana, India, Kenya, Pakistan, Sudan) RCT (2x2x2x2x2 factorial)	Women undergoing first or second CB • N=4639 single layer • N=4647 double layer	Single layer closure	Double layer closure	• Blood transfusion • Further operative procedure • Further operative procedure on wound • Antibiotics for febrile morbidity • Antibiotics for wound infection • Antibiotics for endometritis	
CORONIS 2016 UK (Argentina,	Women in subsequent pregnancy (after CB)	Single layer closure	Double layer closure	• Uterine rupture • Uterine scar dehiscence • Placenta praevia	Follow up to CORONIS 2013 (RCT)

Study	Population	Intervention	Comparison	Outcomes	Comments
Chile, Ghana, India, Kenya, Pakistan, Sudan) RCT follow up (3 years)	• N=1611 single layer • N=1624 double layer			• Morbidly adherent placenta • Hysterectomy in 6 weeks postpartum • CB	
Darj 1999 Sweden RCT	Women undergoing first CB • N=25 Misgav-Ladach (single layer) • N=25 Pfannenstiel (double layer)	Misgav-Ladach (single layer)	Pfannenstiel (double layer)	• Antibiotics required	Compared different CB techniques
El-Gharib 2013 Egypt RCT	Women undergoing scheduled/ elective first CB • N=75 single layer • N=75 double layer	Single layer closure	Double layer closure	• Wound sepsis	Wound sepsis used as a proxy for antibiotic use
Hauth 1992 USA RCT	Women undergoing CB • N=457 single layer • N=449 double layer	Single layer closure	Double layer closure	• Blood transfusion • Postpartum endometritis	Endometritis used as a proxy for antibiotic use
Nabhan 2008 Egypt RCT	Women undergoing first CB • N=300 Modified Misgav-Ladach (single layer) • N=300 Standard (double layer) Same women at repeat CB • N=62 Modified Misgav-Ladach (single layer) • N=62 Standard	Modified Misgav-Ladach (single layer)	Standard/ Pfannenstiel (double layer)	• Blood transfusion • Wound infection requiring antibiotics	Compared different CB techniques Data was available in subgroups: • first CB (N=600) • repeat CB (N= 124/600)

Study	Population	Intervention	Comparison	Outcomes	Comments
	(double layer)				
Ohel 1996 Israel RCT	Women undergoing CB • N=100 single layer • N=100 double layer	• Single layer uterine closure • Visceral and parietal peritoneum were left open	• Double layer uterine closure • Visceral and parietal peritoneum were closed	• Wound infection	Compared different CB techniques Wound infection used as a proxy for antibiotic use
Poonam 2006 Nepal RCT	Women undergoing elective or emergency first CB • N=200 Misgav-Ladach (single layer) • N=200 Control (double layer)	Misgav-Ladach (single layer)	Conventional/ Pfannenstiel (double layer)	• Post-operative transfusion • Wound infection – abdominal wound dehiscence	Compared different CB techniques Post-operative transfusion used as blood transfusion outcome Infection used as a proxy for antibiotic use
Sood 2005 India RCT	Women undergoing emergency or elective CB • N=102 (single layer) • N=106 (double layer)	Single layer closure	Double layer closure	• Wound infection	Infection used as a proxy for antibiotic use
Xavier 2005 Portugal RCT	Women undergoing elective or emergency CB • N=77 Modified Misgav-Ladach (single layer) • N=69 Pfannenstiel-Kerr (double layer)	Modified Misgav-Ladach (single layer)	Pfannenstiel-Kerr (double layer)	• Post-operative antibiotics	Compared different CB techniques
Yasmin 2011 Pakistan RCT	Women undergoing repeat CB • N=30 single layer • N=60 double layer	Single layer closure	• Double layer closure (control) • Modified double	• Wound sepsis requiring antibiotics	Both groups of double layer closure have been combined to form “all those with

Study	Population	Intervention	Comparison	Outcomes	Comments
			layer closure		double layer closure"

CB: caesarean birth; N: number of women; RCT: randomised controlled trial

See the full evidence tables in appendix D and the forest plots in appendix E.

Quality assessment of clinical outcomes included in the evidence review

See the clinical evidence profiles (GRADE tables) in appendix F.

Economic evidence

Included studies

A systematic review of the economic literature was conducted but no economic studies were identified which were applicable to this review question.

See the literature search strategy in appendix B.

Economic model

No economic modelling was undertaken for this review because the committee agreed that other topics were higher priorities for economic evaluation.

Evidence statements

Comparison 1. Single versus double layer closure of the uterus

Critical outcomes

Need for blood transfusion

- Three randomised controlled trials (N=13171) provided very low quality evidence to show no clinically important difference in the need for blood transfusion between single layer and double layer uterine closure.

Additional surgical procedures

- One randomised controlled trial (N=9286) provided very low quality evidence to show no clinically important difference in the incidence of any further operative procedures between single layer and double layer uterine closure.
- One randomised controlled trial (N=9286) provided very low quality evidence to show no clinically important difference in the incidence of any further operative procedures on the wound between single layer and double layer uterine closure.

Uterine rupture (in subsequent pregnancy)

- One randomised controlled trial (N=3234) provided very low quality evidence to show no clinically important difference in the incidence of uterine rupture in a subsequent pregnancy between single layer and double layer uterine closure.
- Two randomised controlled trials (N=3378) provided very low quality evidence to show no clinically important difference in the incidence of uterine scar dehiscence in a subsequent pregnancy between single layer and double layer uterine closure.

Important outcomes

Use of antibiotics

- Five randomised controlled trials (N=12713) provided low quality evidence to show no clinically important difference in the use of antibiotics for wound infection (and wound sepsis) between single layer and double layer uterine closure.
- Two randomised controlled trials (N=12265) provided very low quality evidence to show no clinically important difference in the use of antibiotics for febrile morbidity between single layer and double layer uterine closure.
- Two randomised controlled trials (N=10192) provided very low quality evidence to show no clinically important difference in the use of antibiotics for endometritis between single layer and double layer uterine closure.

Morbidly adherent placenta/abnormal invasion of placenta (in subsequent pregnancy)

- One randomised controlled trial (N=3233) provided very low quality evidence to show no clinically important difference in the incidence of morbidly adherent placenta in a subsequent pregnancy between single layer and double layer uterine closure.

Peri-partum hysterectomy (in subsequent pregnancy)

- One randomised controlled trial (N=3234) provided very low quality evidence to show no clinically important difference in the incidence of hysterectomy (during the 6 weeks postpartum) in a subsequent pregnancy between single layer and double layer uterine closure

Caesarean birth (in subsequent pregnancy)

- Two randomised controlled trials (N=3421) provided low quality evidence to show no clinically important difference in the incidence of caesarean birth in a subsequent pregnancy between single layer and double layer uterine closure

Comparison 2. Trials comparing different caesarean birth techniques

Critical outcomes

Need for blood transfusion

- Three randomised controlled trials (N=1324) provided very low quality evidence to show a clinically important reduction in the need for blood transfusion when using a caesarean birth (CB) technique that included single layer closure, as compared to a technique that included double layer closure.

Additional surgical procedures

- No evidence was available for this outcome.

Uterine rupture (in subsequent pregnancy)

- No evidence was available for this outcome.

Important outcomes

Use of antibiotics

- Two randomised controlled trials (N=196) provided very low quality evidence to show no clinically important difference in the use of antibiotics (for an unspecified reason) between CB techniques that included single or double layer uterine closure.
- Three randomised controlled trials (N=1324) provided very low quality evidence to show no clinically important difference in the use of antibiotics (for wound infection or wound sepsis) between CB techniques that included single or double layer uterine closure.

Subgroup analysis:

- Two randomised controlled trials (N=1000) provided very low quality evidence to show no clinically important difference in the use of antibiotics (for wound infection or wound sepsis) between single layer and double layer uterine closure in a subgroup of women undergoing primary CB.
- One randomised controlled trial (N=124) provided very low quality evidence to show no clinically important difference in the use of antibiotics (for wound infection or wound sepsis) between single layer and double layer uterine closure in a subgroup of women undergoing a repeat CB.

Morbidly adherent placenta/abnormal invasion of placenta (in subsequent pregnancy)

- No evidence was available for this outcome.

Peri-partum hysterectomy (in subsequent pregnancy)

- No evidence was available for this outcome.

Caesarean birth (in subsequent pregnancy)

- No evidence was available for this outcome.

Economic evidence statements

No economic evidence was identified which was applicable to this review question.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

As double layer closure is currently standard practice, the committee wished to determine if single layer closure is as effective and safe. The committee therefore specified three critical outcomes, which were of primary importance for this review. These were the need for blood transfusion as this is an indication of how successful the surgical closure is, the need for additional surgical procedures in the short term as failure of the closure may require the patient to return to theatre, and the occurrence of uterine rupture in a subsequent pregnancy.

In addition, four important outcomes were identified. These were the use of antibiotics within 7 days of the caesarean birth which may be an indicator of wound infection, and three outcomes related to future pregnancies - the presence of morbidly adherent/abnormally invasive placenta, the need for peri-partum hysterectomy, and caesarean birth in a future pregnancy.

The quality of the evidence

Despite a number of large, well conducted trials in this area, the evidence was downgraded in all studies for a high risk of performance bias (due to the inability to blind the surgeon to allocation). Some studies did not blind outcome assessors to the allocated intervention, therefore were also at high risk of detection bias.

Studies comparing different caesarean surgical methods (comparison 2) were downgraded for indirectness as they compared other differences in technique as well as uterine closure (differences in uterine incision, exteriorisation of the uterus, peritoneal closure, skin closure, and suture material). Finally, a number of rare events were included as relevant outcomes in this evidence review (such as uterine rupture and peri-partum hysterectomy). The small number of events that occurred led to a wide confidence interval around the result, meaning that the data was downgraded for imprecision.

Overall the data was considered to be low to very low quality.

Benefits and harms

The committee reviewed the evidence presented as two separate comparisons. For the trials that specifically compared single and double layer closure, no clinically important difference was identified for any of the outcomes. These trials were considered to most accurately reflect the difference between single and double layer closure. When assessing evidence from the trials which randomised women to different caesarean surgical techniques, the committee noted that the only difference in outcomes was an increased chance of requiring a blood transfusion when a double layer uterine closure technique was used. This comparison had multiple confounding factors as it compared completely different caesarean techniques, and not just uterine closure technique. The committee agreed that the additional blood loss would also be anticipated as a result of the difference in method of opening the abdomen and uterus: in the arm that included double layer closure this involved cutting using scissors/scalpel, compared to the blunt entry used in the arm that included single layer closure.

The committee discussed the low event rate of uterine rupture in a subsequent pregnancy using either technique, as historically this concern was used as the rationale for double layer closure, and agreed that the low incidence and lack of difference between the techniques was reassuring, and indicated that either method could be used safely.

The committee discussed the length of the caesarean procedure, and the desire for clinicians to close the abdomen as quickly as possible, in order to minimise the potential for infection. The committee agreed that the lack of difference in infection rates (antibiotic use) between single and double layer closure was encouraging as it suggested the additional time taken to close the uterus using a second layer of sutures did not give rise to an increased chance of infection.

As there was no difference between single and double layer closure for the majority of outcomes the committee agreed that either technique could be used. The committee added the information about the similar risks of bleeding or uterine rupture in a subsequent pregnancy to the recommendation to provide further context for surgeons who may not be familiar with single layer closure and who may be concerned that single layer closure could increase the risk of these adverse events.

The committee discussed the differing levels of experience of those performing a caesarean procedure, and whether a separate recommendation should be made for those with less experience, but agreed that by recommending that either closure method could be used, the decision to use single or double layer could be made on an individual basis for each woman. The committee discussed which factors should be taken into consideration when deciding which closure to use, and agreed that surgeons would make an individual choice based on the clinical circumstance which would include an assessment of the woman's clinical presentation. The committee discussed the fact that surgeons may also have different preferences for single or double closure, and that this is in turn may be influenced by their level of experience.

The committee reiterated that where additional layers of suturing were required (for example, due to ongoing bleeding), the surgeon or treating clinician would continue to respond appropriately, as is current practice.

The committee discussed the fact that as double layer uterine closure is currently recommended, surgeons who, for clinical reasons, decide to carry out single layer closure currently document this in the notes. As the recommendation now allows the choice of either single or double layer closure, it will no longer be seen as necessary to justify why a single layer uterine closure has been carried out.

Cost effectiveness and resource use

Allowing surgeons to use single layer closure of the uterus may bring about some small savings due to the use of less suture material, and saving approximately 2 to 15 minutes of operative time.

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Appendices

Appendix A – Review protocols

Review protocol for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Table 3: Review protocol for uterine closure techniques

Field (based on PRISMA-P)	Content
Actual review question	What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?
Type of review question	Intervention
Objective of the review	To ascertain whether there are differences in efficacy between single versus two-layer closure of the uterus. Surgical technique differs between individual surgeons at present, and the existing guideline does not discuss which technique may be most appropriate.
Eligibility criteria – population/disease/condition/issue/domain	Women undergoing planned (elective) or unplanned (emergency/intrapartum) caesarean birth • pregnancy at or near term (≥ 34 weeks) • lower segment transverse uterine incision
Eligibility criteria – intervention(s)/exposure(s)/prognostic factor(s)	Single layer closure of the uterus
Eligibility criteria – comparator(s)/control or reference (gold) standard	Double layer closure
Outcomes and prioritisation	**Critical outcomes:** • Need for blood transfusion (within 7 days of operation) • Additional surgical procedures (within 7 days of operation) • Uterine rupture in subsequent pregnancy

Field (based on PRISMA-P)	Content
	Important outcomes: • Use of antibiotics (within 7 days of operation) • Morbidly adherent placenta/abnormal invasion of placenta in subsequent pregnancy • Peri-partum hysterectomy in subsequent pregnancy • Caesarean birth in subsequent pregnancy
Eligibility criteria – study design	Only published full text papers Systematic reviews of RCTs RCTs
Other inclusion/exclusion criteria	Exclude classical incision and vertical incision
Proposed stratified, sensitivity/sub-group analysis, or meta-regression	If heterogeneity identified: subgroup analysis for different numbers of caesarean birth (CB) (i.e. first CB versus repeat CB, need to include multiple repeat CB)
Selection process – duplicate screening/selection/analysis	Duplicate screening/selection/analysis will not be undertaken for this review as this question was not prioritised for it. Included and excluded studies will be cross checked with the committee and with published systematic reviews when available.
Data management (software)	If pairwise meta-analyses are undertaken, they will be performed using Cochrane Review Manager (RevMan5). 'GRADE' will be used to assess the quality of evidence for each outcome. STAR will be used for bibliographies/citations and study sifting, data extraction and quality assessment/critical appraisal.
Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR and Embase. Limits (e.g. date, study design): All study designs. Standard animal/non-English language filters will be applied. No date limit will be applied and no supplementary search techniques will be used.

Field (based on PRISMA-P)	Content
	See appendix B for full strategies.
Identify if an update	Yes, this question was included in the 2011 guideline. Studies meeting the current protocol criteria and previously included in the 2011 guideline (CG132) will be included in this update.
Author contacts	Developer: National Guideline Alliance NGA-enquiries@RCOG.ORG.UK
Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual
Search strategy – for one database	For details please see appendix B
Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables).
Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables).
Methods for assessing bias at outcome/study level	Appraisal of methodological quality: The methodological quality of each study will be assessed using an appropriate checklist: ROBIS for systematic reviews Cochrane risk of bias tool for randomised studies For details please see section 6.2 of Developing NICE guidelines: the manual The risk of bias across all available evidence will evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
Criteria for quantitative synthesis	For details please see section 6.4 of Developing NICE guidelines: the manual

Field (based on PRISMA-P)	Content
Methods for quantitative analysis – combining studies and exploring (in)consistency	Synthesis of data: Meta-analysis will be conducted where appropriate using Review Manager. For detailed methods for meta-analysis, please see full guideline methods chapter. Minimum important differences Any significant difference will be used as the MID for the following outcomes: • Uterine rupture in subsequent pregnancy • Morbidly adherent placenta/abnormal invasion of placenta in subsequent pregnancy • Peri-partum hysterectomy in subsequent pregnancy For the remaining outcomes, default values will be used of: 0.8 and 1.25 relative risk for dichotomous outcomes; 0.5 times the control group SD for continuous outcomes, unless more appropriate values are identified by the guideline committee or in the literature. Double sifting, data extraction and methodological quality assessment: Sifting, data extraction, appraisal of methodological quality and GRADE assessment will be performed by the systematic reviewer. Quality control will be performed by the senior systematic reviewer. Dual quality assessment and data extraction will not be performed
Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual.
Confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual
Rationale/context – what is known	For details please see the introduction to the evidence review
Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Sarah Fishburn in line with section 3 of Developing NICE guidelines: the manual.

Field (based on PRISMA-P)	Content
	Staff from the National Guideline Alliance undertook systematic literature searches, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the committee. For details please see the methods chapter.
Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for the NHS in England.
PROSPERO registration number	Not registered with PROSPERO

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; NGA: National Guideline Alliance; NHS: National health service; NICE: National Institute for Health and Care Excellence; RCT: randomised controlled trial; RoB: risk of bias; SD: standard deviation

Appendix B – Literature search strategies

Literature search strategies for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Review question search strategies

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

Date of last search: 21/11/2018

#	Searches
1	exp CESAREAN SECTION/
2	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
3	or/1-2
4	SUTURE TECHNIQUES/
5	(sutur$ adj3 technique?).ti,ab.
6	((one or "1" or singl$ or two or "2" or doubl$ or second) adj5 layer?).ti,ab.
7	((uterus$ or uterin$) adj3 clos$).ti,ab.
8	or/4-7
9	misgav ladach.ti,ab.
10	(Pfannensteil or Pfannenstiel).ti,ab.
11	Joel Cohen.ti,ab.
12	or/9-11
13	3 and 8
14	3 and 12
15	or/13-14
16	limit 15 to english language
17	LETTER/
18	EDITORIAL/
19	NEWS/
20	exp HISTORICAL ARTICLE/
21	ANECDOTES AS TOPIC/
22	COMMENT/
23	CASE REPORT/
24	(letter or comment*).ti.
25	or/17-24
26	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
27	25 not 26
28	ANIMALS/ not HUMANS/
29	exp ANIMALS, LABORATORY/
30	exp ANIMAL EXPERIMENTATION/
31	exp MODELS, ANIMAL/
32	exp RODENTIA/
33	(rat or rats or mouse or mice).ti.
34	or/27-33
35	16 not 34

Databases: Embase; and Embase Classic

Date of last search: 21/11/2018

#	Searches
1	exp CESAREAN SECTION/
2	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
3	or/1-2
4	SUTURE TECHNIQUE/
5	(sutur$ adj3 technique?).ti,ab.
6	((one or "1" or singl$ or two or "2" or doubl$ or second) adj5 layer?).ti,ab.
7	((uterus$ or uterin$) adj3 clos$).ti,ab.
8	or/4-7
9	misgav ladach.ti,ab.
10	(Pfannensteil or Pfannenstiel).ti,ab.

