National Institute for Health and Care Excellence

Draft for Consultation

Twin and Triplet Pregnancy

[D] Evidence review for timing of birth

NICE guideline tbc

Evidence reviews

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Draft for Consultation

These evidence reviews were developed by the National Guideline Alliance hosted by the Royal College of Obstetricians and Gynaecologists

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Timing of birth

Review question

What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Introduction

Twin and triplet pregnancies are at high risk of stillbirth compared with singleton pregnancies. The aim of this review was to determine the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies. These risks were assessed according to the chorionicity and the amnionicity of the pregnancy. The information is then used to draw conclusions about the most appropriate (i.e. least risky) week of pregnancy for women to give birth to twins or triplets taking into account the chorionicity and amnionicity.

This is an update of a question covering timing of birth in the 2011 version of the guideline, but protocols but the review questions and protocols differed so a full new review was conducted.

Summary of the protocol

See Table 1 for a summary of the population, exposure, and outcome characteristics of this review.

Table 1: Summary of the protocol

Population	For twin pregnancies: • Monochorionic diamniotic • Monochorionic monoamniotic • Dichorionic diamniotic For triplet pregnancies: • Trichorionic triamniotic • Dichorionic triamniotic • Monochorionic triamniotic • Dichorionic, diamniotic (containing a monochorionic twins set) and • Monochorionic monoamniotic (contain a monoamniotic triplet set) Setting: Secondary or tertiary care centres.
Exposure	Gestational age at death (in utero), or when clinician noted death (in utero), or gestational age at birth (for neonatal outcomes) cross-classified by chorionicity and amnionicity Note: Incidence of stillbirth, perinatal/neonatal mortality and/or neonatal morbidities

Outcomes	**Critical**
	• Stillbirth
	• Perinatal/neonatal mortality
	Important:
	• Neonatal morbidities including:
	  ○ Respiratory distress syndrome,
	  ○ Need for respiratory support (respiratory ventilation),
	  ○ Septicaemia or meningitis,
	  ○ Bronchopulmonary dysplasia,
	  ○ Hypoxic ischaemic encephalopathy,

	○ Necrotising enterocolitis, ○ Intraventricular haemorrhage, ○ Cystic periventricular leukomalacia, ○ Retinopathy of prematurity

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 and for a full description of the methods see supplementary document C.

Declaration of interests were recorded according to NICE's 2014 conflicts of interest policy from March 2017 until March 2018. From April 2018 onwards they 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 Interests Register).

Clinical evidence

Included studies

One prospective cohort study (Breathnach 2012) and 9 retrospective cohort studies (Baxi 2010; Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016; Wood 2014) were included in this evidence review. The quality of the evidence was based on the risk of bias only.

Evidence was identified for monochorionic diamniotic (MCDA), monochorionic monoamniotic (MCMA) and dichorionic diamniotic (DCDA) twin pregnancies. Evidence was available for critical outcomes including stillbirth and perinatal or neonatal mortality, and for important outcomes including respiratory distress syndrome, need for respiratory support (respiratory ventilation), sepsis, necrotising enterocolitis (NEC) and intraventricular haemorrhage (IVH).

No evidence was available for important outcomes such as meningitis, bronchopulmonary dysplasia (BPD), hypoxic ischaemic encephalopathy, cystic periventricular leukomalacia and retinopathy of prematurity.

One retrospective cohort study reporting on over 17,000 twin births (8,862 twin pregnancies) (Wood 2014) was included as evidence but was not included in the pooled summary statistics as the total for MCMA, MCDA, DCDA, and unknown chorionicity, could not be determined (denominator was not available as an absolute value). Data were available for stillbirth by chorionicity (numerator) as number per 1,000 fetuses at risk). This is due to identification of chorionicity taking place only in the case of stillbirth, at birth. This study also reported gestational age (exposure) as age at intrauterine death (IUFD) when the information was available, otherwise as gestational age when the clinician noted fetal death, or lastly as gestational age at birth when intrauterine/fetal death was confirmed (in line with the studies included here).

One prospective cohort study (Breathnach 2012) was also included as evidence but excluded from the pooled summary statistics, as data were not reported separately for stillbirth and neonatal mortality (death within 7 days of live birth). For MCDA twins, the study reported data for perinatal mortality (sum of stillbirth and neonatal mortality) per number of ongoing pregnancies, and has been presented separately to the data for stillbirth and neonatal mortality. Data for DCDA twins was reported as zero cases/events of perinatal mortality at weekly gestational age, but number of ongoing pregnancies was not reported, and so could not be presented.

Where studies described twin pregnancies as complicated or uncomplicated, this was noted, and pooled separately where possible.

There was no evidence identified for triplet pregnancies.

The clinical studies included in this evidence review are summarised in Table 2.

See also the literature search strategy in appendix B, study selection flow chart in appendix C, study evidence tables in appendix D, and graphical representation of the pooled data in appendix M.

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in appendix K.

Summary of clinical studies included in the evidence review

The included studies are summarised in Table 2.

Table 2: Summary of included studies for twin pregnancy

Study	Population	Outcomes (n/N unless otherwise stated)	Comments
Baxi 2010 Retrospective cohort USA	N=25 MCMA pregnancies (only N=8 pregnancies with relevant data)	• Stillbirth (IUFD) • Neonatal death • Necrotising enterocolitis	Complicated pregnancies[a]
Berezowsky 2016 Retrospective cohort Israel	N=166 MCDA pregnancies	• Stillbirth (IUFD) • Respiratory distress syndrome • Oxygen requirement • Ventilation • Necrotising enterocolitis • Intraventricular haemorrhage	Uncomplicated pregnancies[a]
Breathnach 2012 Prospective cohort Ireland	N=200 MCDA and N=801 DCDA pregnancies	• Perinatal mortality	Uncomplicated pregnancies[a]
Burgess 2014 Retrospective cohort USA	N=167 MCDA and N=601 DCDA pregnancies	• Stillbirth (IUFD) • Neonatal death • Sepsis or sepsis work up • Necrotising enterocolitis • Intraventricular haemorrhage	Uncomplicated pregnancies[a]
Hack 2011 Retrospective cohort The Netherlands	N=465 MCDA pregnancies	• Stillbirth (IUFD) • Perinatal mortality • Early neonatal death • Late neonatal death	Majority of pregnancies uncomplicated (13% intrauterine growth restriction)[a]

Study	Population	Outcomes (n/N unless otherwise stated)	Comments
Lee 2010 Retrospective cohort South Korea	N=171 MCDA and N=526 DCDA pregnancies	• Fetal death in utero (IUFD) • Perinatal mortality • Neonatal morality • Respiratory distress syndrome • Mechanical ventilator support	Uncomplicated pregnancies[a]
Masheer 2017 Retrospective cohort Pakistan	N=84 MCDA and N=310 DCDA pregnancies	• Stillbirth (IUFD) – risk as % • Perinatal death – risk as % • Neonatal sepsis • Necrotising enterocolitis	Rate of complicated pregnancies not clearly described 'approximated one-third of women giving birth at this hospital are high-risk'.
Morikawa 2012 Retrospective cohort Japan	N=3,241 MCDA and N=6,581 DCDA pregnancies	• Stillbirth • Early neonatal death	Rate of complicated pregnancies not clearly described.
Sung 2016 Retrospective cohort South Korea	N=302 MCDA and N=896 DCDA	• Fetal death (IUFD) • Neonatal death • Perinatal death	Uncomplicated pregnancies[a]
Wood 2014 Retrospective cohort Canada	N=17,724 twin births (8,862 twin sets); MCMA, MCDA and DCDA	• Stillbirth (IUFD) – reported as risk per 1000	Reported gestational age at death (in utero), or when clinician noted the death, or lastly GA at birth if nothing else was available

DCDA: dichorionic diamniotic; IUFD: intrauterine fetal death; MCDA: monochorionic diamniotic; MCMA: monochorionic monoamniotic; N: number of pregnancies; n: number of events
a complicated/uncomplicated pregnancies as described by study (see appendix D)

See appendix D for the full evidence tables.

Quality assessment of clinical studies included in the evidence review

The evidence presented here originates from observational studies and the quality assessment for these studies was performed based on risk of bias using an adapted version of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn 2015) for incidence studies.

The evidence for DCDA twin pregnancy is presented in Table 3 to Table 9, for MCDA twin pregnancy in Table 10 to Table 17, and for MCMA twin pregnancy in Table 18 to Table 20. These tables present data for the following outcomes by number of weeks' gestation:

- incidence of stillbirths per number of ongoing pregnancies (n/N, median and interquartile range, crude risk per 1000 ongoing pregnancies).

- incidence of neonatal mortality per number of neonates born (n/N, median and IQR, crude risk per 1000 neonates born)
- incidence of neonatal morbidities per number of neonates born (n/N, median and IQR, crude risk per 1000 neonates born) (summary data presented by morbidity).

Where possible data reported in the identified studies were pooled; i.e. different studies contributed data at each time point. These summary data are also presented graphically in appendix M.

In addition, data from two studies (Wood 2014 and Breathnach 2012) are also presented in the tables by number of weeks' gestation. In Wood (2014) data were available for stillbirth by chorionicity (numerator) as a number per 1000 fetuses at risk. Due to these differences these studies were not included in the pooled summary estimates.

Table 3: Summary clinical evidence profile for stillbirth in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No of ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
Studies in pooled analysis						
1 (Morikawa 2012)	22	3291 (0)	4 (0)	4/6581	0.61	Low
1 (Morikawa 2012)	23	6569 (0)	8 (0)	8/6569	1.22	Low
1 (Morikawa 2012)	24	6541 (0)	0 (0)	0/6541	0.00	Low
2 (Masheer 2017; Morikawa 2012)	25	3408 (3098)	3 (2)	7/6815	1.01	Low
2 (Masheer 2017; Morikawa 2012)	26	3389 (3079)	2 (1)	4/6777	0.60	Low
2 (Masheer 2017; Morikawa 2012)	27	3368 (3064)	4 (1)	8/6735	1.17	Low
2 (Masheer 2017; Morikawa 2012)	28	3337 (3036)	4 (1)	8/6673	1.17	Low

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No of ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
2 (Masheer 2017; Morikawa 2012)	29	3304 (3005)	5 (0)	10/6608	1.53	Low
1 (Morikawa 2012)	30	6215 (0)	6 (0)	6/6215	0.97	Low
2 (Masheer 2017; Morikawa 2012)	31	3201 (2915)	4 (0)	8/6402	1.25	Low
2 (Masheer 2017; Morikawa 2012)	32	3134 (2854)	4 (1)	8/6268	1.29	Low
2 (Masheer 2017; Morikawa 2012)	33	3029 (2764)	3 (1)	5/6058	0.84	Low
4 (Burgess 2014; Masheer 2017; Morikawa 2012; Sung 2016)	34	427 (485)	1 (2)	6/1752	3.43	Low
5 (Burgess 2014; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	35	526 (291)	1 (1)	9/7049	1.28	Moderate[c]
5 (Burgess 2014; Lee 2016; Masheer 2017; Morikawa	36	486 (305)	0 (0)	10/6608	1.53	Moderate[c]

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No of ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
2012; Sung 2016)						
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016)	37	362 (705)	2 (2)	11/3751	2.93	Moderate[c]
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016)	38	97 (160)	0 (1)	5/965	5.18	Moderate[c]
1 (Morikawa 2012)	39	149 (0)	2 (0)	2/149	13.42	Low
1 (Morikawa 2012)	40	37 (0)	1 (0)	1/37	27.03	Low
1 (Morikawa 2012)	41	2 (0)	0 (0)	0/2	0.00	Low
Studies not included in pooled analysis						
1 (Wood 2014)	23	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	24	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	25	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	26	NR	NR	NR	6/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	27	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	28	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	29	NR	NR	NR	2/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	30	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood	31	NR	NR	NR	2/1000	Moderate[b]