#	Searches
11	Joel Cohen.ti,ab.
12	or/9-11
13	3 and 8
14	3 and 12
15	or/13-14
16	limit 15 to english language
17	letter.pt. or LETTER/
18	note.pt.
19	editorial.pt.
20	CASE REPORT/ or CASE STUDY/
21	(letter or comment*).ti.
22	or/17-21
23	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
24	22 not 23
25	ANIMAL/ not HUMAN/
26	NONHUMAN/
27	exp ANIMAL EXPERIMENT/
28	exp EXPERIMENTAL ANIMAL/
29	ANIMAL MODEL/
30	exp RODENT/
31	(rat or rats or mouse or mice).ti.
32	or/24-31
33	16 not 32

Databases: Cochrane Central Register of Controlled Trials; and Cochrane Database of Systematic Reviews

Date of last search: 21/11/2018

#	Searches
#1	MeSH descriptor: [CESAREAN SECTION] explode all trees
#2	(cesarean* or caesarean* or "c section*" or csection* or (deliver* near/3 abdom*)):ti,ab
#3	#1 or #2
#4	MeSH descriptor: [SUTURE TECHNIQUES] this term only
#5	(sutur* near/3 technique*):ti,ab
#6	((one or "1" or singl* or two or "2" or doubl* or second) near/5 layer*):ti,ab
#7	((uterus* or uterin*) near/3 clos*):ti,ab
#8	#4 or #5 or #6 or #7
#9	"misgav ladach":ti,ab
#10	(Pfannensteil or Pfannenstiel):ti,ab
#11	"Joel Cohen":ti,ab
#12	#9 or #10 or #11
#13	#3 and #8
#14	#3 and #12
#15	#13 or #14

Health economics search strategies

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

Date of last search: 21/11/2018

#	Searches
1	ECONOMICS/
2	VALUE OF LIFE/
3	exp "COSTS AND COST ANALYSIS"/
4	exp ECONOMICS, HOSPITAL/
5	exp ECONOMICS, MEDICAL/
6	exp RESOURCE ALLOCATION/
7	ECONOMICS, NURSING/
8	ECONOMICS, PHARMACEUTICAL/
9	exp "FEES AND CHARGES"/
10	exp BUDGETS/
11	budget*.ti,ab.

#	Searches
12	cost*.ti,ab.
13	(economic* or pharmaco?economic*).ti,ab.
14	(price* or pricing*).ti,ab.
15	(financ* or fee or fees or expenditure* or saving*).ti,ab.
16	(value adj2 (money or monetary)).ti,ab.
17	resourc* allocat*.ti,ab.
18	(fund or funds or funding* or funded).ti,ab.
19	(ration or rations or rationing* or rationed).ti,ab.
20	ec.fs.
21	or/1-20
22	exp CESAREAN SECTION/
23	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
24	or/22-23
25	SUTURE TECHNIQUES/
26	(sutur$ adj3 technique?).ti,ab.
27	((one or "1" or singl$ or two or "2" or doubl$ or second) adj5 layer?).ti,ab.
28	((uterus$ or uterin$) adj3 clos$).ti,ab.
29	or/25-28
30	misgav ladach.ti,ab.
31	(Pfannensteil or Pfannenstiel).ti,ab.
32	Joel Cohen.ti,ab.
33	or/30-32
34	24 and 29
35	24 and 33
36	or/34-35
37	limit 36 to english language
38	LETTER/
39	EDITORIAL/
40	NEWS/
41	exp HISTORICAL ARTICLE/
42	ANECDOTES AS TOPIC/
43	COMMENT/
44	CASE REPORT/
45	(letter or comment*).ti.
46	or/38-45
47	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
48	46 not 47
49	ANIMALS/ not HUMANS/
50	exp ANIMALS, LABORATORY/
51	exp ANIMAL EXPERIMENTATION/
52	exp MODELS, ANIMAL/
53	exp RODENTIA/
54	(rat or rats or mouse or mice).ti.
55	or/48-54
56	37 not 55
57	21 and 56

Databases: Embase; and Embase Classic

Date of last search: 21/11/2018

#	Searches
1	HEALTH ECONOMICS/
2	exp ECONOMIC EVALUATION/
3	exp HEALTH CARE COST/
4	exp FEE/
5	BUDGET/
6	FUNDING/
7	RESOURCE ALLOCATION/
8	budget*.ti,ab.
9	cost*.ti,ab.
10	(economic* or pharmaco?economic*).ti,ab.
11	(price* or pricing*).ti,ab.
12	(financ* or fee or fees or expenditure* or saving*).ti,ab.
13	(value adj2 (money or monetary)).ti,ab.
14	resourc* allocat*.ti,ab.
15	(fund or funds or funding* or funded).ti,ab.
16	(ration or rations or rationing* or rationed).ti,ab.

#	Searches
17	or/1-16
18	exp CESAREAN SECTION/
19	(c?esar#an$ or c section$ or csection$ or (deliver$ adj3 abdom$)).ti,ab.
20	or/18-19
21	SUTURE TECHNIQUE/
22	(sutur$ adj3 technique?).ti,ab.
23	((one or "1" or singl$ or two or "2" or doubl$ or second) adj5 layer?).ti,ab.
24	((uterus$ or uterin$) adj3 clos$).ti,ab.
25	or/21-24
26	misgav ladach.ti,ab.
27	(Pfannensteil or Pfannenstiel).ti,ab.
28	Joel Cohen.ti,ab.
29	or/26-28
30	20 and 25
31	20 and 29
32	or/30-31
33	limit 32 to english language
34	letter.pt. or LETTER/
35	note.pt.
36	editorial.pt.
37	CASE REPORT/ or CASE STUDY/
38	(letter or comment*).ti.
39	or/34-38
40	RANDOMIZED CONTROLLED TRIAL/ or random*.ti,ab.
41	39 not 40
42	ANIMAL/ not HUMAN/
43	NONHUMAN/
44	exp ANIMAL EXPERIMENT/
45	exp EXPERIMENTAL ANIMAL/
46	ANIMAL MODEL/
47	exp RODENT/
48	(rat or rats or mouse or mice).ti.
49	or/41-48
50	33 not 49
51	17 and 50

Database: Cochrane Central Register of Controlled Trials

Date of last search: 21/11/2018

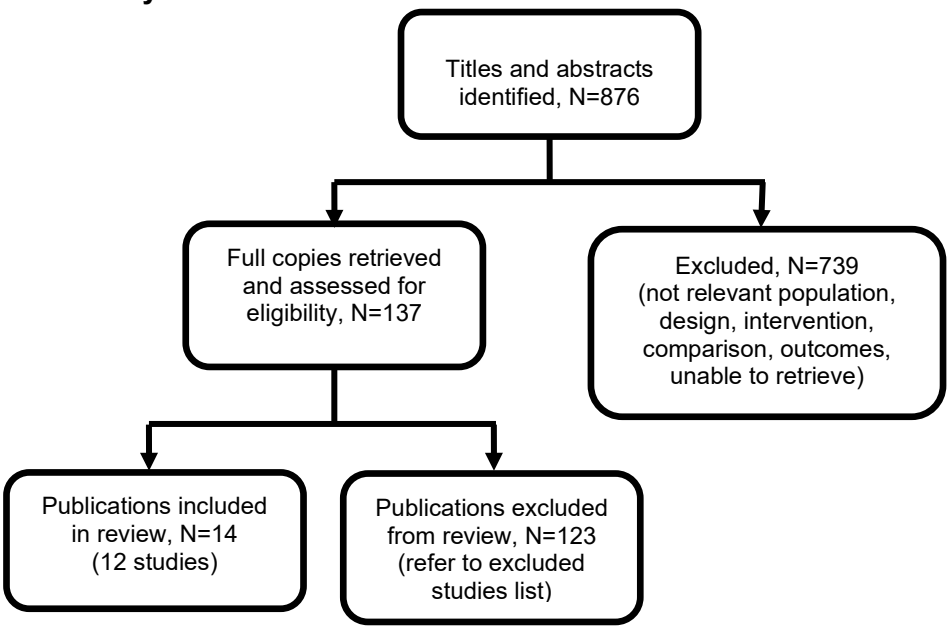
#	Searches
#1	MeSH descriptor: [ECONOMICS] this term only
#2	MeSH descriptor: [VALUE OF LIFE] this term only
#3	MeSH descriptor: [COSTS AND COST ANALYSIS] explode all trees
#4	MeSH descriptor: [ECONOMICS, HOSPITAL] explode all trees
#5	MeSH descriptor: [ECONOMICS, MEDICAL] explode all trees
#6	MeSH descriptor: [RESOURCE ALLOCATION] explode all trees
#7	MeSH descriptor: [ECONOMICS, NURSING] this term only
#8	MeSH descriptor: [ECONOMICS, PHARMACEUTICAL] this term only
#9	MeSH descriptor: [FEES AND CHARGES] explode all trees
#10	MeSH descriptor: [BUDGETS] explode all trees
#11	budget*:ti,ab
#12	cost*:ti,ab
#13	(economic* or pharmaco?economic*):ti,ab
#14	(price* or pricing*):ti,ab
#15	(financ* or fee or fees or expenditure* or saving*):ti,ab
#16	(value near/2 (money or monetary)):ti,ab
#17	resourc* allocat*:ti,ab
#18	(fund or funds or funding* or funded):ti,ab
#19	(ration or rations or rationing* or rationed) .ti,ab.
#20	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19
#21	MeSH descriptor: [CESAREAN SECTION] explode all trees
#22	(cesarean* or caesarean* or "c section*" or csection* or (deliver* near/3 abdom*)):ti,ab
#23	#21 or #22
#24	MeSH descriptor: [SUTURE TECHNIQUES] this term only
#25	(sutur* near/3 technique*):ti,ab
#26	((one or "1" or singl* or two or "2" or doubl* or second) near/5 layer*):ti,ab
#27	((uterus* or uterin*) near/3 clos*):ti,ab

#	Searches
#28	#24 or #25 or #26 or #27
#29	"misgav ladach":ti,ab
#30	(Pfannensteil or Pfannenstiel):ti,ab
#31	"Joel Cohen":ti,ab
#32	#29 or #30 or #31
#33	#23 and #28
#34	#23 and #32
#35	#33 or #34
#36	#20 and #35

Appendix C – Clinical evidence study selection

Clinical study selection for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Figure 1: Study selection flow chart



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Table 4: Clinical evidence tables for uterine closure techniques

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Brocklehurst,P., Caesarean section surgical techniques: A randomised factorial trial (CAESAR), BJOG: An International Journal of Obstetrics and Gynaecology, 117, 1366-1376, 2010 **Ref Id** 109401 **Country/ies where the study was carried out** UK and Italy **Study type** RCT (2x2x2 factorial) **Aim of the study** Determine whether any of the following alternative surgical	**Sample size** n=3033 1483 single layer closure; 1496 double layer closure **Characteristics** mean age: 30.6 SD 5.9 years mean GA at study entry: 39.0 SD 2.0 weeks **Inclusion criteria** Women undergoing delivery by their first caesarean section, this was planned to be performed through the lower uterine segment and there was no clear indication for any particular technique to be used.	**Interventions** Single versus double layer uterine closure. Single layer closure involves bringing both edges of the uterine incision together with a single layer of sutures. In double-layer closure, the uterine incision is closed with two layers of sutures. The first layer opposes the endometrial aspect of the uterine muscle layer and the second brings together the serosal layer.	**Details** Antibiotics as standard: not reported Type of incision used: Pfannenstiel or Joel-Cohen, surgeon's discretion, asked to remain consistent Uterine closure: single or double layer Exteriorisation of uterus: not reported Suture material: no restrictions on the type of suture material that could be used, but should remain consistent (vicryl/ dexon/ other) Type of suture/stitch pattern: not reported Peritoneal closure: Half closure, half non-closure Skin closure: same whether single or double layer (subcuticular/ staples/ clips/ interrupted/ other) Statistics used: Patients were analysed in the groups to which they were	**Results** single layer: allocated n=1505; received allocated: 1377; analysed 1483; excluded 22 double layer: allocated 1506; received allocated 1477; analysed 1496; excluded 10 <u>Antibiotics for febrile morbidity</u> single: n=12/1483; RR=1.09 (0.38-3.19) double: n=11/1496 <u>Antibiotics for wound infection</u> single: n=188/1483; RR=1.01 (0.79-1.29) double: n=188/1496 <u>Blood transfusion</u> single: n=54/1483; RR=0.93 (0.57-1.49) double: n=59/1496	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *telephone randomisation service was employed to allocate the interventions using a minimisation algorithm to ensure comparability between women (**LOW**)* • **Allocation concealment** *Allocation was made available to the operating surgeon prior to the onset of surgery (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *no information (**UNCLEAR**)* • **Blinding of personnel:** *Allocation was made available to the operating surgeon prior to the onset of surgery (**HIGH**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
techniques affect the risk of adverse outcomes: single- versus double-layer closure of the uterine incision; closure versus nonclosure of the pelvic peritoneum; liberal versus restricted use of a subrectus sheath drain? **Study dates** November 2000 - June 2006 **Source of funding** The trial was funded by the NHS South East Region Research and Development Office. The funding source had no role in the study design, the collection and interpretation of the data, writing of the report or decision to submit the paper for publication.	**Exclusion criteria** Women under 16years old		assigned, regardless of deviation from the protocol or treatment received. Comparative statistical analysis entailed the calculation of the relative risk (RR) plus the 95% confidence interval (95% CI) for the primary outcome and 99% CI for the secondary outcomes to take account of multiple comparisons. Pairwise interactions between the different interventions were examined		**Detection bias - Blinding of outcome assessment:** *information from medical records/patient notes (**LOW**)* **Attrition bias - Incomplete outcome data:** *Analysis by intention-to-treat. Exclusions due to vaginal delivery (not CS), withdrawal of consent, clinical reason at time of surgery, error, or lost to follow up - single layer 1.5%, double layer 0.7% (**LOW**)* **Reporting bias - Selective reporting:** *Appears to report as per protocol (**LOW**)* **Other information**
Full citation Chapman, S. J., Owen, J., Hauth, J. C., One- versus two-layer	**Sample size** n=164 from original 906 women (Hauth 1992); n=83/164 had	**Interventions** One layer or two layer closure of uterine incision in previous pregnancy	**Details** As described by Hauth 1992 - low transverse uterine incision; 1-0 chromic catgut sutures	**Results** n=70/145 single layer; n=75/145 double layer used in final analysis Vaginal delivery	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW (as in Hauth 1992)**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
closure of a low transverse cesarean: The next pregnancy, Obstetrics and Gynecology, 89, 16-8, 1997 **Ref Id** 652438 **Country/ies where the study was carried out** USA **Study type** Retrospective (medical record search) Follow up to RCT (Hauth 1992) **Aim of the study** determine whether a low transverse cesarean closure method in one or two layers affects subsequent pregnancy outcome. **Study dates** Follow up to Hauth 1992 in subsequent 4 years	single layer; n=81/163 had two layer n=19/164 had elective c-section without labour, and were excluded from analysis n=70/145 single layer; n=75/145 double layer used in final analysis **Characteristics** Not reported - full cohort data in Hauth 1992 **Inclusion criteria** Women with subsequent pregnancy in 4 years after Hauth 1992 study Gestation longer than 18 weeks Delivered at study institution **Exclusion criteria** Twin gestations (violates the assumption of independence) excluded from neonatal analyses		Statistics used: Statistical analyses were conducted with the Statistical Analysis System (SAS Institute, Inc., Cary, NC) version 6.04. Chi-square, Fisher exact test, the Student t-test, and Wilcoxon rank-sum test were used for comparisons where appropriate. Continuous data are presented as mean +/-1 standard deviation (SD). P </=0.05 represented statistical significance.	single: 56% (n=39/70); double: 64% (n=48/75) <u>Uterine dehiscence</u> single: n=1/70; double: n=0/75	• **Random sequence generation** *computer generated randomisation (**LOW**)* • **Allocation concealment** *Envelopes were opened before initiation of c-section to preclude selection/operator bias (**LOW**)* **Performance bias: LOW** • **Blinding of participants:** Outcomes from medical records - no effect from prior knowledge of study allocation *(**LOW**)* • **Blinding of personnel:** Outcomes from medical records - no effect from prior knowledge of study allocation *(**LOW**)* **Detection bias - Blinding of outcome assessment:** *Outcomes from medical records - no effect from prior knowledge of study allocation (**LOW**)* **Attrition bias - Incomplete outcome data (for each outcome):** Large number of women excluded from analysis (n=19/164; 12%) *(**HIGH**)* **Reporting bias - Selective reporting:** *No access to protocol for long term outcomes (**UNCLEAR**)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Not reported					
Full citation Chitra, K. L. S., Nirmala, A. P., Gayetri, R., Jayanthi, N. V., Shanthi, J. S., Misgav Ladach cesarean section vs Pfannenstiel cesarean section, Journal of obstetrics and gynaecology of India, 54, 473-477, 2004 **Ref Id** 930777 **Country/ies where the study was carried out** India **Study type** RCT **Aim of the study** assess the efficacy, safety, duration, blood loss, need for suture material and post-operative stay, and compare it to Pfannenstiel caesarean section in	**Sample size** n=200: 100 randomly allocated per group **Characteristics** mean age: (Group1) 24.93 years; (Group2) 24.98 years mean GA: (1) 39.15 weeks; (2) 38.84 weeks mean birthweight: (1) 3020g; (2) 3039g **Inclusion criteria** all women posted for elective or emergency primary caesarean section **Exclusion criteria** • women with previous c-section • obstructed labour • previous abdominal surgery • twin pregnancy • placenta praevia • abruptio placenta	**Interventions** **Group 1: Pfannenstiel:** incision: pfannenstiel; closure: double layer **Group 2: Misgav-Ladach**: incision: Joel-Cohen; closure: single layer continuous locking	**Details** Antibiotics as standard: elective c-sections: 1g cephalexin 6 hourly for 3 doses; emergency cases cephalexin 500mg 6 hourly for 5days Type of incision used: (1) pfannenstiel; (2) joel-cohen Uterine closure: (1) two-layers; (2) one-layer Exteriorisation of uterus: not reported Suture material: uterine: chromic catgut; skin closure: black silk; rectus sheath closure: proline no1 Type of suture/stitch pattern: single: continuous locking pattern; double "2 layer" Peritoneal closure: not reported Skin closure: with black silk; (1) 7-8 stitches; (2) 3 stitches Other: all c-sections performed under spinal or general anaesthetic. Surgery allocation by random numbers drawn by the floor nurse. floor nurse, surgeon, and scrub nurse	**Results** Blood transfusion Group 1 (double): n=2/100; Group 2 (single): n=1/100	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *Random allocation using random numbers drawn by floor nurse (**LOW**)* • **Allocation concealment** *Staff aware of allocation (**HIGH**)* **Performance bias: HIGH** • **Blinding of participants:** *Women under anaesthesia (**UNCLEAR**)* • **Blinding of personnel:** *Surgeon and surgical staff aware of allocation* - unable to blind staff to allocation *(**HIGH**)* **Detection bias - Blinding of outcome assessment:** *Surgical staff collected outcomes - floor nurse measured operation time, blood loss estimated by surgeon and nurses from suction bottle, gauzes and pack used, scrub nurse counted number of sutures used (**HIGH**)* **Attrition bias - Incomplete outcome data (for each outcome):** No detail regarding exclusions *(**UNCLEAR**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
women undergoing c-section **Study dates** Not reported **Source of funding** Not reported	• ruptured uterus		recorded outcome measures		**Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation CORONIS Collaborative Group., Caesarean section surgical techniques (CORONIS): a fractional, factorial, unmasked, randomised controlled trial, Lancet (London, England), 382, 234-48, 2013 **Ref Id** 930877 **Country/ies where the study was carried out** UK (Argentina, Chile, Ghana, India, Kenya, Pakistan, Sudan) **Study type** RCT 2x2x2x2x2	**Sample size** total enrolled in study n=15,935 n=9416 allocated to closure of uterus; single: n=4705; double: n=4711 received allocated treatment: single: n=3913 (83%); double: n=4603 (98%) final analysis: single: n=4639 (99%); double: n=4647 (99%) **Characteristics** Maternal age: single: 26.9±5.4 years; double: 26.8±5.4 years Nulliparous: single: n=2160/4639 (47%); double: n=2248/4647 (48%) No previous c-section: single: n=3182/4639	**Interventions** **Blunt v sharp entry:** For sharp entry, the abdomen was entered using a scalpel to divide the abdominal skin. Each subsequent layer of the abdomen was then separately identified and divided using either a scalpel or scissors. In blunt entry, the abdomen was entered using a scalpel to divide the abdominal skin. The scalpel was then used to divide the fat and rectus sheath in the midline and the rectus sheath incision extended manually. The parietal peritoneum was then entered digitally and the defect enlarged manually. **Exteriorisation of the uterus** for repair versus intraabdominal repair: once the placenta had been delivered, either the uterus was drawn from the pelvis to rest on the anterior abdominal wall so that the uterine incision could clearly be visualised or the	**Details** Suture pattern: could be a continuous, continuous locking, or an interrupted layer of sutures. For sites where chromic catgut versus polyglactin-910 was one of the assigned intervention pairs, surgeons were asked to restrict their use of the allocated suture material to repair of the uterine incision and to use their usual suture material for all other layers. All non-allocated surgical elements and all other aspects of the caesarean section procedure were undertaken at the discretion of the surgeon. In particular, there were no restrictions on the type of suture material that could be used, and standard measures to achieve haemostasis were	**Results** antibiotics for febrile morbidity single: n=47/4639; double: n=47/4647; RR=1.0 (95%CI 0.59-1.70) antibiotics for wound infection single: n=353/4639; double: n=379/4647; RR=0.93 (0.78-1.12) antibiotics for endometritis single: n=38/4639; double: n=34/4647; RR=1.12 (0.61-2.05) further operative procedures single: n=74/4639; double: n=87/4647; RR=0.85 (0.57-1.28) further operative procedures on wound single: n=30/4639; double: n=38/4647; RR=0.79 (0.42-1.48) blood transfusion	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *Randomisation was done using a bespoke secure web-based system, with a 24-h automated telephone back-up. The system allocated a number corresponding to a unique allocation envelope held at participating sites. The allocation numbers were generated by computer implementation of a pseudo-random generating algorithm. Each envelope contained an allocation sheet detailing the three allocated interventions for a woman, as a reminder to the surgeon. In instances where there was no internet or telephone connectivity, the recruiting clinician selected the lowest sequentially numbered allocation envelope. (**LOW**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Aim of the study examined five elements of the caesarean section technique in intervention pairs: • blunt versus sharp abdominal entry; • exteriorisation of the uterus for repair versus intraabdominal repair; • single-layer versus double-layer closure of the uterus; • closure versus non-closure of the peritoneum (pelvic and parietal); • chromic catgut versus polyglactin-910 for uterine repair **Study dates** 20 May 2007 - 31 Dec 2010 **Source of funding**	(69%); double: n=3183/4647 (69%) One previous c-section: single: 1457 (31%); double: 1464 (31%) **Inclusion criteria** women who were to undergo birth by lower segment caesarean section through a transverse abdominal incision, irrespective of fever in labour, gestational age, or multiple pregnancies **Exclusion criteria** • clear indication for a particular surgical technique or material to be used that prevented any of the allocated interventions being used, • if they had more than one previous caesarean section, • if they had already been recruited into the trial	uterus was repaired while in the pelvis. **Single-layer v double-layer** closure of the uterus: the uterine incision was closed with either one or two layers of sutures. Each layer could be closed using any accepted technique. Haemostasis of the incision could be done with additional sutures as judged necessary by the surgeon regardless of the method of closure undertaken. **Peritoneum closure v non-closure:** the pelvic and parietal peritoneum was either closed or not closed. For either technique, haemostasis was achieved as usual, including, where necessary, the use of haemostatic sutures. **Suture material:** chromic catgut versus polyglactin-910 for uterine repair, the uterus was repaired using either number 1 chromic catgut (Medsurge, Philadelphia, PA, USA) or number 1 polyglactin-910 (Ethicon, Livingston,NJ, UK).	employed regardless of the allocated intervention. A sample size of 15,000 women was needed, with at least 9000 women in each intervention pair, to have at least 80% power to detect a 15% relative risk reduction in the primary outcome from a baseline incidence of 15%, assuming 15% loss to follow-up.	single: n=76/4639; double: n=79/4647; RR=0.96 (0.64-1.45)	• **Allocation concealment** *All randomisation data were held centrally at the international coordinating centre (National Perinatal Epidemiology Unit Clinical Trials Unit) (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *All investigators, surgeons, and participants were unmasked to treatment allocation (**HIGH**)* • **Blinding of personnel:** *All investigators, surgeons, and participants were unmasked to treatment allocation. (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *All investigators, surgeons, and participants were unmasked to treatment allocation. (**HIGH**)* **Attrition bias - Incomplete outcome data (for each outcome):** *Analysis by intention-to-treat. n=206/15935 (1.3%) women were excluded from the analysis, of whom 143 (0.9%) had a vaginal birth. Women were evenly distributed among the intervention pairs and were excluded from the analysis because they were not at risk of wound-related problems (**LOW**)* **Reporting bias - Selective reporting:** *As described in the protocol (**LOW**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
UK Medical Research Council and WHO					**Other information**
Full citation CORONIS collaborative group., Caesarean section surgical techniques: 3 year follow-up of the CORONIS fractional, factorial, unmasked, randomised controlled trial, Lancet (London, England), 388, 62-72, 2016 **Ref Id** 930878 **Country/ies where the study was carried out** UK (Argentina, Chile, Ghana, India, Kenya, Pakistan, and Sudan) **Study type** RCT follow up **Aim of the study** 3 year follow up of CORONIS study 2013 **Study dates**	**Sample size** Women with subsequent pregnancy (as proportion of number assessed in original study) single: n=1889/3709 (51%); double: n=1904/3702 (51%) women with subsequent viable pregnancy single: n=1611/3709; double n=1624/3702 **Characteristics** Maternal deaths post-CORONIS 2013 single: n=25/4613; double: n=32/4621; RR=0.78 (0.46-1.32) Babies from subsequent viable pregnancy single: n=1630; double: n=1646 Stillbirth in subsequent viable pregnancy single: n=34/1630; double: n=28/1646; RR=1.23 (0.75-2.01) Neonatal death in subsequent viable pregnancy	**Interventions** As in CORONIS 2013	**Details** As in CORONIS 2013	**Results** c-section in subsequent pregnancy single: n=1312/1630 (81%); double: n=1353/1646 (82%); RR=0.98 (0.95-1.01) uterine rupture in subsequent pregnancy single: n=1/1610 (<1%); double: n=2/1624 (<1%); RR=0.50 (0.05-5.51) uterine scar dehiscence in subsequent pregnancy single: n=4/1609 (<1%); double: n=2/1624 (<1%); RR=2.01 (0.37-10.95) placenta previa in subsequent pregnancy single: n=5/1609 (<1%); double: n=4/1624 (<1%); RR=1.23 (0.33-4.57) morbidly adherent placenta in subsequent pregnancy single: n=0/1609 (<1%); double: n=2/1624 (<1%) hysterectomy in 6wks post partum in subsequent pregnancy	**Limitations** As in CORONIS 2013 **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
1 Sept 2011 - 30 Sept 2014 **Source of funding** UK Medical Research Council and the Department for International Development	single: n=32/1595; double: n=34/1616; RR=0.96 (0.59-1.54) **Inclusion criteria** women who participated in CORONIS 2013 study, with subsequent pregnancy in following 3 years **Exclusion criteria** As in CORONIS 2013			single: n=1/1610 (<1%); double: n=1/1624 (0%)	
Full citation Darj, E., Nordstrom, M. L., The Misgav Ladach method for cesarean section compared to the Pfannenstiel method, Acta Obstetricia et Gynecologica Scandinavica, 78, 37-41, 1999 **Ref Id** 930797 **Country/ies where the study was carried out** Sweden	**Sample size** n=50; randomly allocated n=25 to each group **Characteristics** age (mean, range): ML: 29.6 (21-40) years; Pfann: 29.3 (21-37) years GA (mean, range): ML: 38.6 (37-42) weeks; Pfann: 38.3 (37-42) weeks placenta previa: n=2/50 both randomly allocated to Misgav-Ladach group	**Interventions** **Misgav-Ladach**: incision: straight, not through subcutaneous fat; hysterotomy clsore: one layer; visceral and parental pertoneum: open; fascia closure: continuously; skin closure: 2-3 interrupted sutures, skin edges pinched together for 5-7 mins; sutures: 2 Vicryl, 1 Ethion **Pfannenstiel:** incision: curved, through subcutaneous fat; hysterotomy closure: two layers; visceral and parental peritoneum: closed; fascia closure: interrupted sutures; skin closure: continuous intracutaneous suture; sutures: 6 Vicryl	**Details** Antibiotics as standard: prophylactic antibiotics were not used Exteriorisation of uterus: in all cases Statistics used: Sample size was chosen to detect a difference of 10 minutes in mean operating time or a difference of 100 ml of bleeding, which could be of clinical importance, with 80% power at 5% significance level other: spinal anaesthesia in most, general anaesthesia in 2/50 (1/25 each)	**Results** Antibiotics required: n=0/25 in both groups Post-operative wound infection/endometritis: n=0/25 in both groups	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *randomly allocated to two groups and prospectively followed for three months (**LOW**)* • **Allocation concealment** *sealed opaque envelope designating the allocated method, was opened by the woman's husband before initiating the operation (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *woman's husband opened the envelope before the*