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No of ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
2014)					fetuses[a]	
1 (Wood 2014)	32	NR	NR	NR	5/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	33	NR	NR	NR	6/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	34	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	35	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	36	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	37	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	38	NR	NR	NR	7/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	39	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a study presents data as risk per 1000 ongoing pregnancies, but does not report raw data (ongoing pregnancy per week); total n=17,724 twin births (8,862 twin sets)
b exposure was measured using weeks' gestation at death (in utero), or when clinician noted death (in utero), or weeks' gestation at birth; study does not report number of ongoing pregnancies by weeks' gestation
c (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 4: Summary clinical evidence profile for neonatal mortality in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No neonatal mortalities/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Morikawa 2012)	22	24 (0)	9 (0)	9/24	375.00	Low
1 (Morikawa 2012)	23	56 (0)	14 (0)	14/156	250.00	Low
1 (Morikawa 2012)	24	72 (0)	8 (0)	8/172	111.11	Low
1 (Morikawa 2012)	25	76 (0)	4 (0)	4/76	52.63	Low

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No neonatal mortalities/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Morikawa 2012)	26	72 (0)	4 (0)	4/72	55.56	Low
1 (Morikawa 2012)	27	118 (0)	2 (0)	2/118	16.95	Low
1 (Morikawa 2012)	28	126 (0)	4 (0)	4/126	31.75	Low
1 (Morikawa 2012)	29	188 (0)	5 (0)	5/188	26.60	Low
1 (Morikawa 2012)	30	198 (0)	2 (0)	2/198	10.10	Low
1 (Morikawa 2012)	31	256 (0)	1 (0)	1/256	3.91	Low
1 (Morikawa 2012)	32	390 (0)	2 (0)	2/390	5.13	Low
1 (Morikawa 2012)	33	588 (0)	1 (0)	1/588	1.70	Low
3 (Burgess 2014; Morikawa 2012; Sung 2016)	34	440 (357)	1 (2)	7/1610	4.35	Low
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016	35	252 (376)	1 (2)	5/2082	2.4	Moderate[a]
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016)	36	298 (1373)	1 (4)	9/3814	2.36	Moderate[a]
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016)	37	555 (1081)	0 (1)	2/5572	0.36	Moderate[a]

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No neonatal mortalities/No neonates born	Crude risk per 1000 neonates born	RoB
4 (Burgess 2014; Lee 2016; Morikawa 2012; Sung 2016)	38	155 (245)	0 (0)	1/1534	0.65	Moderate[a]
1 (Morikawa 2012)	39	224 (0)	1 (0)	1/224	4.46	Low
1 (Morikawa 2012)	40	70 (0)	1 (0)	1/70	14.29	Low
1 (Morikawa 2012)	41	4 (0)	0 (0)	0/4	0.00	Low

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 5: Summary clinical evidence profile for respiratory distress syndrome in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: RDS median (IQR)	Neonatal morbidities: RDS /No neonates born	Crude risk per 1000 neonates born	RoB
1 (Burgess 2014)	34	440 (0)	71 (0)	71/440	161	Low
2 (Burgess 2014; Lee 2016)	35	173 (93)	26 (21)	52/346	150.29	Moderate[a]
2 (Burgess 2014; Lee 2016)	36	288 (52)	19 (18)	38/576	65.97	Moderate[a]
2 (Burgess 2014; Lee 2016)	37	383 (101)	11 (11)	21/766	27.42	Moderate[a]
2 (Burgess 2014; Lee 2016)	38	140 (14)	6 (6)	11/280	39.29	Moderate[a]

GA: gestational age; IQR: interquartile range; RDS: respiratory distress syndrome; RoB: risk of bias
a (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 6: Summary clinical evidence profile for mechanical ventilator support in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonates ventilator support median (IQR)	Neonatal morbidities: Ventilator support/ No of neonates born	Crude risk per 1000 neonates born	RoB
1 (Lee 2016)	35	80 (0)	5 (0)	5/80	62.50	Moderate[a]
1 (Lee 2016)	36	340 (0)	4 (0)	4/340	11.76	Moderate[a]
1 (Lee 2016)	37	484 (0)	2 (0)	2/484	4.13	Moderate[a]
1 (Lee 2016)	38	126 (0)	0 (0)	0/126	0.00	Moderate[a]

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 7: Summary clinical evidence profile for sepsis in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: Sepsis median (IQR)	Neonatal morbidities: Sepsis / No of neonates born	Crude risk per 1000 neonates born	RoB
1 (Masheer 2017)	25	0 (0)	0 (0)	0/0	0.00	Low
1 (Masheer 2017)	26	12 (0)	3 (0)	3/12	250.00	Low
1 (Masheer 2017)	27	6 (0)	2 (0)	2/6	333.33	Low
1 (Masheer 2017)	28	4 (0)	2 (0)	2/4	500.00	Low
1 (Masheer 2017)	29	12 (0)	4 (0)	4/12	333.33	Low
1 (Masheer 2017)	31	12 (0)	0 (0)	0/12	0.00	Low
1 (Masheer 2017)	32	30 (0)	0 (0)	0/30	0.00	Low
1 (Masheer 2017)	33	26 (0)	1 (0)	1/26	38.46	Low

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: Sepsis median (IQR)	Neonatal morbiditie s: Sepsis / No of neonates born	Crude risk per 1000 neonates born	RoB
2 (Burgess 2014; Masheer 2017)	34	250 (190)	62 (61)	124/500	248.00	Low
2 (Burgess 2014; Masheer 2017)	35	169 (97)	36 (35)	72/338	213.02	Low
2 (Burgess 2014; Masheer 2017)	36	172 (64)	19 (19)	38/334	110.47	Low
1 (Masheer 2017)	37	282 (0)	19 (0)	19/282	67.38	Low
1 (Masheer 2017)	38	154 (0)	12 (0)	12/154	77.92	Low

GA: gestational age; IQR: interquartile range; RoB: risk of bias

Table 8: Summary clinical evidence profile for necrotising enterocolitis in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	No of neonatal morbidities: NEC Median (IQR)	No of neonatal morbidities: NEC /No of neonates born	Crude risk per 1000 neonates born	RoB
1 (Masheer 2017)	25	0 (0)	0 (0)	0/0	0.00	Low
1 (Masheer 2017)	26	12 (0)	1 (0)	1/12	83.33	Low
1 (Masheer 2017)	27	6 (0)	1 (0)	1/6	166.67	Low
1 (Masheer 2017)	28	4 (0)	0 (0)	0/4	0.00	Low
1 (Masheer 2017)	29	12 (0)	1 (0)	1/12	83.33	Low
1 (Masheer 2017)	31	12 (0)	0 (0)	0/12	0.00	Low
1 (Masheer 2017)	32	30 (0)	0 (0)	0/30	0.00	Low
1	33	26 (0)	1 (0)	1/26	38.46	Low

No of studies	GA	Neonates born median (IQR)	No of neonatal morbidities: NEC Median (IQR)	No of neonatal morbidities: NEC /No of neonates born	Crude risk per 1000 neonates born	RoB
(Masheer 2017)						
2 (Burgess 2014; Masheer 2017)	34	250 (190)	1 (1)	2/500	4.00	Low
2 (Burgess 2014; Masheer 2017)	35	169 (97)	0 (0)	0/338	0.00	Low
2 (Masheer 2017)	36	172 (64)	0 (0)	0/344	0.00	Low
1 (Masheer 2017)	37	282 (0)	0 (0)	0/282	0.00	Low
1 (Masheer 2017)	38	154 (0)	0 (0)	0/154	0.00	Low

GA: gestational age; IQR: interquartile range; NEC: necrotising enterocolitis; RoB: risk of bias

Table 9: Summary clinical evidence profile for intraventricular haemorrhage in women with uncomplicated dichorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbiditie s: IVH median (IQR)	No of neonatal morbidities: IVH /No neonates born	Crude risk per 1000 neonates born	RoB
1 (Burgess 2014)	34	440 (0)	3 (0)	3/440	7.00	Low
1 (Burgess 2014)	35	266 (0)	2 (0)	2/266	7.52	Low
1 (Burgess 2014)	36	236 (0)	3 (0)	3/236	12.71	Low
1 (Burgess 2014)	37	282 (0)	1 (0)	1/282	3.55	Low
1 (Burgess 2014)	38	154 (0)	0 (0)	0/154	0.00	Low

GA: gestational age; IQR: interquartile range; IVH: intra-ventricular haemorrhage; RoB: risk of bias

Table 10: Summary clinical evidence profile for stillbirth in women with monochorionic diamniotic twin pregnancy according to number of weeks' gestation

Studies N	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No stillbirths / No ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
Studies included in pooled analysis						
1 (Morikawa, 2012)	22	3241 (0)	15 (0)	15 / 3241	4.63	Low
1 (Morikawa, 2012)	23	3231 (0)	11 (0)	11 / 3231	3.40	Low
1 (Morikawa, 2012)	24	3214 (0)	13 (0)	13 / 3214	4.04	Low
2 (Masheer 2017; Morikawa 2012)	25	1638 (1554)	7 (3)	15 / 3275	4.57	Low
2 (Masheer 2017; Morikawa 2012)	26	1623 (1541)	4 (1)	8 / 3246	2.48	Low
2 (Masheer 2017; Morikawa 2012)	27	1600 (1518)	5 (2)	10 / 3199	3.14	Low
2 (Masheer 2017; Morikawa 2012)	28	1574 (1493)	4 (1)	8 / 3148	2.54	Low
2 (Masheer 2017; Morikawa 2012)	29	1540 (1459)	5 (3)	11 / 3080	3.57	Low
2 (Masheer 2017; Morikawa 2012)	30	1502 (1422)	4 (1)	8 / 3004	2.65	Low
2 (Masheer 2017; Morikawa 2012)	31	1461 (1385)	4 (4)	8 / 2922	2.74	Low
3 (Hack 2011; Masheer 2017; Morikawa 2012)	32	465 (1340)	1 (4)	9 / 3292	2.73	Low
3 (Hack 2011; Masheer 2017; Morikawa 2012)	33	432 (1270)	2 (2)	6 / 3117	1.92	Low
6 (Berezowsky 2016; Burgess 2014; Hack 2011; Masheer 2017; Morikawa 2012; Sung 2016)	34	235 (207)	0 (1)	2 / 3547	0.56	Low
7 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	35	171 (172)	0 (2)	7 / 3313	2.11	Moderate
7 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	36	91 (161)	0 (0)	3 / 2696	1.11	Moderate

Studies N	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No stillbirths / No ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
7 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	37	101 (119)	1 (2)	8 / 1571	5.09	Moderate
5 (Burgess 2014; Hack 2011; Lee 2016; Morikawa 2012; Sung 2016)	38	52 (66)	0 (0)	1 / 434	2.30	Moderate
2 (Hack 2011; Morikawa 2012)	39	37 (15)	0 (0)	0 / 73	0.00	Low
1 (Morikawa, 2012)	40	12 (0)	0 (0)	0 / 12	0.00	Low
1 (Morikawa, 2012)	41	0 (0)	0 (0)	0 / 0	0.00	Low
Studies not included in pooled analysis						
1 (Wood 2014)	23	NR	NR	NR	9/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	24	NR	NR	NR	9/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	25	NR	NR	NR	9/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	26	NR	NR	NR	10/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	27	NR	NR	NR	6/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	28	NR	NR	NR	6/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	29	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	30	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	31	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	32	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	33	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	34	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	35	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	36	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	37	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]