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Study type RCT **Aim of the study** Evaluate the outcome of two different methods of elective caesarean section **Study dates** 1996 - 1997 **Source of funding** Not reported	**Inclusion criteria** women having their first C-Section, but could have delivered vaginally before **Exclusion criteria** previous abdominal operation				*procedure, unclear if woman know allocation (**UNCLEAR**)* • **Blinding of personnel:** *One surgeon, the author, performed all the procedures in the study. Unable to blind personnel to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *operating staff measured operation time and the amount of bleeding , midwives noted mobilisation and infection on the ward, scar appearance assessed by patient and midwife (**HIGH**)* **Attrition bias - Incomplete outcome data (for each outcome):** Women treated as allocated *(**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation EL-Gharib, Mohamed Nabih, Awara, Ahmad. M, Ultrasound Evaluation of the Uterine Scar Thickness after Single Versus Double Layer Closure of Transverse Lower Segment Cesarean Section, Journal of Basic and Clinical Reproductive	**Sample size** N=150; 75 per group **Characteristics** Maternal age: single 28.84±3.4 years; double 28.36±3.2 years GA at birth: single 39.11±0.7 weeks, double 39.16±0.7 weeks	**Interventions** Single layer closure of transverse lower segment c-section. A one-layer closure usually involves a single continuous, locking layer of absorbable suture (0 Vicryl sutures) Double layer closure of transverse lower segment c-section. A two-layer closure typically adds an imbricating layer of absorbable suture (0 Vicryl sutures)	**Details** Antibiotics as standard: Type of incision used: transverse lower segment Uterine closure: single v double layer Exteriorisation of uterus: not reported Suture material: absorbable sutures (0 Vicryl) Type of suture/stitch pattern: single: continuous	**Results** <u>Wound sepsis (as proxy for antibiotic requirement)</u> single n=3/75; double n=6/75	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: HIGH** • **Random sequence generation** *Not reported, just "randomly assigned" (**UNCLEAR**)* • **Allocation concealment** *All the participants' names were hidden and replaced by code numbers to maintain the privacy. After obtaining written consent and*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Sciences, 2, 42-45, 2013 **Ref Id** 939275 **Country/ies where the study was carried out** Egypt **Study type** RCT **Aim of the study** evaluate the uterine scar thickness by ultrasonography in women randomly assigned to one or two layer closure of the uterine incision after primary c-section **Study dates** July 2010 - June 2012 **Source of funding** Not reported	Birthweight: single 2.86±0.6 kg; double 1.6±0.9 kg **Inclusion criteria** Scheduled primary elective caesarean section **Exclusion criteria** • multiple gestations, • abnormalities of fetal heart rate, • polyhydramnios, • uterine malformation, • anterior placenta previa, • placenta accreta, • uterine or cervical fibroid, • fetal macrosomia, • any previous uterine operation • any medical disease that compromises wound healing eg. diabetes mellitus, collagen diseases or anaemia		locking layer; double: +imbricating layer Peritoneal closure: not reported Skin closure: not reported		*confirming entry into the study, each patient was assigned a treatment group by selection of the next consecutive envelope. (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** Not reported *(**UNCLEAR**)* • **Blinding of personnel:** The group-Allocation was revealed to the surgeon during the surgery just before the repair - unable to blind surgeon to allocation *(**HIGH**)* **Detection bias - Blinding of outcome assessment:** *Relevant outcome assessment not reported (**UNCLEAR**)* **Attrition bias - Incomplete outcome data (for each outcome):** All women included in the analysis *(**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation	**Sample size**	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Hauth, J. C., Owen, J., Davis, R. O., Transverse uterine incision closure: one versus two layers, American Journal of Obstetrics and Gynecology, 167, 1108-1111, 1992 **Ref Id** 930890 **Country/ies where the study was carried out** USA **Study type** RCT **Aim of the study** Determine if closure of low transverse uterine caesarean incision with one layer of suture results in less operating time, better homeostasis, and less infectious morbidity than a two-layer closure **Study dates**	n=906; single (one-layer): n=457; double (two-layer): n=449 **Characteristics** age: single closure: 24.2 years; double 24.6 years GA at birth: single: 38 weeks; double: 37.8 weeks Gestational hypertension: single: n=58/457 (13%); double: n=68/449 (15%) Placenta previa: single: n=5/457 (1.1%); double: n=4/449 (0.9%) **Inclusion criteria** Women undergoing caesarean section **Exclusion criteria** • a vertical or T uterine incision was required (n=46) • the operating team could not perform the assigned closure (n=32)	single (one) layer of uterine stitches, or two-layers of uterine stitches all other variables remained the same	Antibiotics as standard: not reported Type of incision used: low transverse incision Uterine closure: one or two layer closure Exteriorisation of uterus: not reported Suture material: no1 chromic catgut, 36 inches Type of suture/stitch pattern: single: continuous locking stitch; double: single + imbricating closure Peritoneal closure: not reported Skin closure: not reported Other detail: randomisation by computer-generated list of random numbers for one or two layer closure. Random assignments placed in sequentially numbers sealed envelopes, opaque to bright lights. Envelopes were opened before initiation of c-section to preclude operator bias (selection bias). Knowledge of allocation was allowed to provide correct number of sutures. Study was powered to 0.90 with alpha=0.05 to detect difference in endometritis as large as 18% vs 27%	single layer: n=457; double layer: n=449 Blood transfusion single: n=9/457 (2.0%); double: n=11/449 (2.5%) Postpartum endometritis (proxy for antibiotic requirement) - excludes women with chorioamnionitis in labour single: n=83/457 (22%); double: n=65/449 (18%)	**Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *computer generated randomisation (**LOW**)* • **Allocation concealment** *Envelopes were opened before initiation of c-section to preclude selection/operator bias (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *unclear if women were told of allocation, unlikely to affect outcomes (**LOW**)* • **Blinding of personnel:** *Envelopes were opened before initiation of c-section so the scrub nurse could lay out the appropriate number of sutures to be used (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *unclear how or who decided if or how many additional sutures were required, other outcomes unlikely to be affected by blinding (**UNCLEAR**)* **Attrition bias - Incomplete outcome data (for each outcome):** Included all women randomised who could be treated with allocation to one or two-layer closure in analysis: n=32 could not have assigned closure *(**HIGH**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
5th June 1989 - 6th July 1991 **Source of funding** Not reported	• incomplete data were available for outcomes (n=7) 85 exclusions equally distributed between groups				**Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation Nabhan, A. F., Long-term outcomes of two different surgical techniques for cesarean, International journal of gynaecology and obstetrics, 100, 69-75, 2008 **Ref Id** 931027 **Country/ies where the study was carried out** Egypt **Study type** RCT **Aim of the study** assess adhesion formation and other long-term outcomes of cesarean delivery by comparing 2 surgical techniques: (1)	**Sample size** n=600 for first-time caesarean section; 300 randomised to each group. of which n=124 (62 per group) were also analysed at repeat caesarean section - end point of the study was reached when the pre-designated number of women (determined at the beginning of the study) who underwent repeat cesarean delivery was achieved **Characteristics** Maternal age: modified: 27.2±0.5 years; standard 28.9±0.82 years **First c-section (n=600)** GA at birth: modified: 38.3±0.34 weeks; standard 37.9±0.61 weeks	**Interventions** (1) "standard": Pfannenstiel incision with development of a bladder flap and in situ suturing of the uterus in 2 layers, (2) "modified": Joel-Cohen incision without bladder flap formation and with exterior suturing of the uterus in 1 layer; modified Misgav Ladach technique	**Details** Antibiotics as standard: not reported Type of incision used: Pfannastiel (with bladder flap) vs Joel-Cohen-Stark/MML (no bladder flap) Uterine closure: Pfannastiel-Kerr (double) vs Joel-Cohen-Stark/MML (single) Exteriorisation of uterus: Pfannaenstiel-Kerr: in situ; Joel-Cohen/MML: exteriorisation Suture material: not reported Type of suture/stitch pattern: not reported Peritoneal closure: Pfanennstiel: closed visceral and parietal; Joel-Cohen/MML: not sutured Skin closure: Joel-Cohen: not closed unless more than 2cm subcut fat Statistics: a sample size of 88 women undergoing repeat cesarean delivery for a 2-sided test and alpha value of 0.05 would	**Results** **First c-section** Blood transfusion modified: n=0/300; standard: n=3/300 (1%) Wound infection requiring additional antibiotics modified: n=5/300 (1.7%); standard n=7/300 (2.3%) **Repeat c-section** Blood transfusion modified: n=0/62; standard: n=5/62 (8.1%) Wound infection requiring additional antibiotics modified: n=4/62 (6.5%); standard n=4/62 (6.5%)	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *randomly assigned to either the standard (Pfannenstiel) group or the modified (Joel-Cohen) group using a computer-generated randomization list drawn up by a statistician and contained in a set of numbered sealed envelopes.(**LOW**)* • **Allocation concealment** *.When a participant was found eligible and had consented to participate in the study, the numbered envelope was opened to determine the operative technique.(**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *Participants did not know which group they had been assigned to for the duration of the study. (**LOW**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Pfannenstiel incision with development of a bladder flap and in situ suturing of the uterus in 2 layers, versus (2) the Joel-Cohen incision without bladder flap formation and with exterior suturing of the uterus in 1 layer **Study dates** 2002 - 2007 **Source of funding** Not reported	Parity (primigravida): modified: n=167/300 (55.7%); standard n=192/300 (64%) Parity (multipara): modified n=133/300; standard n=108/300 **Repeat c-section (n=124)** Maternal age: modified: 28.2±0.4 years; standard 29.8±0.5 years GA at birth: 38.1±0.5 weeks; standard 38.3±0.3 weeks **Inclusion criteria** women with indication for cesarean delivery by lower segment cesarean **Exclusion criteria** Not reported		have a 0.80 power. The present study would have a 0.90 power with a sample size of 116 patients undergoing a repeat cesarean delivery		• **Blinding of personnel:** Unclear who had knowledge of allocation - unable to blind surgeon *(**HIGH**)* **Detection bias - Blinding of outcome assessment:** *No information, likely from case reports/medical records (**UNCLEAR**)* **Attrition bias - Incomplete outcome data (for each outcome):** *Analysis by intention-to-treat (**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation Ohel, G., Younis, J. S., Lang, N., Levit, A., Double-layer closure of uterine incision with visceral and parietal peritoneal closure: are they obligatory steps of routine cesarean sections?, Journal of	**Sample size** n=200 (100 per group) **Characteristics** Gravidity: study 3.1±1.9; control 2.9±1.7 Parity: study 1.8±1.6; control 1.7±1.6	**Interventions** Study group: uterine incision closed by **one layer of continuous non-locking suture**, visceral and parietal peritoneum were left open, fascia was closed using a continuous non-locking suture, and interrupted sutures placed on the skin	**Details** Antibiotics as standard: prophylactic antibiotics used in 84% (control group), 88% (study group) Type of incision used: low transverse or longitudinal abdominal incision; low transverse incision of uterus	**Results** Wound infection (proxy for antibiotic requirement) study (single layer): 4% (n=4/100) control (double layer): 3% (n=3/100)	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: HIGH** • **Random sequence generation** *Used ID number's final digit - evens allocated to study group, odds to control group (**HIGH**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
maternal-fetal medicine, 5, 366-369, 1996 **Ref Id** 931078 **Country/ies where the study was carried out** Israel **Study type** RCT **Aim of the study** examine the feasibility of a modified technique of caesarean section in which uterine incision is sutured in one layer and the visceral and parietal peritoneum are left open **Study dates** Not reported **Source of funding** Not reported	No previous c-section: study 69%; control 54% emergency c-section: study 65%; control 73% **Inclusion criteria** women undergoing caesarean section **Exclusion criteria** Not reported	Control group: uterus closed by 2 **continuous sutures in two layers**, the visceral peritoneum, the parietal peritoneum and fascia were each closed by continuous sutures. Interrupted sutures placed on the skin	Uterine closure: single vs double layer Exteriorisation of uterus: exteriorised in all cases Suture material: skin - Naylon; other layers - Vicryl (polyglactin 910) Type of suture/stitch pattern: continuous pattern (single - non locking) Peritoneal closure: open vs closed Skin closure: all had interrupted sutures Other: c-sections performed by residents in training and assisted by specialists in obstetrics and gynaecology. Anaesthesia was either general or regional. Operative technique similar until closure		• **Allocation concealment** *Allocation clear to anyone aware of ID number (**HIGH**)* **Performance bias: HIGH** • **Blinding of participants:** *No information (**UNCLEAR**)* • **Blinding of personnel:** *No information - unable to blind surgeon to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *No information (**UNCLEAR**)* **Attrition bias - Incomplete outcome data (for each outcome):** *all women included in analysis (**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation	**Sample size** n=400; 200 per group	**Interventions**	**Details**	**Results**	**Limitations**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Poonam,, Banerjee, B., Singh, S. N., Raina, A., The Misgav Ladach method: a step forward in the operative technique of caesarean section, Kathmandu University Medical Journal, 4, 198-202, 2006 **Ref Id** 388049 **Country/ies where the study was carried out** Nepal **Study type** RCT **Aim of the study** compare the intra-operative and short term postoperative outcomes between the conventional and the Misgav-Ladach technique for caesarean section **Study dates** Sept 2001 - Sept 2004	**Characteristics** Maternal age: ML method 24.5 years (range 18-40); control 23.6 (18-40) years GA at birth: ML method 38.6 (38-42 weeks); control 38.5 (37-42 weeks) Primipara: ML method 54%; control 52% **Inclusion criteria** • Single pregnancies at term, undergoing caesarean section • emergency or elective c-section • after an estimated 37 full weeks of gestation **Exclusion criteria** • Multiple pregnancies • Previous caesarean section	**Group 1 Misgav Ladach Technique** 1. Joel Cohen's incision - a straight transverse incision about 3 cms below a line joining the anterior superior iliac spines. 2. Minimal use of instruments - Using the index and third fingers, abdominal wall layers were separated by stretching. Parietal peritoneum was also opened in the same way. 3. Manual lateral stretching of the uterine incision with exteriorization of the uterus. 4. **Single layer** uterine closure. 5. Non-closure of the visceral and parietal peritoneal layers. 6. Closure of the abdomen in two layers - Skin and Fascia **Group 2 Conventional method** 1. Pfannenstiel incision. 2. Use of instruments/sharp dissection while opening the abdomen and extending the incision on lower uterine segment. 3. **Double layer** uterine closure.	Antibiotics as standard: a broad spectrum antibiotic was used for all women Skin closure: skin was closed with non-absorbable suture material and inspected on the 3rd postoperative day. other: The total number of cases were performed by the same surgeon (senior resident) and assisted by junior residents on duty	<u>Intra-operative transfusion</u> *Reported but not relevant to intervention which occurs at closing, only post-operative transfusion data used in analysis* <u>Post-operative transfusion</u> ML method: n=2/200; control: n=10/200 <u>Wound infection - abdominal wound dehiscence (proxy for antibiotic requirement)</u> ML method: n=2/200; control n=13/200	**Risk of Bias assessed using Cochrane ROB tool** **Selection bias: UNCLEAR** • **Random sequence generation** *"The patients under study were divided into two groups by randomization" - no information regarding randomisation of concealment (**UNCLEAR**)* • **Allocation concealment** *No information regarding allocation concealment (**UNCLEAR**)* **Performance bias: HIGH** • **Blinding of participants:** *No information (**UNCLEAR**)* • **Blinding of personnel:** *No information unable to blind surgeon to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *No information (**UNCLEAR**)* **Attrition bias - Incomplete outcome data (for each outcome):** All women analysed as allocated *(**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Source of funding Not reported		4. Closure of the abdomen in layers except for the peritoneum.			
Full citation Sood, Atal Kumar, Single versus double layer closure of low transverse uterine incision at cesarean section, The Journal of Obstetrics and Gynecology of India, 55, 231-236, 2005 **Ref Id** 939274 **Country/ies where the study was carried out** India **Study type** RCT **Aim of the study** assess intraoperative and postoperative morbidity following single layer closure of low transverse uterine incision at cesarean section as compared to double layer closure	**Sample size** n=208; single layer n=102, double layer n=106 **Characteristics** Maternal age: single 26.5±4.5 years; double 25.4±3.5 years parity: single 2.1±0.9, double 1.9±0.6 GA at birth: single 38.2±1.5 weeks, double 37.8±1.8 weeks **Inclusion criteria** Emergency or elective caesarean section All women were eligible for the study, regardless of indication of cesarean delivery, type of skin incision, medical complications, high risk factors, and history of previous cesarean section	**Interventions** single layer: uterine closure was done with continuous nonlocking No.1 polyglactin double layer: an additional imbricating non-locking suture of the same material was employed.	**Details** Antibiotics as standard: All women received prophylactic antibiotics unless already receiving parenteral antibiotics. Cefazoline 2 g was given after cord clamping Type of incision used: Both Pfannenstiel and subumbilical midline incisions were used, and all uterine incisions were low transverse type Uterine closure: single or double layer Exteriorisation of uterus: exteriorised in all women after delivery of placenta Suture material: no1 polyglactin Type of suture/stitch pattern: continuous, non-locking Peritoneal closure: visceral and parietal peritoneum not closed Skin closure: rectus fascia "approximated" with no1 polypropylene, skin "approximated" with subcuticular closure Statistics used: A sample size and power analysis	**Results** Wound infection (proxy for antibiotic requirement) single layer: n=4/102 (3.9%); double: n=9/106 (8.5%); OR=0.43 (95%CI 0.13-1.47)	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *Randomisation was by computer generated random numbers (**LOW**)* • **Allocation concealment** *the randomised allocations were kept secure in sealed envelopes, which were opened in the operation room (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** Treatment allocation was disclosed neither to the nursing or medical staff providing postoperative care, nor to the women *(**LOW**)* • **Blinding of personnel:** *the randomized allocations were kept secure in sealed envelopes, which were opened in the operation room. Treatment allocation was disclosed neither to the nursing or medical staff providing postoperative care, nor*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates October 2001 - December 2003 **Source of funding** Not reported	**Exclusion criteria** None reported		were undertaken prior to the study. 108 women were required in each arm to show a reduction in febrile morbidity from 21% to 7% between double and single layer closure (Power = 0.80, alpha =0.05 and beta= 0.2).		*to the women. - not possible to blind surgeon to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** Relevant outcomes assessed by medical staff - *Treatment allocation was disclosed neither to the nursing or medical staff providing postoperative care, nor to the women (**LOW**)* **Attrition bias - Incomplete outcome data (for each outcome):** All women included in analysis *(**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**
Full citation Xavier, P., Ayres-De-Campos, D., Reynolds, A., Guimarães, M., Costa-Santos, C., Patrício, B., The modified Misgav-Ladach versus the Pfannenstiel-Kerr technique for cesarean section: a randomized trial, Acta Obstetricia et Gynecologica Scandinavica, 84, 878-882, 2005 **Ref Id** 931257	**Sample size** randomised n=162; MML n=88, PK n=74 analysed: MML n=77, PK n=69 n=16 women (9.9%) were excluded after randomisation, 12 because it was not possible to contact them after discharge from hospital and the remaining 4 because they left the hospital before the third postoperative day (11 in the MML group and five in the PK group).	**Interventions** **modified Misgav-Ladach (MML)**: Closure of the uterine incision is accomplished with a **one-layer continuous** #1 poliglactin 910 (Vicryl1) suture, using additional hemostatic stitches if required. After the inspection of the peritoneal cavity and removal of accessible blood and clots, the visceral and parietal peritoneum is left unsutured. The rectus muscles, subfascial space, and subcutaneous tissue are inspected forhemostasis, and the rectus sheath is closed using a continuous #1 polyglactin 910 suture	**Details** Antibiotics as standard: Prophylactic antibiotics were administered to all women after umbilical cord clamping: 2 g of intravenous (i.v.) ampicillin or 500 mg of i.v. erythromycin in patients with hypersensitivity to penicillins Type of incision used: Pfannenstiel incision Exteriorisation of uterus: optional in MML Statistics used: The planned study of 160 patients had an 80%	**Results** <u>Post-operative antibiotics</u> MML (single): n=73/77 (95%); PK (double): n=64/69 (93%)	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *patient were allocated to one of the two study arms according to a sequence of computer-generated random numbers (**LOW**)* • **Allocation concealment** *Pre-allocation concealment was assured by an individual strip of black tape removed from the computer-generated list at the time of randomisation (**LOW**)*

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Country/ies where the study was carried out Portugal **Study type** RCT **Aim of the study** compare intraoperative and short-term postoperative outcomes between the Pfannenstiel–Kerr and the modified Misgav-Ladach (MML) techniques for cesarean section **Study dates** Not reported **Source of funding** Not reported	**Characteristics** Maternal age: MML 28 years (range 19-42); PK 28 years (18-41) GA at birth (median): MML 38 weeks (27-42); PK 38 weeks (29-42) Parity (one): MML n=47/77 (61%); PK n=39/69 (57%) Parity (two): MML n=19/77 (25%); PK n=21/69 (30%) **Inclusion criteria** scheduled for elective or emergency cesarean section by one of three experienced surgeons **Exclusion criteria** • a previous midline infraumbilical skin incision, • axillary temperature exceeding 37.5 C in the 48 hr before surgery, • antibiotic use in the preceding week	**Pfannenstiel-Kerr:** Closure of the uterine incision is accomplished with a **two-layer continuous** #1 polyglactin 910 suture, using additional hemostatic stitches if required. The visceral peritoneum is closed with a continuous #2/0 polyglactin 910 suture. After the inspection of the peritoneal cavity and aspiration of all accessible blood and clots, the parietal peritoneum is closed in a similar fashion. The rectus muscles, subfascial space, and subcutaneous tissue are checked for hemostasis, and the rectus sheath is closed with a continuous #1 polyglactin 910 suture.	power to detect a difference between the two techniques of 20% in bowel restitution by the second postoperative day (assuming 70% and 50% for MML and PK, respectively), at the 5% significance level.		**Performance bias: HIGH** • **Blinding of participants:** *No information (**UNCLEAR**)* • **Blinding of personnel:** *No information - unable to blind surgeon to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *The staff in charge of the postoperative period was unaware of the surgical technique employed in individual patients. Analgesic requirements, antibiotic use, and day of bowel restitution were obtained from the hospital notes and confirmed with patients on the fourth postoperative day (**LOW**)* **Attrition bias - Incomplete outcome data (for each outcome):** *n=16 women (9.9%) were excluded after randomisation, 12 because it was not possible to contact them after discharge from hospital and 4 because they left the hospital before the third postoperative day (11 in the MML group and five in the PK group) (**LOW**)* **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Full citation Yasmin, S., Sadaf, J., Fatima, N., Impact of methods for uterine incision closure on repeat caesarean section scar of lower uterine segment, Journal of the college of physicians and surgeons--pakistan : JCPSP, 21, 522-526, 2011 **Ref Id** 931261 **Country/ies where the study was carried out** Pakistan **Study type** RCT **Aim of the study** compare the effect of different suturing techniques in repeat caesarean section in terms of scar thickness, blood loss, operative time and scar dehiscence at the time of next caesarean section.	**Sample size** n=90 randomised; 30 per group single n=30; double n=60* **both groups of double layer suturing have been combined for purposes of the review* **Characteristics** Maternal age (range): 20-35 years Parity (range): 1-4 GA at birth (range): 37-40 weeks **Inclusion criteria** • singleton term pregnancy, • parity less than 5, • history of previous caesarean section (one to three) **Exclusion criteria** • multiple gestation, • polyhydramnios, • parity greater than 5,	**Interventions** **A - one layer closure**: had their transverse uterine incision closure in one layer with running locking sutures penetrating the full thickness of myometrium with chromic catgut no. 2. **B - two layer closure*:** had an initial closure identical to the one layer closure as above. An additional layer of chromic catgut no. 2 was used to imbricate the first layer in a continuous non-locking suture. **C - modified two layer closure***: had first layer closure by interrupted horizontal mattress sutures taking full thickness of decidua and myometrium. The previous scar tissue was not excised. Care was taken to select the site of each stitch and to avoid withdrawing the needle once it penetrated the myometrium. This minimized the perforation of unligated vessels and subsequent bleeding. The second layer folded muscles over the first layer of sutures in running non-locking sutures. **both groups of double layer suturing have been combined for purposes of the review*	**Details** Antibiotics as standard: All the patients received first dose of first generation cephalosporin antibiotic at umbilical cord clamping. These intravenous antibiotics were continued to all the patients for 24 hours as per hospital protocol Type of incision used: low transverse Uterine closure: A: single layer; B: double layer; C: modified 2 layer Exteriorisation of uterus: not reported Suture material: A&B: chromic catgut no2 Type of suture/stitch pattern: A: one layer running locking sutures penetrating full myometrium; B: "A" + imbricating continuous nonlocking sutures; C: 1st layer interrupted horizontal mattress sutures + 2nd layer folded muscles Peritoneal closure: not reported Skin closure: not reported	**Results** Wound sepsis requiring additional antibiotics n=0/90 (no cases in each group)	**Limitations** **Risk of Bias assessed using Cochrane ROB tool** **Selection bias: LOW** • **Random sequence generation** *random allocation was performed using pre-made allocation cards (**LOW**)* • **Allocation concealment** *each patient was asked to pick the allocation cards from a box (**LOW**)* **Performance bias: HIGH** • **Blinding of participants:** *No information - suggestion participants were aware as they picked the allocation card (blinded) (**UNCLEAR**)* • **Blinding of personnel:** *The group allocation was revealed to the surgeon during the surgery just before the uterine incision closure - unable to blind surgeon to allocation (**HIGH**)* **Detection bias - Blinding of outcome assessment:** *additional haemostatic sutures were placed at the discretion of the operating surgeon and the number of the additional sutures was recorded - aware of allocation (**HIGH**)* **Attrition bias - Incomplete outcome data (for each outcome):** All patients

Study details	Participants	Interventions	Methods	Outcomes and Results	Comments
Study dates June 2005 - June 2010 **Source of funding** Not reported	• maternal diabetes, • anaemia • connective tissue disorder				treated per allocation, all 90 cases analysed as per allocation ***(LOW)*** **Reporting bias - Selective reporting:** *No access to protocol (**UNCLEAR**)* **Other information**

Appendix E – Forest plots

Forest plots for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

This section includes forest plots only for outcomes that are meta-analysed. Outcomes from single studies are not presented here, but the quality assessment for these outcomes is provided in the GRADE profiles in appendix F.

Comparison 1: Trials specifically comparing single and double layer closure

Critical outcomes

Figure 2: Single versus double layer closure: Blood transfusion

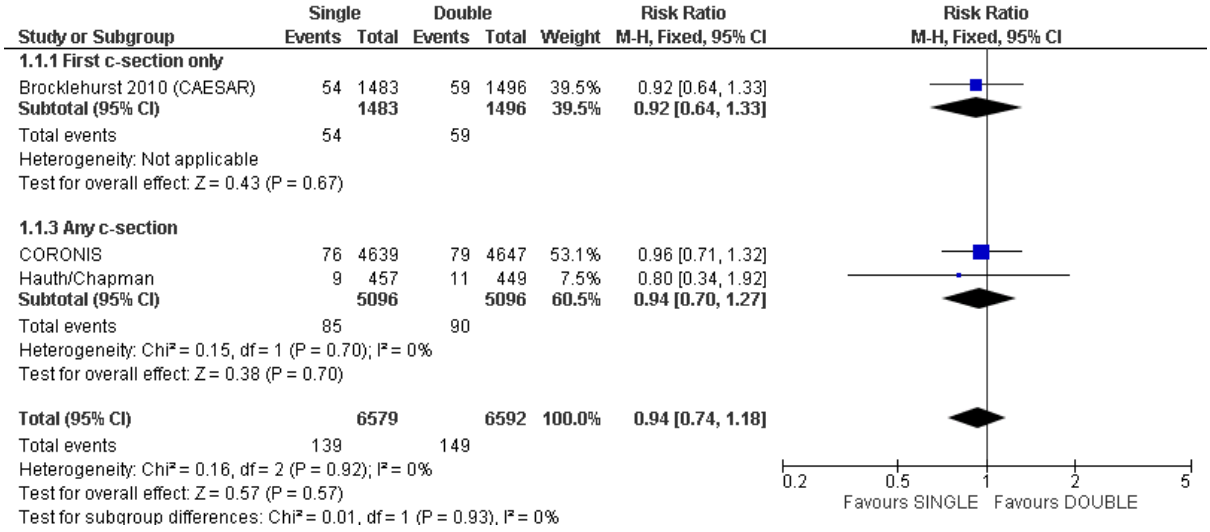
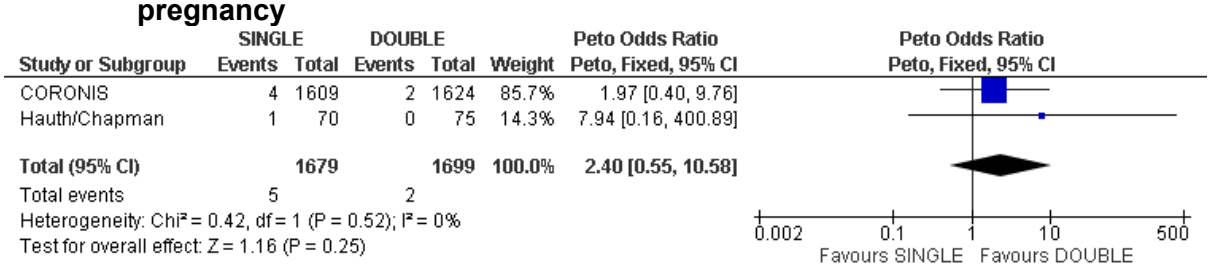


Figure 3: Single versus double layer closure: Uterine scar dehiscence in subsequent pregnancy



Important outcomes

Figure 4: Single versus double layer closure: Antibiotics for wound infection

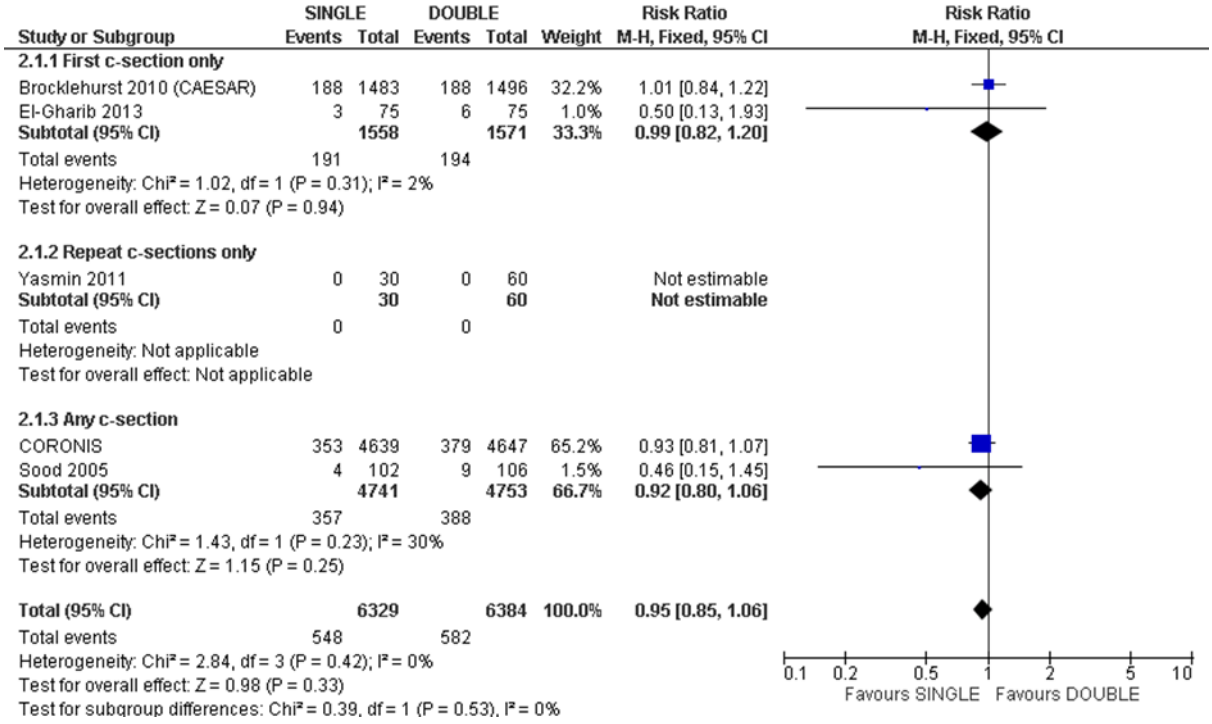


Figure 5: Single versus double layer closure: Antibiotics for febrile morbidity

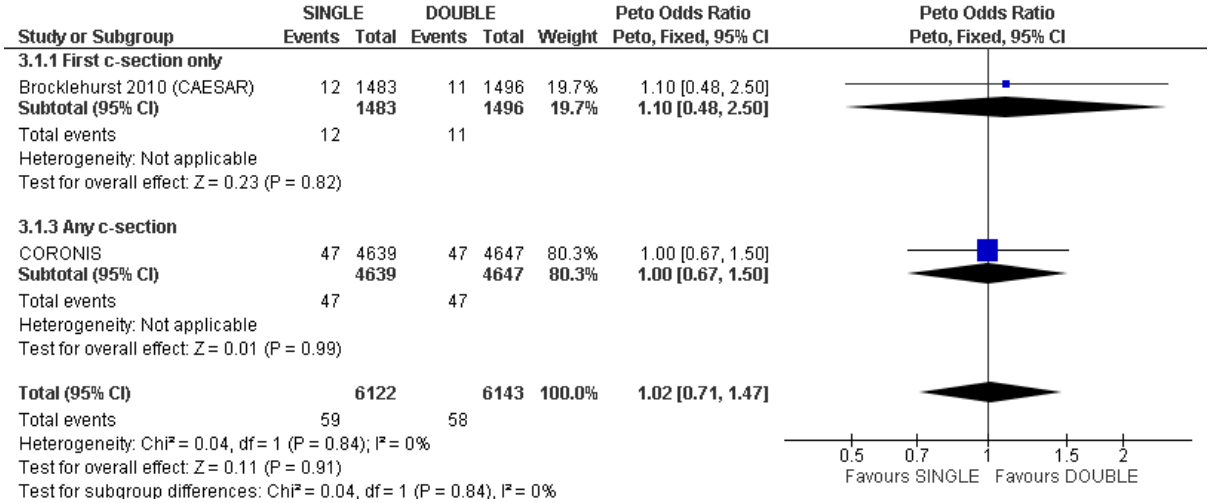


Figure 6: Single versus double layer closure: Antibiotics for endometritis

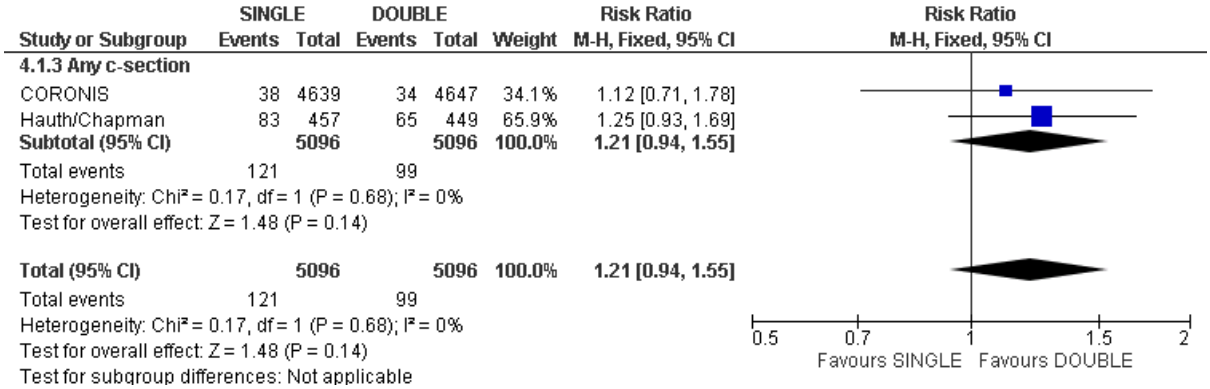
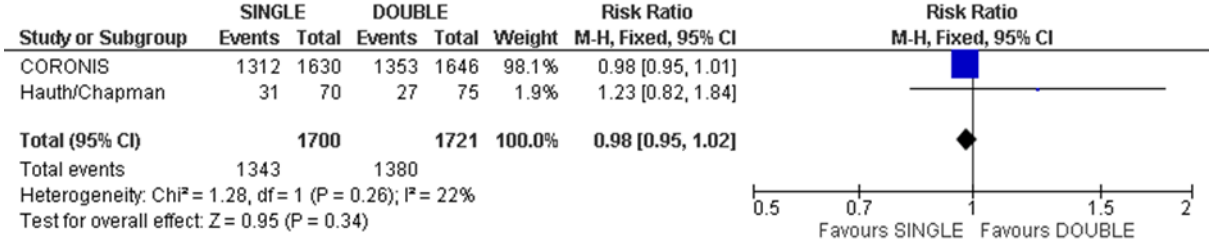


Figure 7: Single versus double layer closure: C-sections in subsequent pregnancy



Comparison 2: Trials comparing different caesarean birth techniques

Figure 8: Trials comparing different CB techniques: Blood transfusion

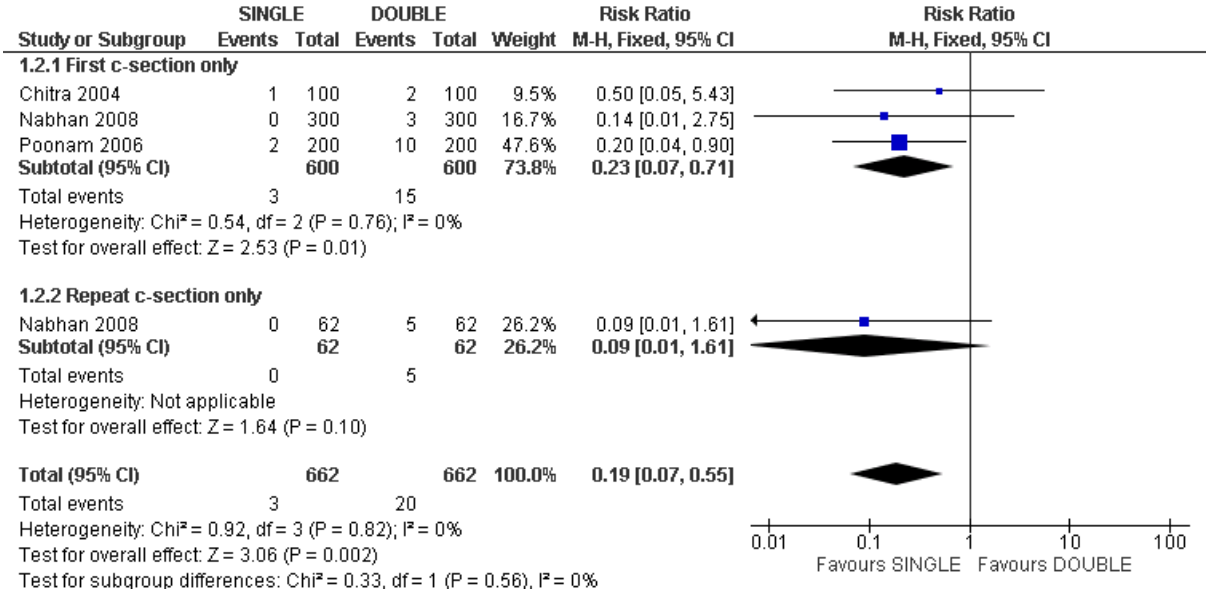


Figure 9: Trials comparing different CB techniques: Antibiotics required (unspecified reason)