Studies N	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No stillbirths / No ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
1 (Wood 2014)	38	NR	NR	NR	10/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)	39	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]

GA: gestational age; IQR: interquartile range; NR: not reported; RoB: risk of bias
a study presents data as risk per 1000 ongoing pregnancies, but does not report raw data (ongoing pregnancy per week); total n=17,724 twin births (8,862 twin sets)
b exposure was measured using weeks' gestation at death (in utero), or when clinician noted death (in utero), or weeks' gestation at birth; study does not report number of ongoing pregnancies by weeks' gestation
c perinatal mortality defined as death of a fetus/neonate weighing at least 500 g or who attained at least 24 completed weeks' gestation, occurring either in utero or within the first 7 days of life
d (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 11: Summary clinical evidence profile for neonatal mortality in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No neonatal mortalities / No neonates born	Crude risk per 1000 neonates born	RoB
1 (Morikawa 2012)	22	20 (0)	5 (0)	5/20	250.00	Low
1 (Morikawa 2012)	23	34 (0)	7 (0)	7/34	205.88	Low
1 (Morikawa 2012)	24	46 (0)	5 (0)	5/46	108.70	Low
1 (Morikawa 2012)	25	54 (0)	7 (0)	7/54	129.63	Low
1 (Morikawa 2012)	26	94 (0)	11 (0)	11/94	117.02	Low
1 (Morikawa 2012)	27	100 (0)	5 (0)	5/100	50.00	Low
1 (Morikawa 2012)	28	136 (0)	3 (0)	3/136	22.06	Low
1 (Morikawa 2012)	29	150 (0)	2 (0)	2/150	13.33	Low
1 (Morikawa 2012)	30	156 (0)	1 (0)	1/156	6.41	Low
1 (Morikawa 2012)	31	186 (0)	2 (0)	2/186	10.75	Low
2 (Hack 2011; Morikawa 2012)	32	174 (108)	2 (1)	3/348	8.62	Low
2 (Hack 2011; Morikawa 2012)	33	198 (128)	3 (3)	6/396	15.15	Low
5 (Berezowsky 2016; Burgess 2014; Hack 2011; Morikawa 2012; Sung 2016)	34	80 (56)	0 (1)	3/848	3.54	Low

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No neonatal mortalities / No neonates born	Crude risk per 1000 neonates born	RoB
6 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Morikawa 2012; Sung 2016)	35	101 (57)	0 (0)	1/1202	0.83	Low
7 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	36	122 (140)	0 (1)	6/2174	2.76	Moderate[a]
7 (Berezowsky 2016; Burgess 2014; Hack 2011; Lee 2016; Masheer 2017; Morikawa 2012; Sung 2016)	37	155 (130)	0 (0)	3/2334	1.29	Moderate[a]
5 (Burgess 2014; Hack 2011; Lee 2016; Morikawa 2012; Sung 2016)	38	38 (104)	0 (0)	1/632	1.58	Moderate[a]
2 (Hack 2011; Morikawa 2012)	39	53 (25)	1 (1)	1/106	9.43	Low
1 (Morikawa 2012)	40	24 (0)	0 (0)	0/24	0.00	Low
1 (Morikawa 2012)	41	0 (0)	0 (0)	0/0	0.00	Low

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 12: Summary clinical evidence profile for respiratory distress syndrome in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born (IQR)	Neonatal morbidities: RDS median (IQR)	Neonatal morbidities: RDS / No neonates born	Crude risk per 1000 neonates born	RoB
2 (Berezowsky 2016; Burgess 2014)	34	82 (42)	9 (5)	17/164	103.7	Low
3	35	62 (22)	2 (6)	16/186	86.0	Moderate[a]

No of studies	GA	Neonates born (IQR)	Neonatal morbidities: RDS median (IQR)	Neonatal morbidities: RDS / No neonates born	Crude risk per 1000 neonates born	RoB
(Berezowsky 2016; Burgess 2014; Lee 2016)						
3 (Berezowsky 2016; Burgess 2014; Lee 2016)	36	74 (75)	3 (4)	7/368	19.0	Moderate[a]
3 (Berezowsky 2016; Burgess 2014; Lee 2016)	37	76 (40)	4 (3)	9/268	33.6	Moderate[a]
2 (Burgess 2014; Lee 2016)	38	33 (1)	1 (1)	2/66	30.3	Moderate[a]

GA: gestational age; IQR: interquartile range; RDS: respiratory distress syndrome; RoB: risk of bias
a (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 13: Summary clinical evidence profile for mechanical ventilator support in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	No neonates born median (IQR)	No of neonatal morbidities: Ventilator support median (IQR)	No of neonatal morbidities: Ventilator support/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Berezowsky 2016)	34	40 (0)	1 (0)	1/40	25.00	Low
2 (Berezowsky 2016; Lee 2016)	35	51 (11)	2 (0)	4/102	39.22	Moderate[a]
2 (Berezowsky 2016; Lee 2016)	36	122 (80)	1 (2)	6/296	20.27	Moderate[a]
2 (Berezowsky 2016; Lee 2016)	37	96 (40)	1 (1)	1/192	5.21	Moderate[a]
1 (Lee 2016)	38	32 (0)	0 (0)	0/32	0.00	Moderate[a]

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a (1 study) unclear if the exposure was measured in a valid and reliable way as not reported; also the outcome measures were not defined

Table 14: Summary clinical evidence profile for oxygen requirement in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonates requiring oxygen support median (IQR)	No neonates requiring oxygen support/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Berezowsky 2016)	34	40 (0)	12 (0)	12	300.00	Low
1 (Berezowsky 2016)	35	62 (0)	5 (0)	5	80.65	Low
1 (Berezowsky 2016)	36	115 (59)	15 (0)	15	86.21	Low
1 (Berezowsky 2016)	37	56 (0)	3 (0)	3	53.57	Low

GA: gestational age; IQR: interquartile range; RoB: risk of bias

Table 15: Summary clinical evidence profile for sepsis in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: Sepsis median (IQR)	No of neonatal morbidities: Sepsis/Neonates born	Crude risk per 1000 neonates born	RoB
1 (Masheer 2017)	25	4 (0)	0 (0)	0/4	0.00	Low
1 (Masheer 2017)	26	0 (0)	0 (0)	0/0	0.00	Low
1 (Masheer 2017)	27	2 (0)	0 (0)	0/2	0.00	Low
1 (Masheer 2017)	28	0 (0)	0 (0)	0/0	0.00	Low
1 (Masheer 2017)	29	2 (0)	1 (0)	1/2	500.00	Low
1 (Masheer 2017)	30	8 (0)	0 (0)	0/8	0.00	Low
1 (Masheer 2017)	31	4 (0)	3 (0)	3/4	750.00	Low
1 (Masheer 2017)	32	2 (0)	0 (0)	0/2	0.00	Low
1 (Masheer 2017)	33	14 (0)	0 (0)	0/14	0.00	Low

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: Sepsis median (IQR)	No of neonatal morbidities: Sepsis/Neonates born	Crude risk per 1000 neonates born	RoB
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	34	40 (50)	1 (11)	25/188	132.98	Low
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	35	62 (26)	2 (12)	28/178	157.30	Low
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	36	64 (36)	3 (4)	9/280	32.14	Low
2 (Berezowsky 2016; Burgess 2014)	37	66 (10)	3 (3)	5/132	37.88	Low
1 (Burgess 2014)	38	34 (0)	4 (0)	4/34	117.65	Low

GA: gestational age; IQR: interquartile range; RoB: risk of bias

Table 16: Summary clinical evidence profile for necrotising enterocolitis in women with uncomplicated monochorionic diamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: NEC median (IQR)	No of neonatal morbidities: NEC /No neonates born	Crude risk per 1000 neonates born	RoB
1 (Masheer 2017)	25	4 (0)	0 (0)	0/4	0.00	Low
1 (Masheer 2017)	26	0 (0)	0 (0)	0/0	0.00	Low
1 (Masheer 2017)	27	2 (0)	0 (0)	0/2	0.00	Low
1 (Masheer 2017)	28	0 (0)	0 (0)	0/0	0.00	Low
1	29	2 (0)	0 (0)	0/2	0.00	Low

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: NEC median (IQR)	No of neonatal morbidities: NEC /No neonates born	Crude risk per 1000 neonates born	RoB
(Masheer 2017)						
1 (Masheer 2017)	30	8 (0)	2 (0)	2/8	250.00	Low
1 (Masheer 2017)	31	4 (0)	1 (0)	1/4	250.00	Low
1 (Masheer 2017)	32	2 (0)	0 (0)	0/2	0.00	Low
1 (Masheer 2017)	33	14 (0)	0 (0)	0/14	0.00	Low
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	34	40 (50)	0 (1)	1/188	5.32	Low
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	35	62 (26)	1 (1)	2/178	11.24	Low
3 (Berezowsky 2016; Burgess 2014; Masheer 2017)	36	64 (36)	0 (0)	0/280	0.00	Low
2 (Berezowsky 2016; Burgess 2014)	37	66 (10)	0 (0)	0/132	0.00	Low
1 (Burgess 2014)	38	34 (0)	0 (0)	0/34	0.00	Low

GA: gestational age; IQR: interquartile range; NEC: necrotising enterocolitis; RoB: risk of bias

Table 17: Summary clinical evidence profile for intraventricular haemorrhage in women with uncomplicated monochorionic diamniotic twin pregnancy according to weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: IVH median (IQR)	No of neonatal morbidities: IVH/Neonates born	Crude risk per 1000 neonates	RoB
2 (Berezowsky 2016; Burgess 2014)	34	82 (42)	1 (1)	1/164	6.10	Low
2 (Berezowsky 2016; Burgess 2014)	35	73 (11)	0 (0)	0/146	0.00	Low
2 (Berezowsky 2016; Burgess 2014)	36	72 (20)	0 (0)	0/246	0.00	Low
2 (Berezowsky 2016; Burgess 2014)	37	66 (10)	0 (0)	0/132	0.00	Low
1 (Burgess 2014)	38	34 (0)	0 (0)	0/34	0.00	Low

GA: gestational age; IQR: interquartile range; IVH: intraventricular haemorrhage; RoB: risk of bias

Table 18: Summary clinical evidence profile for stillbirth in women with monochorionic monoamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
1 (Wood 2014)[a]	23	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Baxi 2010)[c]	24[d]	8[c] (0)	0[c] (0)	0/8[c]	0.00	Moderate[c]
1 (Wood 2014)[a]	24	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Baxi 2010)[c]	25[d]	7[c] (0)	0[c] (0)	0/7[c]	0.00	Moderate[c]
1 (Wood 2014)[a]	25	NR	NR	NR	8/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	26	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]

No of studies	GA	Ongoing pregnancies median (IQR)	Stillbirths median (IQR)	No of stillbirths/No ongoing pregnancies	Crude risk per 1000 ongoing pregnancies	RoB
1 (Wood 2014)[a]	27	NR	NR	NR	4/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	28	NR	NR	NR	3/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	29	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	30	NR	NR	NR	2/1000 fetuses[a]	Moderate[b]
1 (Baxi 2010)[c]	31[d]	6[c] (0)	1[c] (0)	1/6[c]	166.67	Moderate[c]
1 (Wood 2014)[a]	31	NR	**NR**	NR	4/1000 fetuses[a]	Moderate[b]
1 (Baxi 2010)[c]	32[d]	5[c] (0)	0[c] (0)	0/5[c]	0.00	Moderate[d]
1 (Wood 2014)[a]	32	NR	NR	NR	2/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	33	NR	NR	NR	1/1000 fetuses[a]	Moderate[b]
1 (Baxi 2010)[c]	34[d]	4[c] (0)	0[c] (0)	0/4[c]	0.00	Moderate[c]
1 (Wood 2014)[a]	34	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	35	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	36	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	37	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	38	NR	NR	NR	0/1000 fetuses[a]	Moderate[b]
1 (Wood 2014)[a]	39	NR	NR	[+]NR	0/1000 fetuses[a]	Moderate[b]

GA: gestational age; IQR: interquartile range; NR: not reported; RoB: risk of bias
a study presents data as risk per 1000 ongoing pregnancies, but does not report raw data (ongoing pregnancy per week); total n=17,724 twin births (8,862 twin sets)
b exposure was measured using weeks' gestation at death (in utero), or when clinician noted death (in utero), or weeks' gestation at birth; study does not report number of ongoing pregnancies by weeks' gestation
c unclear if study participants were sampled in an appropriate way as cases were identified on an ongoing basis and confirmed from a computerised perinatal database, but relevant data only available for 8/25 pregnancies (16

neonates); also the study subjects and the setting were not described in detail as limited information regarding maternal and neonatal characteristics
d complicated pregnancy as described in study (see appendix D)

Table 19: Summary clinical evidence profile for neonatal mortality in women with complicated monochorionic monoamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal mortalities median (IQR)	No of neonatal mortalities/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Baxi 2010)	24[a]	2 (0)	1 (0)	1/2	500.00	Moderate[b]
1 (Baxi 2010)	25[a]	2 (0)	0 (0)	0/2	0.00	Moderate[b]
1 (Baxi 2010)	31[a]	2 (0)	0 (0)	0/2	0.00	Moderate[b]
1 (Baxi 2010)	32[a]	2 (0)	1 (0)	1/2	500.00	Moderate[b]
1 (Baxi 2010)	34[a]	8 (0)	1 (0)	1/8	125.00	Moderate[b]

GA: gestational age; IQR: interquartile range; RoB: risk of bias
a complicated pregnancy as described in study (see appendix D)
b unclear if study participants were sampled in an appropriate way as cases were identified on an ongoing basis and confirmed from a computerised perinatal database, but relevant data only available for 8/25 pregnancies (16 neonates); also the study subjects and the setting were not described in detail as limited information regarding maternal and neonatal characteristics

Table 20: Summary clinical evidence profile for necrotising enterocolitis in women with complicated monochorionic monoamniotic twin pregnancy according to number of weeks' gestation

No of studies	GA	Neonates born median (IQR)	Neonatal morbidities: NEC median (IQR)	No of neonatal morbidities: NEC/No neonates born	Crude risk per 1000 neonates born	RoB
1 (Baxi 2010)	24[a]	2 (0)	1 (0)	1/2	500.00	Moderate[b]
1 (Baxi 2010)	25[a]	2 (0)	0 (0)	0/2	0.00	Moderate[b]
1 (Baxi 2010)	31[a]	2 (0)	0 (0)	0/2	0.00	Moderate[b]
1 (Baxi 2010)	32[a]	2 (0)	0 (0)	0/2	0.00	Moderate[b]
1 (Baxi 2010)	34[a]	8 (0)	0 (0)	0/8	0.00	Moderate[b]

IQR: interquartile range; NEC: necrotising enterocolitis; RoB: risk of bias

a complicated pregnancy as described in study (see appendix D)
b unclear if study participants were sampled in an appropriate way as cases were identified on an ongoing basis and confirmed from a computerised perinatal database, but relevant data only available for 8/25 pregnancies (16 neonates); also the study subjects and the setting were not described in detail as limited information regarding maternal and neonatal characteristics

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 appendix B for the economic search strategy and appendix G for the economic evidence selection flow chart for further information.

However, the model developed for the previous guideline was included for consideration by the committee. Table 21 provides a brief summary.

Table 21: Summary of included studies (economic evidence)

Study	Population	Intervention/Comparison	Perspective and cost year	Comments
CG129 Cost utility analysis England, Wales and Northern Ireland	Women with a multiple pregnancy	Elective birth was assumed to occur at a gestational age of 37+0 weeks versus expectant management	NHS 2011 prices	The “what-if” model did not cost the intervention or outcomes but rather considerd the incremental costs that would be consistent with cost effectiveness. Therefore , the price year is implicit from the publication date of the guideline

For full details see the economic evidence table in appendix H.

Excluded studies

Studies not included in this review with reasons for their exclusion are listed in appendix K.

Summary of studies included in the economic evidence review

No economic studies were identified from a systematic search of the literature which were applicable to this review question. However, a model produced for the previous guideline was included as economic evidence and this is summarised below.

Economic model

No economic modelling was undertaken for this review because this topic was introduced late into guideline development and the committee agreed that other topics were higher priorities for economic evaluation. However, a relevant model was developed for the previous guideline (NICE CG129) and this was considered as economic evidence by the committee

for this review. The model compared the cost effectiveness of elective birth compared to expectant management in uncomplicated twin and triplet pregnancies. In the model, elective birth was assumed to occur at a gestational age of 37^{+0} weeks and expectant management was assumed to take place 1 week later. The analysis modelled the impact of timing of birth on stillbirth and respiratory distress syndrome. Other neonatal outcomes and maternal outcomes were not included as the clinical review did not find statistically significant differences between them after 34 weeks. The model did not explicitly cost the different strategies but used a 'what-if' approach to determine the saving that would be required in order to make expectant management cost effective given the expected lower quality adjusted life years (QALYs) gain arising from a higher stillbirth rate. The results suggested that expected management would have to generate savings of £5,567 or more to be considered cost effective relative to elective birth at a cost effectiveness threshold of £20,000 per QALY. However, it was not thought likely that expectant management would produce these savings. Whilst elective birth may slightly increase the costs of birth as a result of the costs associated with induction of labour, expectant management requires additional monitoring costs as well as potentially incurring higher 'downstream' costs from worse neonatal outcomes. The clinical data underpinning this analysis was largely based on dichorionic twin pregnancies. Whilst triplet and monochorionic twin pregnancies were not excluded there was insufficient data to analyses these groups separately.

Evidence statements

Clinical

In this section evidence statements describe the pattern of incidence (risk per 1000 ongoing pregnancies [stillbirth] or risk per 1000 neonates born [neonatal mortality or neonatal morbidity]) by gestational age according to chorionicity and amnionicity. No formal statistical analysis was conducted. For further detail see the methods in supplementary material C.

Dichorionic diamniotic (DCDA) twin pregnancies

Stillbirth

A total of 6 studies contributed data on the frequency of stillbirths in ongoing DCDA twin pregnancies. All studies were observational (retrospective cohort) studies and of low to moderate risk of bias and reported data from 25 to 38 weeks' gestation. Limited data were available for <30 weeks' gestation (2 studies) and >38 weeks' gestation (1 study), with the majority of studies contributing data for the period 34^{+0} to 38^{+6} weeks' gestation. The estimated crude risk of stillbirth per 1000 ongoing DCDA twin pregnancies increased at 34 weeks' gestation (3.43/1000 [4 studies]),and increased again after 37 weeks' gestation. The highest estimated crude risk of stillbirth per 1000 ongoing pregnancies was highest at 39 and 40 weeks' gestation (13.4/1000 [1 study] and 27.0/1000 [1 study], respectively) (refer to Figure 3, Appendix M).

One study was not included in the pooled analysis:

- One retrospective cohort study (Wood et al. 2014) of moderate risk of bias reported risk of stillbirth per 1000 fetuses by weekly gestation from 23 to 39 weeks' gestation. The risk of stillbirth was highest before 33 weeks' gestation, and then increased again after 38 weeks' gestation (8 stillbirths occurred at 38 to 39 weeks' gestation).

Neonatal mortality

A total of 4 studies contributed data on the frequency of neonatal mortality in ongoing DCDA twin pregnancies. All studies were observational (retrospective cohort) studies and of moderate-to-low risk of bias, and reported data from 22 to 41 weeks' gestation. Limited data were available for <30 weeks' gestation (1 study) and >38 weeks' gestation (1 study), with

the majority of studies contributing data for the period 34^{+0} to 38^{+6} weeks' gestation. The highest estimate of crude risk of neonatal mortality per 1000 neonates born was observed at ≤30 weeks' gestation (375.0/1000 at 22 weeks' gestation reducing to 10.1/1000 at 30 weeks' gestation). Estimates of crude risk of neonatal mortality per 1000 neonates born tended to reducefrom 34 weeks' gestation although a small increase was observed at 39 weeks' gestation (4.5/1000 [1 study] and 14.3/1000 [1 study] at 39 and 40 weeks' gestation, respectively) (refer to Figure 4, Appendix M).

Neonatal morbidities

A total of 3 studies reported data on the frequency of neonatal morbidities among neonates born: respiratory distress syndrome (RDS); ventilator support; oxygen requirement; necrotising enterocolitis (NEC), sepsis, and intraventricular haemorrhage (IVH).

- **RDS:** A total of 2 studies with low or moderate risk of bias, reported data by number of weeks' gestation covering the period 34 to 38 weeks' gestation. Estimated crude risk of RDS per 1000 neonates born was highest at 34 weeks' gestation (161.0/1000 [1 study]). In general, the pattern indicated a decrease in estimated crude risk over time with the lowest estimate of crude risk of RDS per 1000 neonates born at 37 weeks' gestation (27.4/1000 [2 studies]). There was a slight increase at 38 weeks' gestation (39.3/1000 [2 studies]).
- **Ventilator support:** A total of 1 study with moderate risk of bias, reported data by number of weeks' gestation covering the period 35 to 38 weeks' gestation. At 35 weeks' gestation the estimated crude risk of requirement for ventilator support was highest (62.5/1000 [1 study]), and decreased over time (4.1/1000 at 37 week's gestation). iAmong 126 neonates born at 38 weeks' gestation none required ventilation support (0.0/1000 [1 study].
- **Oxygen requirement:** No studies reported data on oxygen requirement among neonates born.
- **Sepsis:** A total of 2 studies with low risk of bias, reported data by number of weeks' gestation covering the period 25 to 38 weeks' gestation..Estimated crude risk of sepsis per 1000 neonates born was highest at <30 weeks' gestation (estimates ranging from 250/1000 to 500/1000). Estimated crude risk of sepsis at 33 weeks' gestation was notably low (38/1000 [1 study]). At 34 weeks' gestation the estimate increased (248.0/1000 [2 studies]) before decreasing gradually over time (213.0/1000, 110.5/1000, 67.4/100, and 77.9/1000 at 35, 36, 37, and 38 weeks' gestation, respectively).
- **NEC:** A total of 2 studies with low risk of bias, reported data by number of weeks' gestation covering the period 25 to 38 weeks' gestation. Estimated crude risk of NEC per 1000 neonates born was highest at 27 weeks' gestation (166.7/1000, 1 study). Lower estimates of cruide risk were observed at 26 and 29 weeks' gestation (both 83.3/1000 [1 study]), 33 weeks' gestation (38.5/1000 [1 study]) and 34 weeks' gestation (4.0/1000 [2 studies]). No events were reported in the identified studies among 1164 neonates born at 25, 28, 31, 32, and ≥35 weeks' gestation. No consistent pattern was observed in the data.
- **IVH:** One study with low risk of bias, reported data by number of weeks' gestation covering the period 34 to 38 weeks' gestation. Estimated crude risk of IVH per 1000 neonates born increased from 7/1000 (1 study) at 34 weeks' gestation to 12.7/1000 (1 study) at 36 weeks' gestation. At 37 weeks' gestation the estimated crude risk per 1000 neonates born decreased to 3.6/1000 (1 study), and at 38 weeks' gestation, no events were reported among 154 neonates born.