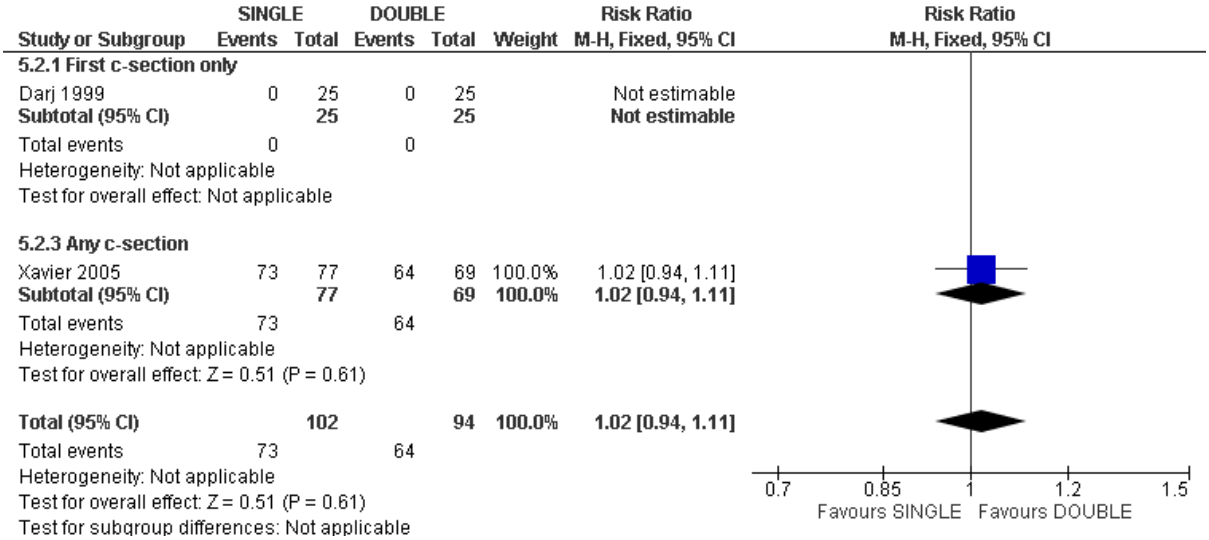
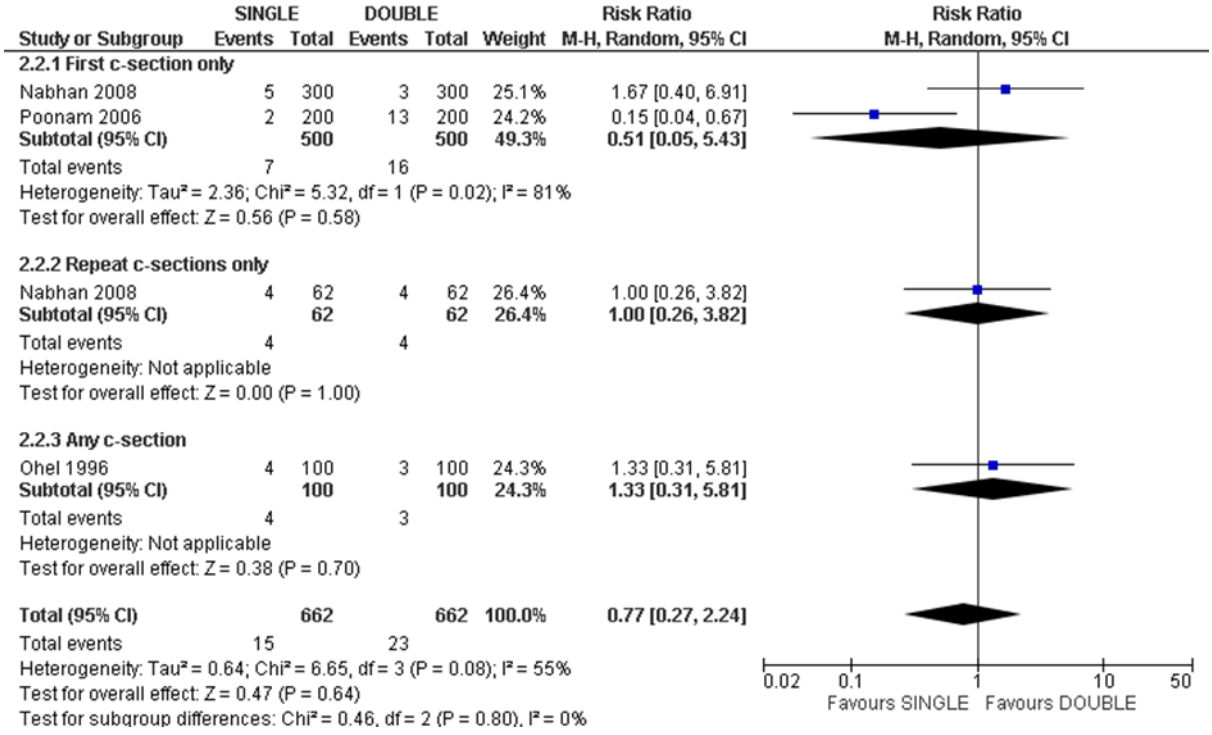


Figure 10: Trials comparing different CB techniques: Antibiotics for wound infection (and wound sepsis)



Appendix F – GRADE tables

GRADE tables for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Table 5: Comparison 1. Trials specifically comparing uterine closure method (single versus double layer closure)

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single-layer uterine closure (intervention)	Double-layer uterine closure (control)	Relative (95% CI)	Absolute		
Blood transfusion												
3 (Brocklehurst 2010, CORONIS, Hauth/Chapman)	Randomised trials	Very serious[1]	No serious inconsistency	No serious indirectness	Serious[2]	None	139/6579 (2.1%)	149/6592 (2.3%)	RR 0.94 (0.74 to 1.18)	1 fewer per 1000 (from 6 fewer to 4 more)	VERY LOW	CRITICAL
Further operative procedures[a]												
1 (CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Serious[2]	None	74/4639 (1.6%)	87/4647 (1.9%)	RR 0.85 (0.63 to 1.16)	3 fewer per 1000 (from 7 fewer to 3 more)	VERY LOW	CRITICAL
Further operative procedures on wound												
1 (CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	30/4639 (0.65%)	38/4647 (0.82%)	POR 0.79 (0.49 to 1.27)	2 fewer per 1000 (from 4 fewer to 2 more)	VERY LOW	CRITICAL
Uterine rupture in subsequent pregnancy												

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single-layer uterine closure (intervention)	Double-layer uterine closure (control)	Relative (95% CI)	Absolute		
1 (CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	1/1610 (0.06%)	2/1624 (0.12%)	POR 0.52 (0.05 to 4.98)	1 fewer per 1000 (from 1 fewer to 5 more)	VERY LOW	CRITICAL
Uterine scar dehiscence in subsequent pregnancy												
2 (CORONIS, Hauth/Chapman)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	Very serious[4]	None	5/1679 (0.3%)	2/1699 (0.12%)	POR 2.40 (0.55 to 10.58)	2 more per 1000 (from 1 fewer to 11 more)	VERY LOW	CRITICAL
Antibiotics for wound infection or wound sepsis												
5 (Brocklehurst 2010, El-Gharib 2013, Yasmin 2011, CORONIS, Sood 2005)	Randomised trials	Very serious[6]	No serious inconsistency	No serious indirectness	No serious imprecision	None	548/6329 (8.7%)	582/6384 (9.1%)	RR 0.95 (0.85 to 1.06)	5 fewer per 1000 (from 14 fewer to 5 more)	LOW	IMPORTANT
Antibiotics for febrile morbidity												
2 (Brocklehurst 2010, CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	59/6122 (0.96%)	58/6143 (0.94%)	POR 1.02 (0.71 to 1.47)	0 more per 1000 (from 3 fewer to 4 more)	VERY LOW	IMPORTANT
Antibiotics for endometritis												
2 (CORONIS, Hauth/Chapman)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	Serious[7]	None	121/5096 (2.4%)	99/5096 (1.9%)	RR 1.21 (0.94 to 1.55)	4 more per 1000 (from 1 fewer to 11 more)	VERY LOW	IMPORTANT
Morbidly adherent placenta in subsequent pregnancy												

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single-layer uterine closure (intervention)	Double-layer uterine closure (control)	Relative (95% CI)	Absolute		
1 (CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	0/1609 (0%)	2/1624 (0.12%)	POR 0.14 (0.01 to 2.18)	1 fewer per 1000 (from 1 fewer to 1 more)	VERY LOW	IMPORTANT
Hysterectomy in 6 weeks postpartum in subsequent pregnancy												
1 (CORONIS)	Randomised trials	Very serious[3]	No serious inconsistency	No serious indirectness	Very serious[4]	None	1/1610 (0.06%)	1/1624 (0.06%)	POR 1.01 (0.06 to 16.13)	0 more per 1000 (from 1 fewer to 9 more)	VERY LOW	IMPORTANT
C-sections in subsequent pregnancy												
2 (CORONIS, Hauth/Chapman)	Randomised trials	Very serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	None	1343/1700 (79%)	1380/1721 (80.2%)	RR 0.98 (0.95 to 1.02)	16 fewer per 1000 (from 40 fewer to 16 more)	LOW	IMPORTANT

a Includes any operative procedures on caesarean wound, curettage, laparotomy, artery ligation, brace suture, and hysterectomy.
1 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, and attrition bias
2 The quality of the evidence was downgraded by 1 level for imprecision as the 95%CI crosses the lower boundary of the default MID threshold (0.80)
3 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, and detection bias
4 The quality of the evidence was downgraded by 2 levels for imprecision as the 95%CI crosses the upper and lower boundaries of the default MID thresholds (0.80 and 1.25)
5 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, detection bias, and attrition bias
6 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, detection bias, and selection bias
7 The quality of the evidence was downgraded by 1 level for imprecision as the 95%CI crosses the upper boundary of the default MID threshold (1.25)

Table 6: Comparison 2. Trials comparing different caesarean birth techniques

Quality assessment							Number of women		Effect		Quality	Importance
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Single-layer uterine closure (intervention)	Double-layer uterine closure (control)	Relative (95% CI)	Absolute		
Blood transfusion												
3 (Chitra 2004, Nabhan 2008, Poonam 2006)	Randomised trials	Very serious[1]	No serious inconsistency	Very serious[2]	No serious imprecision	None	3/662 (0.45%)	20/662 (3%)	RR 0.19 (0.07 to 0.55)	24 fewer per 1000 (from 14 fewer to 28 fewer)	VERY LOW	CRITICAL
Antibiotics required (unspecified reason)												
2 (Darj 1999, Xavier 2005)	Randomised trials	Very serious[1]	No serious inconsistency	Very serious[2]	No serious imprecision	None	73/102 (71.6%)	64/94 (68.1%)	RR 1.02 (0.94 to 1.11)	14 more per 1000 (from 41 fewer to 75 more)	VERY LOW	IMPORTANT
Antibiotics for wound infection (and wound sepsis) (pooled all CS)												
3 (Nabhan 2008, Poonam 2006, Ohel 1996)	Randomised trials	Very serious[3]	Serious[4]	Very serious[2]	Very serious[5]	None	15/662 (2.3%)	23/662 (3.5%)	RR 0.77 (0.27 to 2.24)	8 fewer per 1000 (from 25 fewer to 43 more)	VERY LOW	IMPORTANT
Antibiotics for wound infection (and wound sepsis) (Subgroup analysis, first CS only)												
2 (Nabhan 2008, Poonam 2006)	Randomised trials	Very serious[6]	Very serious[7]	Very serious[2]	Very serious[5]	None	7/500 (1.4%)	16/500 (3.2%)	RR 0.51 (0.05 to 5.43)	16 fewer per 1000 (from 30 fewer to 142 more)	VERY LOW	IMPORTANT
Antibiotics for wound infection (and wound sepsis) (Subgroup analysis, repeat CS only)												
1 (Nabhan 2008)	Randomised trials	Serious[8]	No serious inconsistency	Very serious[2]	Very serious[5]	None	4/62 (6.5%)	4/62 (6.5%)	RR 1 (0.26 to 3.82)	0 fewer per 1000 (from 48 fewer to 182 more)	VERY LOW	IMPORTANT

1 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, and detection bias

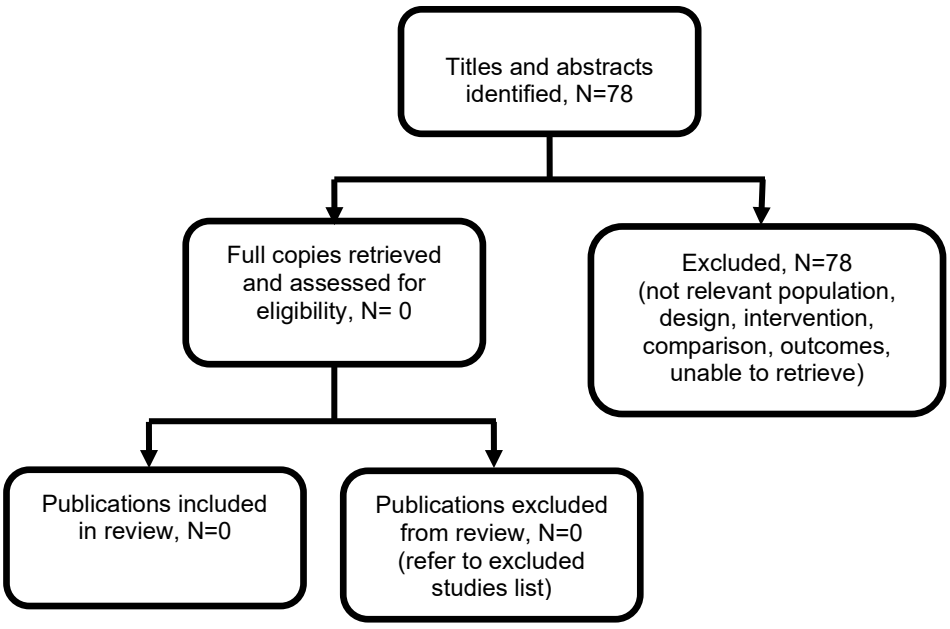
2 The quality of the evidence was downgraded by 2 levels for indirectness as the comparison also examined uterine incision, exteriorisation of the uterus, peritoneal closure, skin closure, and suture material
3 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias, and selection bias
4 The quality of the evidence was downgraded by 1 level for inconsistency as heterogeneity was high (I^2=55%, random effects model)
5 The quality of the evidence was downgraded by 2 levels for imprecision as the 95%CI crosses the upper and lower boundaries of the default MID thresholds (0.80 and 1.25)
6 The quality of the evidence was downgraded by 2 levels for risk of bias as the outcome had high risk of performance bias in more than 1 study
7 The quality of the evidence was downgraded by 2 levels for inconsistency as heterogeneity was high (I^2=81%, random effects model)
8 The quality of the evidence was downgraded by 1 level for risk of bias as the outcome had high risk of performance bias in 1 study

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

No evidence was identified which was applicable to this review question.

Figure 11: Study selection flow chart



Appendix H – Economic evidence tables

Economic evidence tables for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

No evidence was identified which was applicable to this review question.

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

No evidence was identified which was applicable to this review question.

Appendix J – Economic analysis

Economic evidence analysis for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

No economic analysis was conducted for this review question.

Appendix K – Excluded studies

Excluded studies for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

Clinical studies

Table 7: Excluded studies and reasons for their exclusion

Study	Reason for Exclusion
Abalos, E., Addo, V., Brocklehurst, P., El Sheikh, M. A., Farrell, B., Gray, S., Hardy, P., Juszczak, E., Mathews, J. E., Masood, S. N., Oyarzun, E., Oiyeke, J., Sharma, J., Spark, P., Caesarean section surgical techniques long term outcomes: Follow-up of the CORONIS trial, BJOG: An International Journal of Obstetrics and Gynaecology, 123, 30, 2016	Conference abstract
Abalos, E., Oyarzun, E., Addo, V., Sharma, J. B., Matthews, J., Oyieke, J., Masood, S. N., El Sheikh, M. A., Brocklehurst, B., Farrell, F., Gray, S., Hardy, P., Jamieson, N., Juszczak, E., Spark, P., CORONIS - International study of caesarean section surgical techniques: The follow-up study, BMC Pregnancy and Childbirth, 13 (no pagination), 2013	CORONIS study protocol
Abraham, C., A randomized clinical trial of knotless barbed suture vs conventional suture for closure of the uterine incision at cesarean delivery, American Journal of Obstetrics and Gynecology, 219, 220â□□221, 2018	Short communication/ Letter to the Editor
Adam, Y., Mwinyoglee, J., Masuku, B., Nicolaou, E., An evaluation of the indications for caesarean sections at Chris Hani Baragwanath academic Hospital, South African Journal of Obstetrics and Gynaecology, 24, 11-14, 2018	Retrospective cross-sectional study (non RCT)
Ahn, J. W., Lee, S. J., Kwon, Y. S., Impact of uterine closure on residual myometrial thickness after cesarean: a randomized controlled trial, American Journal of Obstetrics and Gynecology, 216, 81â□□82, 2017	Letter to the Editor (response to published article)
Babu, K. M., Magon, N., Uterine closure in cesarean delivery: A new technique, North American Journal of Medical Sciences, 4, 358-361, 2012	Description of new techniques for closure (single layer excluding decidual layer)
Bamberg, C., Hinkson, L., Dudenhausen, J. W., Bujak, V., Kalache, K. D., Henrich, W., Longitudinal transvaginal ultrasound evaluation of cesarean scar niche incidence and depth in the first two years after single- or double-layer uterotomy closure: a randomized controlled trial, Acta Obstetricia et Gynecologica Scandinavica, 96, 1484â□□1489, 2017	No relevant outcomes (C-section scar niche observed by ultrasound)
Bamberg, Christian, Dudenhausen, Joachim W., Bujak, Verena, Rodekamp, Elke, Brauer, Martin, Hinkson, Larry, Kalache, Karim, Henrich, Wolfgang, A Prospective Randomized Clinical Trial of Single vs. Double Layer Closure of Hysterotomy at the Time of Cesarean Delivery: The Effect on Uterine Scar Thickness, Der Effekt auf die Narbendicke nach	Article in German

Study	Reason for Exclusion
einschichtigem oder zweischichtigem Verschluss der Uterotomie bei der Sectio Cesarea: Eine prospektiv randomisierte Studie., 39, 343-351, 2018	
Batioglu, S., Kuscu, E., Duran, E. H., Haberal, A., One-layer closure of low segment transverse uterine incision by the Lembert technique, Journal of Gynecologic Surgery, 14, 11â□□14, 1998	No relevant outcomes
Belci, D., Di Renzo, G. C., Stark, M., Duric, J., Zoricic, D., Belci, M., Peteh, L. L., Morbidity and chronic pain following different techniques of caesarean section: A comparative study, Journal of obstetrics and gynaecology : the journal of the Institute of Obstetrics and Gynaecology, 35, 442-6, 2015	Compared traditional method and Misgav-Ladach method for C-section procedure (both use single layer, continuous locking suture for uterine closure)
Bennich, G., Rudnicki, M., Wilken-Jensen, C., Lousen, T., Lassen, P. D., Wojdemann, K., Impact of adding a second layer to a single unlocked closure of a Cesarean uterine incision: randomized controlled trial, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 47, 417-422, 2016	No relevant outcomes (Residual myometrial thickness, RMT, assessed by ultrasound)
Bij de Vaate, A. J., van der Voet, L. F., Naji, O., Witmer, M., Veersema, S., Brolmann, H. A., Bourne, T., Huirne, J. A., Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 43, 372-382, 2014	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion (only 2 studies of relevance assessed for inclusion).
Bjorklund, K., Kimaro, M., Urassa, E., Lindmark, G., Introduction of the Misgav Ladach caesarean section at an African tertiary centre: a randomised controlled trial, BJOG: An International Journal of Obstetrics & Gynaecology, 107, 209-16, 2000	Compared Misgav Ladach procedure and standard lower midline incision procedure (difference was transverse or longitudinal incision)
Blumenfeld, Yair, Caughey, Aaron B., Lyell, Deirdre J., Re: Uterine exteriorization compared with in situ repair at cesarean delivery: a randomized controlled trial, Obstetrics and Gynecology, 112, 183-183, 2008	Letter to the Editor regarding published article
Borowski, K., Andrews, J., Hocking, M., Hansen, W., Fleener, D., Syrop, C., Ultrasonographic detection of cesarean scar defects in a trial of single versus double layer closure, American Journal of Obstetrics and Gynecology, 197, S62, Abstract no: 183, 2007	Conference abstract
Brocklehurst, P., The CORONIS Trial: international study of caesarean section surgical techniques: a randomised fractional factorial randomised trial, BJOG: an international journal of obstetrics and gynaecology., 120, 3, 2013	Conference abstract
Brocklehurst, P., Abalos, E., Addo, V., El Sheikh, M. A., Farrell, B., Gray, S., Hardy, P., Juszczak, E., Mathews, J. E., Masood, S. N., Oyarzun, E., Oiyeke, J., Sharma, J., Spark, P., Caesarean section surgical techniques long-term outcomes: Follow-up of the CORONIS trial, BJOG: An International Journal of Obstetrics and Gynaecology, 123, 12, 2016	Conference abstract