Monochorionic diamniotic (MCDA) twin pregnancies

Stillbirth

A total of 9 studies contributed data on the frequency of stillbirths in ongoing MCDA pregnancies. All studies were observational (retrospective cohort) studies and of moderate-to-low risk of bias, and reported data from 22 to 41 weeks' gestation . Estimated crude risk

per 1000 ongoing monochorionic diamniotic twin pregnancies high before 30 week's gestation and then increased again after 36 weeks' gestation (highest estimate of 5.1/1000 [7 studies] at 37 weeks' gestation). No stillbirths were reported at >38 weeks' gestation among 85 ongoing monochorionic diamniotic twin pregnancies (2 studies) (refer to Figure 7, Appendix M).

Two studies were not included in the pooled analysis:

- One retrospective cohort study (Wood, 2014) of moderate risk of bias the reported risk of stillbirth per 1000 fetuses at risk by weekly gestation from 23 to 39 weeks' gestation. The still-birth risk was highest before 29 weeks' gestation, and then increased again after 36 weeks' gestation (14 stillbirths occurred at 36 to 38 weeks' gestation).One retrospective cohort study (Breathnach, 2012) of low risk of bias reported risk of perinatal mortality (defined as a fetus/neonate weighing at least 500 g or who attained a gestation of at least 24 completed weeks' gestation, occurring either in utero or within the first 7 days of life) by weekly gestation from 34 to 37 weeks. The crude risk per 1000 ongoing MCDA twin pregnancies was highest at 34 weeks' gestation (16.9/1000).

Neonatal mortality

A total of 7 studies contributed data on the frequency of neonatal mortality among neonates born. All studies were observational (retrospective cohort) studies and of moderate or low risk of bias, and reported data for the period 32^{+0} to 39^{+6} weeks' gestation. The estimated crude risk of neonatal mortality per 1000 neonates born was highest before 30 weeks' gestation (250.0/1000 [1 study] at 22 weeks' gestation and 13.3/1000 at 29 weeks' gestation [1 study]). From 34 weeks' gestation, estimated crude risk per 1000 neonates born tended to reduce although a slight increase was observed at 39 weeks' gestation. No mortalities were reported among 24 neonates born at 40 weeks' gestation (1 study) (refer to Figure 8, Appendix M).

Neonatal morbidities

A total of 3 studies reported data on the frequency of neonatal morbidities among neonates born: respiratory distress syndrome (RDS); ventilator support; oxygen requirement; necrotising enterocolitis (NEC), sepsis, and intraventricular haemorrhage (IVH).

- **RDS:** A total of 3 studies of low or moderate risk of bias, reported data by weekly gestation covering the period 34 to 38 weeks' gestation. Estimated crude risk of RDS per 1000 neonates born was highest at 34 weeks' gestation (103.66/1000). After 34 weeks' gestation estimated crude risk of RDS per 1000 neonates born reduced (86.0/1000, 19.0/1000, 33.6/1000 and 30.3/1000 at 36, 37, 38 weeks' gestation, respectively).
- **Ventilator support:** A total of 2 studies of low or moderate risk of bias, reported data by weekly gestation covering the period 34 to 38 weeks' gestation. Estimated crude risk of requirement for ventilation support per 1000 neonates born was highest at 35 weeks' gestation (39.2/1000 [2 studies]), and decreased over subsequent weeks' gestation. No events were reported among 32 neonates born at 38 weeks' gestation.
- **Oxygen requirement:** A total of 1 study of low risk of bias, reported data by weekly gestation covering the period 34 to 38 weeks' gestation. The estimated crude risk of oxygen requirement per 1000 neonates born was highest at 34 weeks' gestation (300/1000) and decreased over time 54/1000 at 37 weeks' gestation.
- **Sepsis:** A total of 3 studies of low risk of bias, reported data by number of weeks' gestation covering the period 25 to 38 weeks' gestation. The highest estimated crude risk of sepsis per 1000 neonates born was at 31 weeks' gestation (750/1000 [1 study]). The estimated risk reduced over time to 37 weeks' gestation and then appeared to increase again at 38 week's gestation (117.7/1000 [1 study]).
- **NEC:** A total of 3 studies of low risk of bias, reported data by weekly gestation covering the period 25 to 38 weeks' gestation. Estimated crude risk of NEC per 1000 neonates

born was highest at 30 and 31 weeks' gestation (both 250.0/1000, 1 study), decreasing to 5.3/1000 and 11.2/1000 at 34 and 35 weeks' gestation, respectively (3 studies). No events were reported in the identified studies among 436 neonates born at <30, 32, 33, ≥36 weeks' gestation.

- **IVH:** A total of 2 studies of low risk of bias, reported data by weekly gestation covering the period 34 to 38 weeks' gestation. The estimated crude risk of IVH per 1000 neonates born at 34 weeks' gestation was 6.1/1000, and no events were reported among the 558 neonates born at 35 to 38 weeks' gestation.

Monochorionic monoamniotic (MCMA) twin pregnancies

Stillbirth

One retrospective cohort study (Baxi, 2010) with moderate risk of bias reported data for 25 MCMA complicated twin pregnancies for the period 24, 25, 31, 32, and 34 weeks' gestation. Estimated risk of stillbirth at 31 weeks' gestation was 166.7/1000. In this study, no stillbirths were reported at 24,25, 32, 34 weeks' gestationOne retrospective cohort study (Wood, 2014) with moderate risk of bias reported data for MCMA complicated twin pregnancies (total not reported) during the period starting from 23 and ending at 39 weeks' gestation. All stillbirths occurred before 34 weeks' gestation with most occurring before 28 weeks' gestation.

Neonatal mortality

One retrospective cohort study (Baxi, 2010) with moderate risk of bias reported data for 25 MCMA complicated twin pregnancies for the period 24, 25, 31, 32, and 34 weeks' gestation. Highest estimated crude risk per 1000 neonates born was 500.0/100 (1 study) at both 24 and 32 weeks' gestation. The estimated risk per 1000 neonates born decreased to 125.0/1000 at 34 weeks' gestation.

Neonatal morbidities

One retrospective cohort study (Baxi, 2010) with moderate risk of bias reported data for 25 MCMA complicated twin pregnancies over during the period starting from 24 and ending at 34 weeks' gestation. Data for one morbidity of interest – necrotising enterocolitis (NEC) – were reported:

- **NEC:** The estimated crude risk of NEC per 1000 neonates born was 500.0/1000 at 24 weeks' gestation. No cases of NEC were reported among 14 neonates born at the remaining timepoints reported (25, 31, 32, and 34 weeks' gestation).

Economic

One cost utility analysis found that elective birth at a gestational age of 37+0 weeks was cost effective compared to expectant management providing that the incremental costs of elective birth were less than £5,560.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee prioritised stillbirth and perinatal or neonatal mortality as critical outcomes because comparison of death rates before and after birth was viewed as the most important starting point to inform decision making as to the safety of continuing pregnancy versus recommending birth be planned for a given number of weeks' gestation.

The committee agreed that neonatal morbidities such as respiratory distress syndrome, need for respiratory support (respiratory ventilation), septicaemia or meningitis, bronchopulmonary dysplasia, hypoxic ischaemic encephalopathy, necrotising enterocolitis, intraventricular haemorrhage, cystic periventricular leukomalacia, retinopathy of prematurity were important outcomes, because these are severe neonatal morbidities with risks of life-long complications. As such, their incidence should be considered in addition to the risk of neonatal mortality when attempting to balance the neonatal risks of planned birth versus the fetal risks of stillbirth at each weekly gestation.

The quality of the evidence

The risk of bias of the included studies was assessed using an adapted version of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn 2015) for incidence studies. The included studies were rated as being of low or moderate risk of bias. Study design was one of the main factors that lowered the confidence in the evidence: all studies were observational (retrospective). In some studies, reporting omissions hindered the assessment of measurement of exposure and in some cases outcome definitions were unclear.

Nine of the included studies were conducted in OECD countries. One study (Masheer, 2017) was conducted in a non-OECD country (Pakistan). The data from this study aligned with other studies' findings and was therefore included for completeness.

Of note, for each outcome, the studies did not contribute data to all weeks' gestation reported; i.e. at some weeks' gestation there were ≤2 studies contributing data and others >2 studies. The majority of studies contributed data for 34 to 38 weeks' gestation. This could have contributed to the some of the bimodal patterns observed in the data. In addition, there were limited studies that contributed data for neonatal morbidities. Due to these limitations, no formal statistical comparison was made and patterns observed in data extracted from the identified evidence were summarised narratively.

Benefits and harms

Timing recommendations were based on data extracted from the identified evidence. In addition, the committee took into account information from their knowledge of a systematic review (Cheong-See, 2016 [monochorionic diamniotic and dichorionic diamniotic twin pregnancies]) and retrospective study (Van Miegham, 2014 [monochorionic monoamniotic twin pregnancies]). These two studies were excluded (see appendix K) but were used by the the committee as an extra step in the validation of their conclusions.

Where relevant the committee also considered the systematic review that was conducted for the previous guideline (NICE CG129 - 2011) and the associated recommendations. Even though it addressed the same topic the previous review question was broader and did not include amnionicity as a characteristic for investigation. Therefore some of this information was only considered to check for consistency of conclusions.

They noted that this was an unusual type of review question in the context of guideline development and given the seriousness of the outcomes, such as stillbirth, neonatal mortality and morbidities, they were keen to draw on their knowledge of the Cheong-See, 2016 and Van Miegham, 2014 studiesas well as the previous guideline to discuss the identified evidence in a wider context.

Twin pregnancy:

Information to support planning the timing of birth

The committee agreed that it was critical to give women who are pregnant with twins the information they need to participate in shared decisions about when their babies are born.

The committee agreed that the evidence based estimate from the previous guideline of women giving birth prematurely (approximately 60 in 100 twin pregnancies result in spontaneous birth before 37 weeks), was still appropriate for the current update. They agreed on the importance of this number and that it should be explained to the woman to enable shared decision making about timing of birth. They therefore retained the recommendation from 2011.

In addition, in twin pregnancy preterm birth is also linked to an increased risk of admission to a neonatal unit. The committee therefore recognised that many women would give birth earlier than the times specified in the recommendations. They agreed that optimal timing of planned birth should be discussed with the woman as early as 24 weeks but no later than 28 weeks pregnancy. This timing was recommended to aid expectations of pregnancy duration and/or increase knowledge of the risks and implications of spontaneous or emergency preterm birth before the optimal recommended timing of birth.

Uncomplicated dichorionic diamniotic

The recommendation for timing of birth in uncomplicated dichorionic diamniotic twins was based on the balance of risks of stillbirth, neonatal mortality, and neonatal morbidity. Conversations should take place with the woman to explain why the specific gestational weeks are chosen for her type of pregnancy to enable her to make an informed choice about timing of birth.

For women with uncomplicated dichorionic diamniotic twin pregnancies, 37^{+0} weeks gestation was chosen because the evidence showed that planned birth at this time does not appear to be linked to an increased risk of neonatal mortality or morbidities, but the evidence also indicated that continuing the pregnancy beyond 37^{+6} weeks increases the risk of fetal death.

The woman should be offered planned birth at the recommended gestational week (see above). The committee was reassured that this is also in line with the findings from the Cheong-See 2016 systematic review for this group and acknowledged also that it was consistent with the timing of birth recommended for this type of pregnancy in 2011.

Uncomplicated monochorionic diamniotic

The recommendation for timing of birth in uncomplicated monochorionic diamniotic twin pregnancies was based on the balance of risks of stillbirth, neonatal mortality, and neonatal morbidity. Conversations should take place with the woman to explain why the specific gestational weeks are chosen for her type of pregnancy to enable her to make an informed choice about timing of birth.