Study	Reason for Exclusion
Brocklehurst, P., Abalos, E., Addo, V., Sharma, J. B., Matthews, J., Oyieke, J., Naz Masood, S., El Sheikh, M. A., The CORONIS Trial. International study of caesarean section surgical techniques: A randomised fractional, factorial trial, BMC Pregnancy and Childbirth, 7, 24, 2007	CORONIS study protocol
Bujold, E., The optimal uterine closure technique during caesarean, North American Journal of Medical Sciences, 4, 362-363, 2012	Short communication
Capmas, P., Guyot, A., Stirnemann, J., Ville, Y., Fernandez, H., Comparing sonographic aspect of cesarean scar after a continuous single-or double-layer suture: a randomized trial, Journal of Minimally Invasive Gynecology, 20, S165, 2013	Conference abstract
Cardona-Osuna, M. E., Avila-Vergara, M. A., Peraza-Garay, F., Meneses-Valderrama, V., Flores-Pompa, E., Corrales-López, A., Comparison of pregnancy outcomes Caesarean techniques: modified Misgav-Ladach, Pfannenstiel-Kerr and Kerr-half infraumbilical, Ginecologia y Obstetricia de Mexico, 84, 514â□□522, 2016	Article in Spanish
Catling-Paull, Christine, Johnston, Rebecca, Ryan, Clare, Foureur, Maralyn J., Homer, Caroline S. E., Clinical interventions that increase the uptake and success of vaginal birth after caesarean section: a systematic review, Journal of advanced nursing, 67, 1646-61, 2011	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion (2 studies - follow up of one RCT - assessed for inclusion).
Ceci, O., Scioscia, M., Bettocchi, S., Cantatore, C., Nardelli, C., Laera, A., Vimercati, A., Ultrasound evaluation of the uterine scar after cesarean delivery: A randomized controlled trial of one- and two-layer closure, Obstetrics and Gynecology, 111, 452, 2008	Letter to the Editor regarding published article
Chamberlain, G., Steer, P., ABC of labour care: operative delivery, BMJ (Clinical research ed.), 318, 1260-4, 1999	Description of c-section procedure (educational material)
Charoenkwan, K., Double-layer continuous parallel uterine closure for low transverse cesarean incisions, International Journal of Gynecology and Obstetrics, 94, 137-138, 2006	Short communication regarding two-layer technique
Chauhan, R., Nagrath, A., Mathura, V., Singh, S., Mathur, R. K., Comparison of single layer closure with conventional multilayer closure of the abdominal wall in caesarean section, Journal of obstetrics and gynaecology of India, 52, 33â□□36, 2002	No relevant outcomes. Unclear if women were randomly allocated to study or "control" groups. Multi-layer (study group) closure: (1) peritoneum closure, (2) rectus sheath closure, (3) subcutaneous closure. Single layer (control) closure of peritoneum, rectus sheath, subcutaneous using round body needle
Corso, E., Hind, D., Beever, D., Fuller, G., Wilson, M. J., Wrench, I. J., Chambers, D., Enhanced recovery after elective caesarean: a rapid review of clinical protocols, and an umbrella review of systematic reviews, BMC Pregnancy & Childbirth, 17, 91, 2017	No relevant outcomes
Coutinho, I. C., Ramos de Amorim, M. M., Katz, L., Bandeira de Ferraz, A. A., Uterine exteriorization compared with in situ repair at cesarean delivery: a	Compared exteriorized and in-situ repair of uterine wall (uterine incision was closed with a continuous single layer)

Study	Reason for Exclusion
randomized controlled trial, Obstetrics and Gynecology, 111, 639â□□647, 2008	
Dahlke,J.D., Mendez-Figueroa,H., Rouse,D.J., Berghella,V., Baxter,J.K., Chauhan,S.P., Evidence-based surgery for cesarean delivery: An updated systematic review, American Journal of Obstetrics and Gynecology, 209, 294-306, 2013	Systematic review with no relevant outcomes. 3 references checked and assessed for inclusion.
Dani C, , Reali M, , Oliveto R, , Temporin G, , Bertini G,, Rubaltelli F. , Short-term outcome of newborn infants born by a modified procedure of cesarean section: a prospective randomized study, Acta Obstetricia et Gynecologica Scandinavica, 77, 929-31, 1998	No relevant outcomes (neonatal outcomes only)
Di Spiezio Sardo, A., Saccone, G., McCurdy, R., Bujold, E., Bifulco, G., Berghella, V., Risk of Cesarean scar defect following single- vs double-layer uterine closure: systematic review and meta-analysis of randomized controlled trials, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 50, 578-583, 2017	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion (included studies with relevant outcomes already included).
Dodd, J. M., Anderson, E. R., Gates, S., Surgical techniques for uterine incision and uterine closure at the time of caesarean section, Cochrane Database of Systematic Reviews, CD004732, 2008	More recent version assessed for inclusion
Dodd, J. M., Anderson, E. R., Gates, S., Grivell, R. M., Surgical techniques for uterine incision and uterine closure at the time of caesarean section, Cochrane Database of Systematic Reviews, 7, CD004732, 2014	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion
Dodson, M. K., Magann, E. F., Meeks, G. R., A randomized comparison of secondary closure and secondary intention in patients with superficial wound dehiscence, Obstetrics and Gynecology, 80, 321-4, 1992	Skin closure
E. Mathews J, Ashworth, F., Chippington Derrick, D., Cousens, S., Neilson, J., Purwar, M., Roberts, M., Waddington, C., Bewley, S., Campbell, O., Deeks, J., Mirembe, F., El Sheikh, M., Farrell, B., Gray, S., Mathews, J. E., Sharma, J. B., Armstrong, N., Bowler, U., Brocklehurst, P., Farrell, B., Gray, S., Hardy, P., Juszczak, E., Nowicki, M., Quigley, M., Spark, P., Zhao, R., Abalos, E., Burqueno, N. F., Campodonico, L., Carroli, B., D'Aloisio, L., Dalonso, M., Giordano, D., Novaro, J., Toumani, B., Zanello, R., Garay, C., Ihnen, O., Mora, S., Oyarzun, E., Addo, V., Ansah, A., Asamoa, P., Ashong, R., Attrams, I., Boateng, K., Senya, L., Bahadur, A., Batra, D., Chaudhary, A., Devi, S. G., Dhanai, S., Dharmendra, S., Gandhi, S., Gupta, A., Gupta, H., Kumar, M., Kumar, N., Kumar, P., Kumar, V., Kumari, S., Naha, M., Pushpraj, M., Roy, B. K., Shankar, M., Sharma, J. B., Sharma, S., Shukla, H., Singla, S., Wangdi, T., Nayana, E. J., Jacob, S., Mathews, J. E., Thomas, W., Jeyasudha, R., Nirmala, M., Sukumar, K., Bwana, K. M., Mulange, J., Ndeda, M., O'Goro, K., Okoti, D., Oyieke, J., Abdul	Conference abstract

Study	Reason for Exclusion
Muhammad, Z., Ali, A., Arain, S., Bhatia, J., Bibi, F., Imran Shah, S., Malik, S., Naz Masood, S., Rafiq, S., Rizvi, S., Soomro, S., Abdelhafiz, Z., El Sheikh, E., El Sheikh, M., El Sheikh, T., Etayeb, E., Hamad, T., Hashim, A., Khatim, M., Mohamed, S., Yousif, A., Arias, C. A., Bosquiazzo, L. M., Bruna, J. A., Fabrica, M. C., Mascotti, C., Bertin, M. S., Castaldi, J. L., Mendoza, S. J., Partida, L. Y., Zyla, A., Castilla, L., Di Gerolano, E., Espinoza, M., Koch, G., Tulian, M., Melis, M., Miriam, M., Palermo, M., Pappalardo, J., Quinones, M., Cabrera, F., Campos, S., Curioni, M. A., Fernandez, J., Grasselli, C., Abarzua, F., Araya, G., Caro, M., Gonzalez, C., Vera, C., Araneda, M., De La Cuadra, S., Kusanovic, J. P., Ortiz, J. A., Silva, K., Bofa, W. K., Djokoto, R. M., Konney, T. O., Larbi, Y. O., Quashie, E., Kriplani, A., Kumar, S., Mittal, S., Gupta, U., Puri, M., Raghunandan, C., Trivedi, S. S., Batra, S., Kumar, A., Manaktala, U., Prasad, S., Goel, N., Guleria, K., Radhakrishnan, G., Suneja, A., Vaid, N. B., Beck, M., D'Souza, A., Sebastian, A., Thomas, A. E., Thomas, E., Vijayaselvi, R., Butt, F., Kaliti, S., Nyaboga, E. O., Owiti, M. J., Wameyo, A., Akram, S., Junejo, A., Khatoon, J., Siddiqui, S., Zafar, S., Abbasi, F., Aijaz, S., Firdous, A., Khuwaja, A., Zulfiqar, B., Batool, S., Hashmi, H., Hussaini, S., Naqvi, Z., Tahir, S., Ibrahim, S., Khalil, S. E., Kuna, A., Saboni, M., Salman, M., Abubakar, M. S., Awad, M., Elbashir, M., Gaffar, N., Hussain, S., Caesarean section surgical techniques (CORONIS): A fractional, factorial, unmasked, randomised controlled trial, Journal of Obstetrics and Gynaecology Research, 41, 23-24, 2015	
El-Khayat, W., Elsharkawi, M., Hassan, A., A randomized controlled trial of uterine exteriorization versus in situ repair of the uterine incision during cesarean delivery, International journal of gynaecology and obstetrics, 127, 163â□□166, 2014	Compared extra-abdominal and in-situ repair of uterine incision (uterus was closed with absorbable continuous Vicryl 1 sutures in a continuous double layer)
El-Sokkary, M., Wahba, K., El-Shahawy, Y., Uterine salvage management for atonic postpartum hemorrhage using "modified lynch suture", BMC Pregnancy and Childbirth, 16, 251, 2016	Not relevant population or comparison (women who suffered from PPH during lower segment caesarean section and were not responding to uterotonics were operated upon by the modified technique or the classic B-lynch)
Enkin, M. W., Wilkinson, C., WITHDRAWN: Single versus two layer suturing for closing the uterine incision at Caesarean section, Cochrane database of systematic reviews (Online), CD000192, 2007	Withdrawn and replaced with more recent review; Dodd 2014
Enkin, M. W., Wilkinson, C., Single versus two layer suturing for closing the uterine incision at caesarean section, Cochrane Database of Systematic Reviews, CD000192, 2000	Withdrawn and replaced with more recent review; Dodd 2014
Enkin, M. W., Wilkinson, C. S., Single versus two layer suturing for closing the uterine incision at Caesarean section, Cochrane Database of Systematic Reviews, 2006	Withdrawn and replaced with more recent review; Dodd 2014

Study	Reason for Exclusion
Ezechi, O. C., Kalu, B. K., Njokanma, F. O., Nwokoro, C. A., Okeke, G. C., Uterine incision closure at caesarean section: a randomised comparative study of intraperitoneal closure and closure after temporary exteriorisation, West african journal of medicine, 24, 41â□□43, 2005	Compared exteriorization and in-situ uterine repair (two layer closure of uterine incision)
Farrell, B., The CORONIS trial: International study of caesarean section surgical techniques-a randomised non-regular fractional, factorial trial, Clinical Trials, 10, S50, 2013	Conference abstract
Ferrari, A. G., Frigerio, L. G., Candotti, G., Buscaglia, M., Petrone, M., Taglioretti, A., Calori, G., Can Joel-Cohen incision and single layer reconstruction reduce cesarean section morbidity?, International Journal of Gynaecology & Obstetrics, 72, 135-43, 2001	Compared classic C-section technique with "modified technique" (different incision, exteriorization, closure). No relevant outcomes reported
Franchi, M., Ghezzi, F., Balestreri, D., Beretta, P., Maymon, E., Miglierina, M., Bolis, P. F., A randomized clinical trial of two surgical techniques for cesarean section, American Journal of Perinatology, 15, 589-94, 1998	Compared Joel-Cohen incision with the parietal and pelvic peritoneum left open, and the Pfannenstiel incision with both peritoneal layers sutured (continuous single layer non-locking uterine closure in all)
Gaskin, I. M., Concerns about single-layer suturing of the uterus after cesarean surgery, Midwifery today with international midwife, 32-34, 2002	Oral presentation
Gezginc, Kazim, Yazici, Fatma, Koyuncu, Tuba, Results of hysterosalpingogram in women with previous B-Lynch suture, International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 115, 68-9, 2011	Short communication; case-series
Gutiérrez, J. G., Coló, J. A., Arreola, M. S., Comparative trial between traditional cesarean section and Misgav-Ladach technique, Ginecologia y Obstetricia de Mexico, 76, 75â□□80, 2008	Article in Spanish
Gyamfi, C., Juhasz, G., Gyamfi, P., Blumenfeld, Y., Stone, J. L., Single- versus double-layer uterine incision closure and uterine rupture, Journal of Maternal-Fetal & Neonatal Medicine, 19, 639-43, 2006	Non RCT (retrospective cohort/case-control)
Hamar, B. D., Saber, S. B., Cackovic, M., Magloire, L. K., Pettker, C. M., Abdel-Razeq, S. S., Rosenberg, V. A., Buhimschi, I. A., Buhimschi, C. S., Ultrasound evaluation of the uterine scar after cesarean delivery: a randomized controlled trial of one- and two-layer closure, Obstetrics and Gynecology, 110, 808â□□813, 2007	No relevant outcomes
Hamar, B. R., Saber, S. B., Cackovic, M., Magloire, L. K., Pettker, C. M., Abdel-Razeq, S. S., Ultrasound evaluation of uterine incision healing after cesarean delivery - a randomized controlled study of one- versus two-layer closure, American Journal of Obstetrics and Gynecology, 195, S57, 2006	Conference abstract
Hamid,R., Arulkumaran,S., Management of scarred uterus in subsequent pregnancies, Current Obstetrics and Gynaecology, 16, 168-173, 2006	Narrative review

Study	Reason for Exclusion
Hayakawa,H., Itakura,A., Mitsui,T., Okada,M., Suzuki,M., Tamakoshi,K., Kikkawa,F., Methods for myometrium closure and other factors impacting effects on cesarean section scars of the uterine segment detected by the ultrasonography, Acta Obstetricia et Gynecologica Scandinavica, 85, 429-434, 2006	No relevant outcomes (wedge defects one month post-partum)
Hegde, C. V., The never ending debate single-layer versus double-layer closure of the uterine incision at cesarean section, Journal of obstetrics and gynaecology of India, 64, 239-40, 2014	Narrative, short communication
Hofmeyr,J.G., Novikova,N., Mathai,M., Shah,A., Techniques for cesarean section, American Journal of Obstetrics and Gynecology, 201, 431-444, 2009	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion (examined complete methods/technique of C-section, not individual aspects).
Humphries, G., Suturing a cesarean wound, Midwifery today with international midwife, 22-3, 2001	Oral presentation
Jacobs-Jokhan, D., Hofmeyr, G., Extra-abdominal versus intra-abdominal repair of the uterine incision at caesarean section, Cochrane Database of Systematic Reviews, CD000085, 2004	Compared extra-abdominal and intra-abdominal repair of uterine incision
Jacobsâ□□Jokhan, D., Hofmeyr, G. J., Extraâ□□abdominal versus intraâ□□abdominal repair of the uterine incision at caesarean section, Cochrane Database of Systematic Reviews, 2004	Duplicate of 387390 (Cochrane SR, Jacobs-Jokhan 2004)
Jacobson, P., Improved uterine closure in classical cesarean section, Western journal of surgery, obstetrics, and gynecology, 59, 431-3, 1951	Narrative overview
Juszczak, E., Farrell, B., The CORONIS Trial: International study of caesarean section surgical techniques, Trials. Conference: Clinical Trials Methodology Conference, 12, 2011	Poster presentation
Kostu, B., Ercan, O., Ozer, A., Bakacak, M., Ozdemir, O., Avci, F., A comparison of two techniques of uterine closure in caesarean section, Journal of Maternal-Fetal and Neonatal Medicine, 29, 1573-1576, 2016	No relevant intervention (compared direction the surgeon pulled suture during closure)
Kumar, S., Single versus double layer closure of low transverse uterine incision at cesarean section, Journal of obstetrics and gynaecology of India, 55, 231â□□236, 2005	Duplicate (Sood et al 2005)
Lal, K., Tsomo, P., Comparative study of single layer and conventional closure of uterine incision in cesarean section, International journal of gynaecology and obstetrics, 27, 349â□□352, 1988	No relevant outcomes (scar deformities visualised by ultrasound)
Landon,M.B., Vaginal birth after cesarean delivery, Clinics in Perinatology, 35, 491-504, 2008	Narrative review
Matsubara, Shigeki, Yano, Hitoshi, Ohkuchi, Akihide, Kuwata, Tomoyuki, Usui, Rie, Suzuki, Mitsuaki, Uterine compression sutures for postpartum hemorrhage: an overview, Acta Obstetricia et Gynecologica Scandinavica, 92, 378-85, 2013	Narrative review regarding brace sutures