The evidence for women with uncomplicated monochorionic diamniotic twin pregnancies indicated that planned birth from 36^{+0} weeks' gestation does not appear to be linked to an increased risk of neonatal mortality or morbidities. The evidence also showed that continuing an uncomplicated monochorionic diamniotic twin pregnancy beyond 36^{+6} weeks is associated with an increase in the risk of fetal death.

The woman should be offered planned birth at the recommended gestational week (see above). For women with uncomplicated monochorionic diamniotic twin pregnancy planned birth should be offered after a course of antenatal corticosteroids. The committee was reassured that this is also in line with the findings from the Cheong-See 2016 systematic review for this group and acknowledged also that it was consistent with the timing of birth recommended for this type of pregnancy in 2011.

Uncomplicated monochorionic monoamniotic

In this guideline update, the committee clarified the recommendation for uncomplicated monochorionic monoamniotic twins which were not specifically mentioned in the previous guideline. The recommendation was made on the basis of the limited evidence meeting the eligibility criteria for the evidence review.

In monochorionic monoamniotic twin pregnancy, the available evidence suggest planned birth between 32^{+0} and 33^{+6} weeks' gestation is not associated with an increased risk of serious neonatal adverse outcome. However, the evidence also showed that birth beyond this gestation is associated with an increased risk of fetal death. Stillbirths in MCMA occurred before 34 weeks' gestation with the majority occurring before 28 weeks' gestation. The evidence suggested that it is likely that most of these twins will have an increased risk of respiratory problems and will be admitted to a neonatal unit as a result.

The woman should be offered planned birth at the recommended gestational week (see above). For women with uncomplicated monochorionic monoamniotic twin pregnancy planned birth should be offered after a course of antenatal corticosteroids.

Based on their knowledge the committee also discussed the retrospective study (Van Miegham, 2014) they were aware of which indicated that the prospective risk of a nonrespiratory neonatal complication was lower than the prospective risk of fetal death after 32 weeks' gestation; i.e. monoamniotic twins delivered at approximately 33 weeks' gestation have the best outcome. At 33 weeks of gestation, neonatal respiratory complications can still occur, but these are usually manageable if glucocorticoids for pulmonary maturation have been administered. This type of twin pregnany is rare and complicated and the committee noted that evidence is naturally scarce. They were therefore reassured that the conclusions drawn from the identified evidence match the findings of this additional study.

Triplet pregnancy

Information to support planning the timing of birth

The committee agreed that it was critical to give women who are pregnant with triplets the information they need to participate in shared decisions about when their babies are born. The committee agreed that the consensus based estimate from the previous guideline of women giving birth prematurely (approximately 75 in 100 triplet pregnancies result in spontaneous birth before 35 weeks), was still appropriate for the current update. They agreed on the importance of this number and that this should be explained to the woman to enable shared decision making about timing of birth.

Based on evidence presented in the previous guideline, the committee knew that in triplet pregnancies the risk of preterm birth is significantly increased. In addition, in triplet pregnancy preterm birth is also linked to an increased risk of admission to a neonatal unit. The committee therefore recognised that many women would give birth earlier than the times specified in the recommendations. They agreed that optimal timing of planned birth should be discussed with the woman as early as 24 weeks but no later than 28 weeks pregnancy. This timing was recommended to aid expectations of pregnancy duration and/or increase knowledge of the risks and implications of spontaneous or emergency preterm birth before before the optimal recommended timing of birth.

Uncomplicated trichorionic triamniotic and dichorionic triamniotic

No evidence was identified in the current review for triplet pregnancies. The committee clarified the position on triplet pregnancy by chorionicity and amnionicity according to risk and complexity rather than considering all triplet pregnancies as one generic group as was

the case in the previous guidance. Compared to twin pregnancies, triplet pregnancies are rare. The majority of triplet pregnancies are trichorionic, triamniotic.

The committee considered based on their clinical experience that continuing an uncomplicated trichorionic triamniotic or a dichorionic triamniotic triplet pregnancy beyond 35^{+6} weeks' gestation would lead to an increased risk of fetal death.

Once conversations have taken place with the woman to explain this, the woman should be offered planned birth at week 35 of pregnancy. For women with uncomplicated trichorionic triamniotic or dichorionic triamniotic triplet pregnancy planned birth at the recommended timings should be offered after a course of antenatal corticosteroids. It was acknowledged that this is consistent with the previous 2011 recommendations for this group.

Monochorionic triamniotic triplet pregnancy or a triplet pregnancy that involves a shared amnion

No evidence was identified for this group. The committee noted that these types of triplet pregnancies are very rare and are usually complicated (see below). The committee agreed that the timing of birth for these groups of triplets would need to be tailored to each particular pregnancy. To allow the woman to take part in shared decision making about the birth of her baby a conversation should take place where this is explained. Having this explanation will reassure the woman that the timing of birth of her babies will be individualised to her needs. This retains the previous 2011 recommendation.

Even though no evidence was identified for triplet pregnancy the committee decided not to make a research recommendation because they noted that the recommended mode of birth was by caesarean section and that the timing of this is easier to plan. Therefore they agreed that other topics should be prioritised for research.

Any complicated twin or triplet pregnancy

Based on the committee's experience and expertise, it was acknowledged that twin pregnancies can be complicated by many different conditions (some of these are referred to in evidence reviews A1 to A3). Twin and triplet pregnancies with a shared chorion or shared amnion are inherently more complex than other twin or triplet pregnancies. These are also significantly less common then other less complicated pregnancies. The committee decided that where complications are identified the approach to timing of birth would need to be individualised and tailored to the woman's needs and circumstances. The time of birth that is then offered should depend on an individual assessment which would weigh up the benefits and risks related to birth at a particular week of pregnancy.

When planned birth is declined

The committee considered, based on their experience, that women who decline planned birth at the timings recommended, should be offered routine monitoring and weekly appointments with the specialist obstetrician. This would provide an opportunity for the attending clinicians to assess the pregnancy and reiterate the offer of birth to reduce the likelihood of adverse outcomes.

Cost effectiveness and resource use

In the absence of any new economic evidence or de novo analysis, the committee made a largely qualitative assessment about the cost effectiveness of optimal timing of birth, although a model produced for the previous guideline was also considered.

The committee noted that whilst there may be some additional costs associated with earlier birth such as more induction of labour and potentially more operative birth, these costs are relatively small. Furthermore, delayed birth results in increased monitoring costs and

increased 'downstream' costs are also likely where there is an increased risk of neonatal morbidity. Therefore, the committee concluded that clinical outcomes are likely to drive the cost effectiveness of the optimal timing of birth. This is also consistent with the economic evidence presented in the previous 2011 guideline.

The recommendations made in this guideline update largely reflect existing guidance although some new recommendations were made to clarify recommendations by pregnancy type where this was not explicitly addressed in the previous guideline. Although the recommendation to clarify the timing of when women with monochorionic monoamniotic pregnancy should be offered planned birth represents a change from the previous guideline, the committee considered that it reinforces current practice.

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Appendices

Appendix A – Review protocols

Review protocol – review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Table 22: Review protocol for identifying the incidence of stillbirth and neonatal death and morbidity by gestational age in monochorionic/dichorionic twin and all triplet pregnancies according to amnionicity

ID	Field (based on PRISMA-P)	Content
I	Review question	What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and all triplet pregnancies according to chorionicity and amnionicity?
II	Type of review question	Incidence
III	Objective of the review	To determine the optimal timing of birth based on the incidence of stillbirth and neonatal death or neonatal morbidity by gestational age in monochorionic/dichorionic twin and all triplet pregnancies
IV	Eligibility criteria – population/disease/condition/issue/domain	**For twin pregnancies:** • Monochorionic diamniotic • Monochorionic monoamniotic (contain monoamniotic pair) • Dichorionic diamniotic **For triplet pregnancies:** • Trichorionic triamniotic • Dichorionic triamniotic • Monochorionic triamniotic • Dichorionic diamniotic (contain a monochorionic twins set) and • Monochorionic monoamniotic (contain a monoamniotic triplet set) Setting: Secondary or tertiary care centres
V	Eligibility criteria – interventions	Gestational age at death (in utero), or when clinician noted death (in utero), or gestational age at birth (for neonatal outcomes) cross-classified by chorionicity and amnionicity Note: Data will be extracted from eligible studies as number of events (stillbirth or neonatal death or individual neonatal morbidity outcome) and number births/pregnancies by weekly gestation.
VI	Eligibility criteria – comparators	None
VII	Outcomes and prioritisation	For the baby: **Critical** • stillbirth • perinatal/neonatal mortality

ID	Field (based on PRISMA-P)	Content
		Important: • Neonatal morbidities (respiratory distress syndrome, need for respiratory support (respiratory ventilation), septicaemia or meningitis, bronchopulmonary dysplasia, hypoxic ischaemic encephalopathy, necrotising enterocolitis, intraventricular haemorrhage, cystic periventricular leukomalacia, retinopathy of prematurity admission to neonatal intensive care unit)
VIII	Eligibility criteria – study design	Only published full text papers in English language: • Systematic reviews of observational studies • Prospective or retrospective observational studies (prospective observational studies will be prioritised over retrospective) Conference abstracts will be considered. Note: Data will be extracted from eligible studies as number of events (stillbirth or neonatal death or individual neonatal morbidity outcome) and number of births/pregnancies by weekly gestational age
IX	Other inclusion exclusion criteria	Exclusions: • women with a quadruplet or higher-order pregnancy • studies where chorionicity is not specified or where results are not reported specifically for twin monochorionic, and/or twin dichorionic, and/or triplet pregnancies • studies that do not report results specifically for twin and/or triplet pregnancies • studies where amnionicity is not specified or where results are not reported specifically for monoamniotic or diamniotic in twin and/or triplet pregnancies • women with twin or triplet pregnancy where structural or chromosomal anomalies had been identified in one or more babies
X	Proposed sensitivity/sub-group analysis, or meta-regression	Stratified analysis by: • Amnionicity: ○ For twin pregnancies: - Monochorionic diamniotic - Monochorionic monoamniotic - Dichorionic diamniotic ○ For triplet pregnancies: - Dichorionic triamniotic - Monochorionic triamniotic - Dichorionic, diamniotic (a monochorionic twins set) - Monochorionic monoamniotic • Gestational age dependent on available evidence; for example: ○ <32 weeks' gestation ○ ≥32 weeks' gestation • Presence of complications

ID	Field (based on PRISMA-P)	Content
		○ Uncomplicated ○ Complicated pregnancies (including feto-fetal transfusion syndrome and/or pregnancies complicated by congenital abnormalities) Should evidence allow, the following stratified analysis will also be conducted: • Population: ○ High risk, for example smoking, high blood pressure, genetic factors ○ Not high risk
XI	Selection process – duplicate screening/selection/analysis	Formal duplicate screening will not be undertaken for this question (as it has not been prioritised for economic analysis), although there will be senior supervision of the selection process. Hard copies of retrieved papers will be read by 2 reviewers and any disputes will be resolved in discussion with the Topic Advisor. Data extraction will be supervised by a senior reviewer. Draft excluded studies and evidence tables will be discussed with the Topic Advisor, prior to circulation to the Topic Group for their comments. Resolution of disputes will be by discussion between the senior reviewer, Topic Advisor and Chair.
XII	Data management (software)	NGA STAR software will be used for generating bibliographies/citations, study sifting and data extraction and recording quality assessment using checklists. Meta-analyses will be performed using Cochrane Review Manager (RevMan5) and WinBugs if available data permit.
XIII	Information sources – databases and dates	Sources to be searched: Medline, Medline In-Process, CCTR, CDSR, DARE, HTA, Embase Search limits: • Limit to English language • Limit to human-only studies • Apply standard animal/non-English language exclusion
XIV	Identify if an update	A similar review was conducted for the previous guideline (CG129). However, the focus of the proposed review will be to identify evidence for the research question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in monochorionic (monoamniotic or diamniotic) / dichorionic (monoamniotic or diamniotic) twin and all triplet pregnancies? The research question in the review in the previous guideline (CG129) was: What is the incidence of perinatal and neonatal morbidity and mortality in babies born by elective birth in twin and triplet pregnancies? **Recommendations: 1.7 Timing of birth** 1.7.1.1 Discuss with women with twin and triplet pregnancies the timing of birth and possible modes of delivery] early in the third trimester.