Study	Reason for Exclusion
Mazhar, S. B., Mahsood, S., Single versus double layer uterine closure during cesarean section: a randomised trial, 30th british congress of obstetrics and gynaecology; 2004 july 7-9; glasgow, UK, 63, 2004	Conference abstract
Moreira, P., Moreau, J. C., Faye, M. E., Ka, S., Kane Gueye, S. M., Faye, E. O., Comparison of two cesarean techniques: classic versus misgav ladach cesarean]. [French, Journal de gynecologie, obstetrique ET biologie de la reproduction, 31, 572â□□576, 2002	Article in French
Mukhopadhyay, B., Single layer - vs - two layer closure of uterus during caesarean section - an institutional experience, XVI FIGO world congress of obstetrics & gynecology (book 3); 2000 sept 3-8; washington dc, USA, 43, 2000	Conference abstract
Najam, A., Sial, S., Basharat, A., Usmani, A., Jamil, M., Comparison of perioperative complications between modified Misgav Ladach and Pfannenstiel technique of caesarean section: a randomised controlled trial at a tertiary care hospital, Pakistan, BJOG: an international journal of obstetrics and gynaecology. Conference: 2018 world congress of the royal college of obstretriscians and gynaecologists, RCOG 2018. Singapore, 125, 67, 2018	Conference abstract
Naz Masood, S., Caesarean section surgical techniques (CORONIS): a fractional, factorial, unmasked, randomised controlled trial, Journal of maternal-fetal and neonatal medicine., 27, 16, 2014	Conference abstract
Nct,, Closure of Uterine Incision by Single or Double Layer Technique, Https://clinicaltrials.gov/show/nct02144805, 2014	Clinical trial record (completed - no known publications)
Nct,, Impact of Double-layer Versus Single-layer Uterine Closure Suture in Cesarean Section on the Development of Postoperative Uterine Scar Deficiency, Https://clinicaltrials.gov/show/nct03039803, 2016	Clinical trial record (ongoing trial, actively recruiting)
Nct,, Seprafilm® for Prevention of Adhesions at Repeat Cesarean, Https://clinicaltrials.gov/show/nct00697606, 2008	Clinical trial record (terminated due to lack of funding)
Nct,, Study to Compare Suture Material in Closure of Uterine Incision in Cesarian Section, Https://clinicaltrials.gov/show/nct02517710, 2014	Clinical trial record (completed - no known publications)
Nct,, Trial Comparing Barbed and Non-barbed Suture for Uterine Incision Closure at Cesarean Section, Https://clinicaltrials.gov/show/nct02962011, 2016	Clinical trial register (completed - no known publications)
Nct,, Long Term Comparison of Two Different Techniques of Uterine Cesarean Incision Closure, Https://clinicaltrials.gov/show/nct01289262, 2011	Clinical trial record (completed - no known publications)
Nct,, Plication of the Rectus Abdominis in Two Planes and in One Continuous Suture Plan, Https://clinicaltrials.gov/show/nct02674035, 2015	Clinical trial record (completed - no known publications)
Nct,, Rectus Muscle Re-approximation at Cesarean Delivery, Https://clinicaltrials.gov/show/nct03296969, 2017	Clinical trial record (ongoing trial, not yet recruiting)

Study	Reason for Exclusion
Nct,, Suture of UTerus and Ultrasound Repair Evaluation, Https://clinicaltrials.gov/show/nct01860859, 2013	Clinical trial record (completed -no known publications)
Nct,, NIche Development With Closure of Cesarean Uterotomy by Modified or Conventional Two-layer Technique, Https://clinicaltrials.gov/show/nct02410395, 2015	Clinical trial record (ongoing trial, no longer recruiting)
Nct,, Impact of Uterine Closure Techniques on the Cesarean Scar Thickness After Repeated Cesarean Section, Https://clinicaltrials.gov/show/nct03644433, 2018	Clinical trial record (ongoing trial, actively recruiting)
O'Leary, J. L., O'Leary, J. A., Uterine artery ligation for control of postcesarean section hemorrhage, Obstetrics and Gynecology, 43, 849-53, 1974	Ligation of uterine artery to control post c-section haemorrhage
Olyaeemanesh, Alireza, Bavandpour, Elahe, Mobinizadeh, Mohammadreza, Ashrafinia, Mansoor, Bavandpour, Maryam, Nouhi, Mojtaba, Comparison of the Joel-Cohen-based technique and the transverse Pfannenstiel for caesarean section for safety and effectiveness: A systematic review and meta-analysis, Medical journal of the Islamic Republic of Iran, 31, 54, 2017	No relevant outcomes. SR compared vertical Joel-Cohen-based and transverse Pfannenstiel incision (focus on incision)
Paglia, M. J., Parham, T., Sinclair, T., Murtha, A. P., Dermal closure time in cesarean delivery Pfannenstiel incision using a barbed suture, Obstetrics and Gynecology, 105, 32S, 2005	Conference abstract
Paglia, M., Sinclair, T., Murtha, A., Evaluation of a novel technique for cesarean section closure via Pfannenstiel incision using a barbed suture, American Journal of Obstetrics and Gynecology, 191, S155, 2004	Conference abstract
Park, I. Y., Kim, M. R., Lee, H. N., Gen, Y., Kim, M. J., Risk factors for Korean women to develop an isthmocele after a cesarean section, BMC Pregnancy and Childbirth, 18, 162, 2018	Non RCT (case-control study of women who underwent C-section and had an isthmocele)
Peleg, D., Ahmad, R. S., Warsof, S. L., Marcus-Braun, N., Sciaky-Tamir, Y., Ben Shachar, I., A randomized clinical trial of knotless barbed suture vs conventional suture for closure of the uterine incision at cesarean delivery, American Journal of Obstetrics and Gynecology, 218, 343.e1â□□343.e7, 2018	Compared knotless barbed and conventional sutures (in all cases the uterine incision was closed in 2 layers)
Peleg, D., Ahmad, R. S., Warsof, S. L., Marcus-Braun, N., Sciaky-Tamir, Y., Shachar, I. B., Knotless barbed suture closure of the uterine incision at cesarean-a randomized controlled trial, American journal of obstetrics and gynecology. Conference: 38th annual meeting of the society for maternal-fetal medicine: the pregnancy meeting. United states, 218, S25, 2018	Conference abstract
Roberge, S., Bujold, E., Single versus double layer closure and risk of uterine rupture: Systematic review and meta-analysis, American Journal of Obstetrics and Gynecology, 201, S198, 2009	Conference abstract
Roberge, S., Chaillet, N., Boutin, A., Moore, L., Jastrow, N., Brassard, N., Gauthier, R. J., Hudic, I.,	Systematic review: analyses cannot be used in entirety, included studies (cohort

Study	Reason for Exclusion
Shipp, T. D., Weimar, C. H. E., Fatusic, Z., Demers, S., Bujold, E., Single- versus double-layer closure of the hysterotomy incision during cesarean delivery and risk of uterine rupture, International Journal of Gynecology and Obstetrics, 115, 5-10, 2011	and case-control trials, and 1 RCT) checked for inclusion
Roberge, S., Demers, S., Berghella, V., Chaillet, N., Moore, L., Bujold, E., Impact of single- vs double-layer closure on adverse outcomes and uterine scar defect: A systematic review and metaanalysis, American Journal of Obstetrics and Gynecology, 211, 453-460, 2014	Systematic review: only 2 RCTs relevant, assessed for inclusion
Roberge, S., Demers, S., Girard, M., Vikhareva, O., Markey, S., Chaillet, N., Moore, L., Paris, G., Bujold, E., Impact of uterine closure on residual myometrial thickness after cesarean: a randomized controlled trial, American Journal of Obstetrics and Gynecology, 214, 507.e1â□□507.e6, 2016	No relevant outcomes
Rozenberg, P., Re: Risk of Cesarean scar defect following single- vs double-layer uterine closure: systematic review and meta-analysis of randomized controlled trials. A. Di Spiezio Sardo, G. Saccone, R. McCurdy, E. Bujold, G. Bifulco and V. Berghella. Ultrasound Obstet Gynecol 2017; 50: 578-583, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 50, 557-558, 2017	Short communication/Letter to the Editor
Sahin, N., Genc, M., Turan, G. A., Kasap, E., Guclu, S., A comparison of 2 cesarean section methods, modified Misgav-Ladach and Pfannenstiel-Kerr: a randomized controlled study, Advances in clinical and experimental medicine, 27, 357â□□361, 2018	Compared Pfannestiel-Kerr and modified Misgav-Ladach method (both used single layer continuous sutures for uterine closure)
Scioscia, M., Iannone, P., Morano, D., Pontrelli, G., Greco, P., Comment on "Longitudinal transvaginal ultrasound evaluation of cesarean scar niche incidence and depth in the first two years after single- or double-layer uterotomy closure: a randomized controlled trial", Acta Obstetricia et Gynecologica Scandinavica, (no pagination), 2018	Letter to the Editor
Sevket, O., Ates, S., Molla, T., Ozkal, F., Uysal, O., Dansuk, R., Hydrosonographic assessment of the effects of 2 different suturing techniques on healing of the uterine scar after cesarean delivery, International journal of gynaecology and obstetrics, 125, 219â□□222, 2014	No relevant outcomes
Shan, D., Mathew, B. S., Wu, Y., Hu, Y., Qiu, P., New lower segment repairing surgery to control bleeding in repeated caesarean section, a randomized controlled trail, International Journal of Clinical and Experimental Medicine, 11, 3932â□□3939, 2018	No relevant outcomes. Compared new suture method for repeat c-section and standard c-section technique
Shi, Z., Ma, L., Yang, Y., Wang, H., Schreiber, A., Li, X., Tai, S., Zhao, X., Teng, J., Zhang, L., Lu, W., An, Y., Alla, N. R., Cui, T., Adhesion formation after previous caesarean section-a meta-analysis and systematic review, BJOG: An International Journal of Obstetrics & Gynaecology, 118, 410-22, 2011	Systematic review, based on retrospective observational studies (not RCTs); comparison of 3 caesarean sections procedures

Study	Reason for Exclusion
Shmakov, R. G., Vinitskiy, A. A., Chuprinin, V. D., Yarotskaya, E. L., Sukhikh, G. T., Alternative approaches to surgical hemostasis in patients with morbidly adherent placenta undergoing fertility-sparing surgery, Journal of Maternal-Fetal and Neonatal Medicine, 1-7, 2018	Ligation techniques of uterine artery/ internal iliac arteries/ common iliac artery
Shrestha, Pravin, Shrestha, Smita, Gyawali, Merina, Ultrasound Evaluation of Uterine Scar in Primary Caesarean Section: A Study of Single versus Double Layer Uterine Closure, American Journal of Public Health Research, 3, 178-181, 2015	No relevant outcomes (scar thickness by ultrasound)
Sivasuriya, M., Sriskanthan, R., Sriskandarajah, M. N., A new technique for closure of the uterus at Caesarean section, Australian and New Zealand Journal of Obstetrics and Gynaecology, 28, 96-98, 1988	Narrative review, description of single layer technique
Stark, M., Evidence-based facts concerning caesarean section, Journal of Maternal-Fetal and Neonatal Medicine, 23, 72, 2010	Conference abstract
Stegwee, S. I., Jordans, I. P. M., van der Voet, L. F., van de Ven, P. M., Ket, J. C. F., Lambalk, C. B., de Groot, C. J. M., Hehenkamp, W. J. K., Huirne, J. A. F., Uterine caesarean closure techniques affect ultrasound findings and maternal outcomes: a systematic review and meta-analysis, BJOG: An International Journal of Obstetrics and Gynaecology, 125, 1097-1108, 2018	Systematic review: analyses cannot be used in entirety, included studies checked for inclusion (no relevant outcomes).
Studzinski Z. , The Misgav-Ladach method for cesarean section compared to the Pfannenstiel technique [Ciecie cesarskie sposobem Misgavâ□“Ladach w porownaniu z technika Pfannenstiela]., Ginekologia Polska, 73, 672-6, 2002	Article in Polish
Surico, D., Amadori, R., Vigone, A., D'Agostino, C., Dessole, M., Surico, N., Successful delivery after surgical repair of uterine rupture at 15 weeks of gestation: case report and brief review, European Journal of Obstetrics Gynecology and Reproductive Biology, 204, 5-8, 2016	Case-series
Tekiner, N. B., Cetin, B. A., Turkgeldi, L. S., Yilmaz, G., Polat, I., Gedikbasi, A., Evaluation of cesarean scar after single- and double-layer hysterotomy closure: a prospective cross-sectional study, Archives of Gynecology and Obstetrics, 297, 1137-1143, 2018	No relevant outcomes (scar defects)
Tucker, J. M., Hauth, J. C., Hodgkins, P., Owen, J., Winkler, C. L., Trial of labor after a one- or two-layer closure of a low transverse uterine incision, American Journal of Obstetrics and Gynecology, 168, 545-546, 1993	Non RCT (retrospective cohort)
Turan, C., Buyukbayrak, E. E., Onan Yilmaz, A., Karageyim Karsidag, Y., Pirimoglu, M., Purse-string double-layer closure: a novel technique for repairing the uterine incision during cesarean section, Journal of Obstetrics and Gynaecology Research, 41, 565â□□574, 2015	Compares new form of double layer closure to classic double layer closure (intervention should be single layer closure)

Study	Reason for Exclusion
Turan, G. A., Gur, E. B., Tatar, S., Gokduman, A., Guclu, S., Uterine closure with unlocked suture in cesarean section: safety and quality, Pakistan journal of medical sciences, 30, 2014	Compared locked and unlocked sutures (all single layer closure of uterus)
Unterscheider, J., Kent, E., Murray, A., Flood, K., Breathnach, F., Malone, F. D., Single versus double layer closure at caesarean delivery-an ongoing debate, Irish Journal of Medical Science, 180, S157, 2011	Conference abstract
Vachon-Marceau, C., Demers, S., Bujold, E., Roberge, S., Gauthier, R. J., Pasquier, J. C., Girard, M., Chaillet, N., Boulvain, M., Jastrow, N., Single versus double-layer uterine closure at cesarean: impact on lower uterine segment thickness at next pregnancy, American journal of obstetrics and gynecology., 05, 2017	Non RCT (secondary analysis of prospective cohort study); no relevant outcomes (lower uterine segment thickness)
van Dongen, P. W., Nijhuis, J. G., Jongsma, H. W., Reduced blood loss during caesarean section due to a controlled stapling technique, European Journal of Obstetrics, Gynecology, & Reproductive BiologyEur J Obstet Gynecol Reprod Biol, 32, 95-102, 1989	Intervention: use of staples to "seal blood vessels and all three uterine layers" before uterine incision
Wahab,M.A., Karantzis,P., Eccersley,P.S., Russell,I.F., Thompson,J.W., Lindow,S.W., A randomised, controlled study of uterine exteriorisation and repair at caesarean section, British Journal of Obstetrics and Gynaecology, 106, 913-916, 1999	Compared exteriorization and in-situ uterine repair (double layer closure of uterine incision in all cases)
Wallin, G., Fall, O., Modified joel-cohen technique for caesarean section. A prospective randomised study, Acta Obstetricia et Gynecologica Scandinavica, 76 Suppl, 24, 1997	Abstract only/ short communication
Wallin, G., Fall, O., Modified Joel-Cohen technique for caesarean delivery, British Journal of Obstetrics and Gynaecology, 106, 221â□□226, 1999	Compared Joel-Cohen technique and Pfannenstiel technique (both used interrupted sutures in one layer)
Walsh,C.A., Evidence-based cesarean technique, Current Opinion in Obstetrics and Gynecology, 22, 110-115, 2010	Narrative review. Relevant references checked and assessed for inclusion
Waniorek, A., Hysterography after cesarean section for evaluation of suturing technic, Obstetrics and Gynecology, 29, 192-199, 1967	No relevant outcomes (scar deformity)
Wilkinson, C., Enkin, M. W., Uterine exteriorization versus intraperitoneal repair at caesarean section, Cochrane Database of Systematic Reviews, CD000085, 2000	Compared exteriorization and in-situ repair of uterine incision
Wojdemann, K., Bennich, G., Long term follow-up from a randomized trial comparing one- and two-layer closure techniques in caesarean section (cs), Ultrasound in obstetrics & gynecology, 36, 141, 2010	Conference abstract
Xu, Dabao, Cheng, Chunxia, Xue, Min, Wan, Yajun, Retained permanent uterine suture after cesarean, International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 100, 78-9, 2008	Short communication
Yazicioglu, F., Gokdogan, A., Kelekci, S., Aygun, M., Savan, K., Incomplete healing of the uterine incision after caesarean section: Is it preventable?, European	Compared suturing techniques: full thickness including the endometrial (decidual) layer, and split thickness

Study	Reason for Exclusion
Journal of Obstetrics Gynecology and Reproductive Biology, 124, 32-36, 2006	excluding the endometrial layer (both used single layer continuous locking sutures)
Ying, Hao, Duan, Tao, Bao, Yi-Rong, Song, Yue-Hua, Wang, De-Fen, Transverse annular compression sutures in the lower uterine segment to control postpartum hemorrhage at cesarean delivery for complete placenta previa, International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics, 108, 247-8, 2010	Short communication
Zaphiratos, Valerie, George, Ronald B., Boyd, J. Colin, Habib, Ashraf S., Uterine exteriorization compared with in situ repair for Cesarean delivery: a systematic review and meta-analysis, Canadian journal of anaesthesia = Journal canadien d'anesthesie, 62, 1209-20, 2015	Systematic review compared exteriorization and in-situ uterine repair
Zayed, M. A., Fouda, U. M., Elsetohy, K. A., Zayed, S. M., Hashem, A. T., Youssef, M. A., Barbed sutures versus conventional sutures for uterine closure at cesarean section; a randomized controlled trial, Journal of Maternal-Fetal and Neonatal Medicine, 1-8, 2017	Compared barbed and conventional sutures in uterine closure (both used two-layer uterine closure)

Economic studies

No economic evidence was identified for this review.

Appendix L – Research recommendations

Research recommendations for review question: What is the efficacy of single layer closure of the uterus as compared with double layer closure at caesarean birth?

No research recommendations were made for this review question.