ID	Field (based on PRISMA-P)	Content
		1.7.1.2 Inform women with twin pregnancies that about 60% of twin pregnancies result in spontaneous birth before 37 weeks 0 days. 1.7.1.3 Inform women with triplet pregnancies that about 75% of triplet pregnancies result in spontaneous birth before 35 weeks 0 days. 1.7.1.4 Inform women with twin and triplet pregnancies that spontaneous preterm birth and elective preterm birth are associated with an increased risk of admission to a special care baby unit. 1.7.1.5 Inform women with uncomplicated monochorionic twin pregnancies that elective birth from 36 weeks 0 days does not appear to be associated with an increased risk of serious adverse outcomes, and that continuing uncomplicated twin pregnancies beyond 38 weeks 0 days increases the risk of fetal death. 1.7.1.6 Inform women with uncomplicated dichorionic twin pregnancies that elective birth from 37 weeks 0 days does not appear to be associated with an increased risk of serious adverse outcomes, and that continuing uncomplicated twin pregnancies beyond 38 weeks 0 days increases the risk of fetal death. 1.7.1.7 Inform women with triplet pregnancies that continuing uncomplicated triplet pregnancies beyond 36 weeks 0 days increases the risk of fetal death. 1.7.1.8 Offer women with uncomplicated: monochorionic twin pregnancies elective birth from 36 weeks 0 days, after a course of antenatal corticosteroids has been offered dichorionic twin pregnancies elective birth from 37 weeks 0 days triplet pregnancies elective birth from 35 weeks 0 days, after a course of antenatal corticosteroids has been offered. [1] Antenatal care' (NICE clinical guideline 62) recommends determination of gestational age from 10 weeks 0 days. However, the aim in this recommendation is to keep to a minimum the number of scan appointments that women need to attend within a short time, especially if it is already known that a woman has a twin or triplet pregnancy. [6] Specific recommendations about mode of delivery are outside the scope of this guideline.
XV	Author contacts	Developer: National Guideline Alliance https://www.nice.org.uk/guidance/indevelopment/gid-ng10063
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual 2014
XVII	Search strategy – for one database	For details please see appendix B.

ID	Field (based on PRISMA-P)	Content
XVIII	Data collection process – forms/duplicate	A standardised evidence table format will be used, and published as appendix D (clinical evidence tables) or H (economic evidence tables).
XIX	Data items – define all variables to be collected	For details please see evidence tables in appendix D (clinical evidence tables) or H (economic evidence tables).
XX	Methods for assessing bias at outcome/study level	Quality assessment of individual studies will be performed using the following checklists: AMSTAR for systematic reviews, an adapted version of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn et al., 2015) for incidence studies. For details please see section 6.2 of Developing NICE guidelines: the manual 2014.
XXI	Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual 2014 A systematic review of observational studies that included meta-analysis has recently published so it is anticipated that quantitative synthesis will be possible. Data will be extracted from eligible studies as number of events (stillbirth or neonatal death or individual neonatal morbidity outcome) and number births/pregnancies by weekly gestational age. These will be presented in summary evidence tables and, where appropriate, narratively summarised. Meta-analyses will be conducted for this review only from studies of the same study design, and where the study populations assessed are from Organisation for Economic Co-operation and Development (OECD) countries. In all other cases, the results will be reported separately.
XXII	Methods for analysis – combining studies and exploring (in)consistency	For each outcome, the proportion of an event of interest (refer to Point VII) will be calculated as the number of events of interest divided by the total number of pregnancies/births. Standard errors and/or confidence intervals for a single proportion will be derived. The results will be plotted with their 95% confidence interval, plots in Review Manager, and if possible (see Point XXI), the results will be pooled. The forest plots will be used to visually see the studies alongside each other and to explore similarities and differences between them. Where possible (see Point XXI), the results will be pooled using a random-effects model and the Der Simonian & Laird method to derive the summary estimate. Prior to analysis, to incorporate the influence of study size on the outcome, adjusted proportions and standard errors will be calculated using a logit transformation. Heterogeneity will be assessed using the I^2 value. In cases of significant heterogeneity, potential sources of heterogeneity will be investigated. In addition, where data allow, the crude risk will be calculated by gestational weeks (≥32 weeks): **Crude** risk of stillbirth and neonatal mortality per 1000 pregnancies (95% CI) will be calculated based on the raw data (number of events of interest divided by the total

ID	Field (based on PRISMA-P)	Content
		number of pregnancies/births) reported for each individual study. **Crude** risk of neonatal morbidities per 1000 deliveries (95% CI) will be calculated based on the raw data (number of events of interest divided by the total number of pregnancies/births) reported for each individual study.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see section 6.2 of Developing NICE guidelines: the manual 2014. For this review no assessment for publication bias was conducted.
XXIV	Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual 2014
XXV	Rationale/context – Current management	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee developed the guideline. The committee was convened by the National Guideline Alliance and chaired by Anthony Pearson in line with section 3 of Developing NICE guidelines: the manual 2014. 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. A full description of this is provided in the methods in supplementary material C.
XXVII	Sources of funding/support	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
XXVIII	Name of sponsor	The National Guideline Alliance is funded by NICE and hosted by the Royal College of Obstetricians and Gynaecologists
XXIX	Roles of sponsor	NICE funds the National Guideline Alliance to develop guidelines for those working in the NHS, public health, and social care in England
XXX	PROSPERO registration number	This protocol is not registered with PROSPERO

AMSTAR: Assessing the Methodological Quality of Systematic Reviews; CCTR: Cochrane Controlled Trials Register; CDSR: Cochrane Database of Systematic Reviews; CI: confidence interval; DARE: Database of Abstracts of Reviews of Effects; HTA: Health Technology Assessment; NICE: National Institute for Health and Care Excellence; NGA: National Guideline Alliance

Appendix B – Literature search strategies

Literature search for review question: What is the incidence of stillbirth, neonatal death and morbidity by gestational age in monochorionic/dichorionic twin and triplet pregnancies according to amnionicity?

Focused Clinical Searches

Date of search: 06/11/2018

Database(s): Embase 1980 to 2018 Week 45, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November 05, 2018

Search Strategy:

#	Searches
1	exp Pregnancy, Multiple/ use ppez
2	exp multiple pregnancy/ use emez
3	((multiple* or twin* or triplet* or monozygotic or dizygotic or trizygotic) adj3 (birth* or pregnan* or gestation* or f?etus* or f?etal)).tw.
4	(monochorionic* or dichorionic* or trichorionic*).tw.
5	or/1-4
6	(monoamnio* or diamnio* or triamnio* or (amnio* and chorio*)).tw.
7	((amnio* or membrane* or placenta*) adj2 (share* or sharing)).tw.
8	6 or 7
9	5 and 8
10	exp Delivery, Obstetric/
11	exp Labor, Obstetric/
12	exp Parturition/
13	exp Obstetric Labor, Premature/
14	Stillbirth/
15	Pregnancy Outcome/
16	(or/10-15) use ppez
17	labor onset/
18	exp obstetric delivery/
19	exp childbirth/
20	birth/
21	exp "immature and premature labor"/
22	stillbirth/
23	pregnancy outcome/
24	(or/17-23) use emez
25	(deliver* or childbirth* or birth* or labo?r* or parturition or stillbirth* or outcome*).tw.
26	16 or 24 or 25
27	Letter/ use ppez
28	letter.pt. or letter/ use emez

#	Searches
29	note.pt.
30	editorial.pt.
31	Editorial/ use ppez
32	News/ use ppez
33	exp Historical Article/ use ppez
34	Anecdotes as Topic/ use ppez
35	Comment/ use ppez
36	Case Report/ use ppez
37	case report/ or case study/ use emez
38	(letter or comment*).ti.
39	or/27-38
40	randomized controlled trial/ use ppez
41	randomized controlled trial/ use emez
42	random*.ti,ab.
43	or/40-42
44	39 not 43
45	animals/ not humans/ use ppez
46	animal/ not human/ use emez
47	nonhuman/ use emez
48	exp Animals, Laboratory/ use ppez
49	exp Animal Experimentation/ use ppez
50	exp Animal Experiment/ use emez
51	exp Experimental Animal/ use emez
52	exp Models, Animal/ use ppez
53	animal model/ use emez
54	exp Rodentia/ use ppez
55	exp Rodent/ use emez
56	(rat or rats or mouse or mice).ti.
57	or/44-56
58	9 and 26
59	58 not 57
60	limit 59 to english language
61	remove duplicates from 60

Date of search: 01/11/2018

Database(s): The Cochrane Library, issue 11 of 12, November 2018: Cochrane Database of Systematic Reviews (CDSR), issue 11 of 12, November 2018; Cochrane Central Register of Controlled Trials (CCTR): issue 10 of 12, October 2018

ID	Search
#1	MeSH descriptor: [Pregnancy, Multiple] explode all trees
#2	((dizygotic or monozygotic or multiple or triplet* or trizygotic or twin) near/3 (birth* or foetus* or foetal or fetus* or fetal or gestation* or pregnan*))

ID	Search
#3	(monochorionic* or dichorionic* or trichorionic*)
#4	{or #1-#3}
#5	(monoamnio* or diamnio* or triamnio* or (amnio* and chorio*))
#6	((amnio* or membrane* or placenta*) near/2 (share* or sharing))
#7	#5 or #6
#8	#4 and #7
#9	MeSH descriptor: [Labor, Obstetric] explode all trees
#10	MeSH descriptor: [Delivery, Obstetric] explode all trees
#11	MeSH descriptor: [Parturition] explode all trees
#12	MeSH descriptor: [Obstetric Labor, Premature] explode all trees
#13	MeSH descriptor: [Stillbirth] this term only
#14	MeSH descriptor: [Pregnancy Outcome] this term only
#15	(birth* or childbirth or deliver* or labor* or labour* or parturition* or stillbirth* or outcome*)
#16	{or #9-#15}
#17	#8 and #16

Date of search: 01/11/2018

NIHR Centre for Reviews and Dissemination: Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA) and the NHS Economic Evaluation Database (NHS EED)

Search strategy:

ID	Search
1	MeSH DESCRIPTOR Pregnancy, Multiple EXPLODE ALL TREES
2	((monochorionic* or dichorionic* or trichorionic*)) IN DARE, NHSEED, HTA
3	((((dizygotic or monozygotic or multiple or triplet* or trizygotic or twin) near3 (birth* or foetus* or foetal or fetus* or fetal or gestation* or pregnan*)))) IN DARE, NHSEED, HTA
4	#1 OR #2 OR #3
5	((monoamnio* or diamnio* or triamnio* or (amnio* and chorio*))) IN DARE, NHSEED, HTA
6	(((amnio* or membrane* or placenta*) near2 (share* or sharing))) IN DARE, NHSEED, HTA
7	#5 OR #6
8	#4 AND #7

Health economics searches

For the Cochrane Library and CRD databases, see above

Date of search: 06/11/2018

Database(s): Embase 1980 to 2018 Week 45, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November 05, 2018

#	Searches
1	exp Pregnancy, Multiple/ use ppez
2	exp multiple pregnancy/ use emez
3	((multiple* or twin* or triplet* or monozygotic or dizygotic or trizygotic) adj3 (birth* or pregnan* or gestation* or f?etus* or f?etal)).tw.
4	(monochorionic* or dichorionic* or trichorionic*).tw.
5	or/1-4
6	(monoamnio* or diamnio* or triamnio* or (amnio* and chorio*)).tw.
7	((amnio* or membrane* or placenta*) adj2 (share* or sharing)).tw.
8	6 or 7
9	5 and 8
10	exp Delivery, Obstetric/
11	exp Labor, Obstetric/
12	exp Parturition/
13	exp Obstetric Labor, Premature/
14	Stillbirth/
15	Pregnancy Outcome/
16	(or/10-15) use ppez
17	labor onset/
18	exp obstetric delivery/
19	exp childbirth/
20	birth/
21	exp "immature and premature labor"/
22	stillbirth/
23	pregnancy outcome/
24	(or/17-23) use emez
25	(deliver* or childbirth* or birth* or labo?r* or parturition or stillbirth* or outcome*).tw.
26	16 or 24 or 25
27	Letter/ use ppez
28	letter.pt. or letter/ use emez
29	note.pt.
30	editorial.pt.
31	Editorial/ use ppez
32	News/ use ppez
33	exp Historical Article/ use ppez

#	Searches
34	Anecdotes as Topic/ use ppez
35	Comment/ use ppez
36	Case Report/ use ppez
37	case report/ or case study/ use emez
38	(letter or comment*).ti.
39	or/27-38
40	randomized controlled trial/ use ppez
41	randomized controlled trial/ use emez
42	random*.ti,ab.
43	or/40-42
44	39 not 43
45	animals/ not humans/ use ppez
46	animal/ not human/ use emez
47	nonhuman/ use emez
48	exp Animals, Laboratory/ use ppez
49	exp Animal Experimentation/ use ppez
50	exp Animal Experiment/ use emez
51	exp Experimental Animal/ use emez
52	exp Models, Animal/ use ppez
53	animal model/ use emez
54	exp Rodentia/ use ppez
55	exp Rodent/ use emez
56	(rat or rats or mouse or mice).ti.
57	or/44-56
58	9 and 26
59	58 not 57
60	limit 59 to english language
61	remove duplicates from 60

Supplementary Outcomes searches

Date of search: 08/11/2018

Database(s): Embase 1980 to 2018 Week 46, Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily 1946 to November 08, 2018

#	Searches
1	exp Pregnancy, Multiple/ use ppez
2	exp multiple pregnancy/ use emez

#	Searches
3	((multiple* or twin* or triplet* or monozygotic or dizygotic or trizygotic) adj3 (birth* or pregnan* or gestation* or f?etus* or f?etal)).tw.
4	(monochorionic* or dichorionic* or trichorionic*).tw.
5	or/1-4
6	(monoamnio* or diamnio* or triamnio* or (amnio* and chorio*)).tw.
7	Gestational Age/ use ppez
8	gestational age/ use emez
9	((foetal or fetal or foetus* or fetus* or gestation*) adj3 (age or maturity or mature or immatur* or growth or discordan*)).tw.
10	or/6-9
11	5 and 10
12	Fetal Death/
13	Fetal Mortality/
14	Stillbirth/
15	exp Obstetric Labor Complications/
16	Perinatal Death/
17	Perinatal Mortality/
18	Infant Mortality/
19	exp Respiratory Distress Syndrome, Newborn/
20	exp Respiration, Artificial/
21	Neonatal Sepsis/
22	exp Meningitis/
23	Bronchopulmonary Dysplasia/
24	Hypoxia-Ischemia, Brain/
25	Enterocolitis, Necrotizing/
26	Cerebral Intraventricular Hemorrhage/
27	Leukomalacia, Periventricular/
28	Retinopathy of Prematurity/
29	(or/12-28) use ppez
30	twin discordance/
31	fetus death/
32	fetus mortality/
33	stillbirth/
34	exp labor complication/
35	perinatal death/
36	exp perinatal mortality/
37	neonatal respiratory distress syndrome/
38	exp artificial ventilation/
39	newborn sepsis/
40	exp meningitis/
41	lung dysplasia/
42	hypoxic ischemic encephalopathy/

#	Searches
43	necrotizing enterocolitis/
44	brain hemorrhage/
45	leukomalacia/
46	retrolental fibroplasia/
47	(or/30-47) use emez
48	stillbirth.tw.
49	(death or dead or demise or mortality).tw.
50	((foetal or fetal or foetus* or fetus*) adj3 (loss* or outcome*)).tw.
51	((neonat* or preterm or prematur* or newborn or perinatal) adj3 (loss* or outcome* or morbidity or complication* or distress)).tw.
52	(sepsis or septic* or bacteri?emia or meningitis or encephalopath* or enterocolit* or h?emorrhag* or leu?omalac* or fibroplasi* or retinopath* or isch?emi* or respirat* distress* or respirat* insufficien* or ventilat*).tw.
53	(bronchopulmonary dysplas* or BPD).tw.
54	or/49-53
55	29 or 47 or 54
56	11 and 55
57	limit 56 to english language
58	Letter/ use ppez
59	letter.pt. or letter/ use emez
60	note.pt.
61	editorial.pt.
62	Editorial/ use ppez
63	News/ use ppez
64	exp Historical Article/ use ppez
65	Anecdotes as Topic/ use ppez
66	Comment/ use ppez
67	Case Report/ use ppez
68	case report/ or case study/ use emez
69	(letter or comment*).ti.
70	or/58-69
71	randomized controlled trial/ use ppez
72	randomized controlled trial/ use emez
73	random*.ti,ab.
74	or/71-73
75	70 not 74
76	animals/ not humans/ use ppez
77	animal/ not human/ use emez
78	nonhuman/ use emez
79	exp Animals, Laboratory/ use ppez
80	exp Animal Experimentation/ use ppez
81	exp Animal Experiment/ use emez

#	Searches
82	exp Experimental Animal/ use emez
83	exp Models, Animal/ use ppez
84	animal model/ use emez
85	exp Rodentia/ use ppez
86	exp Rodent/ use emez
87	(rat or rats or mouse or mice).ti.
88	or/75-87
89	57 not 88
90	limit 89 to yr="2015 -Current"
91	remove duplicates from 90

Date of search: 08/11/2018

Database(s): The Cochrane Library, issue 11 of 12, November 2018

ID	Search
#1	MeSH descriptor: [Pregnancy, Multiple] explode all trees
#2	((dizygotic or monozygotic or multiple or triplet* or trizygotic or twin) near/3 (birth* or foetus* or foetal or fetus* or fetal or gestation* or pregnan*))
#3	(monochorionic* or dichorionic* or trichorionic*)
#4	{or #1-#3}
#5	(monoamnio* or diamnio* or triamnio* or (amnio* and chorio*))
#6	((amnio* or membrane* or placenta*) near/2 (share* or sharing))
#7	MeSH descriptor: [Gestational Age] this term only
#8	((foetal or fetal or foetus* or fetus* or gestation*) near/3 (age or maturity or mature or immatur* or growth or discordan*))
#9	{or #5-#8}
#10	#4 and #9
#11	MeSH descriptor: [Fetal Death] this term only
#12	MeSH descriptor: [Fetal Mortality] this term only
#13	MeSH descriptor: [Stillbirth] this term only
#14	MeSH descriptor: [Obstetric Labor Complications] explode all trees
#15	MeSH descriptor: [Perinatal Death] this term only
#16	MeSH descriptor: [Perinatal Mortality] this term only
#17	MeSH descriptor: [Infant Mortality] this term only
#18	MeSH descriptor: [Respiratory Distress Syndrome, Newborn] explode all trees
#19	MeSH descriptor: [Respiration, Artificial] explode all trees
#20	MeSH descriptor: [Neonatal Sepsis] this term only
#21	MeSH descriptor: [Meningitis] explode all trees
#22	MeSH descriptor: [Bronchopulmonary Dysplasia] this term only
#23	MeSH descriptor: [Hypoxia-Ischemia, Brain] this term only
#24	MeSH descriptor: [Enterocolitis, Necrotizing] this term only

ID	Search
#25	MeSH descriptor: [Cerebral Intraventricular Hemorrhage] this term only
#26	MeSH descriptor: [Leukomalacia, Periventricular] this term only
#27	MeSH descriptor: [Retinopathy of Prematurity] this term only
#28	stillbirth
#29	(death or dead or demise or mortality)
#30	((foetal or fetal or foetus* or fetus*) near/3 (loss* or outcome*))
#31	((neonat* or preterm or prematur* or newborn or perinatal) near/3 (loss* or outcome* or morbidity or complication* or distress))
#32	(sepsis or septic* or bacteri?emia or meningitis or encephalopath* or enterocolit* or h?emorrhag* or leu?omalac* or fibroplasi* or retinopath* or isch?emi* or respirat* distress* or respirat* insufficien* or ventilat*)
#33	(bronchopulmonary dysplas* or BPD)
#34	{or #11-#33}
#35	#10 and #34 with Publication Year from 2015 to 2018, with Cochrane Library publication date Between Jan 2015 and Jan 2018, in Trials

Date of search: 08/11/2018

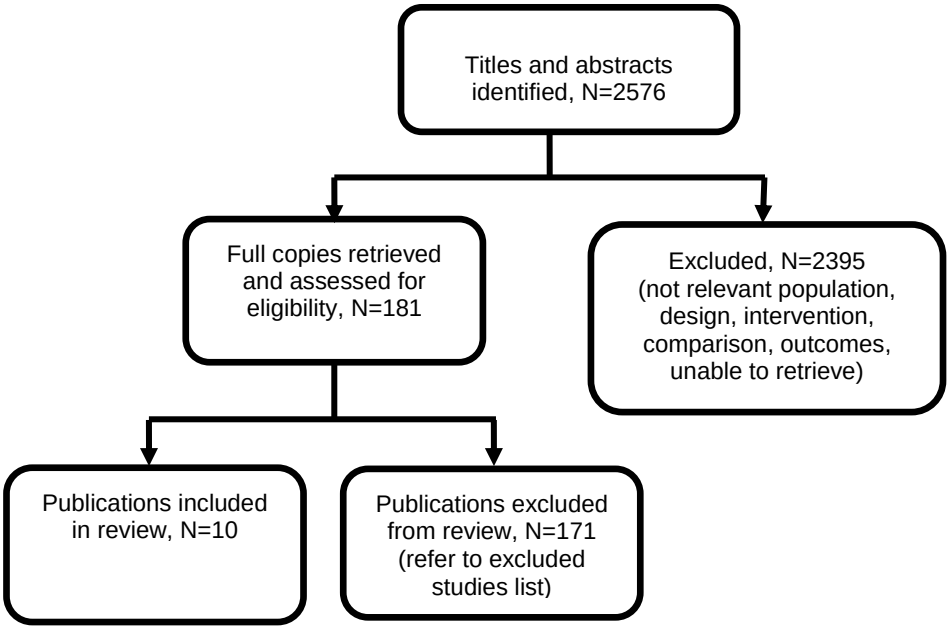
NIHR Centre for Reviews and Dissemination: Database of Abstracts of Reviews of Effects (DARE), Health Technology Assessment Database (HTA) and the NHS Economic Evaluation Database (NHS EED)

ID	Search
1	MeSH DESCRIPTOR Pregnancy, Multiple EXPLODE ALL TREES
2	((monochorionic* or dichorionic* or trichorionic*)) IN DARE, NHSEED, HTA
3	((((dizygotic or monozygotic or multiple or triplet* or trizygotic or twin) near3 (birth* or foetus* or foetal or fetus* or fetal or gestation* or pregnan*)))) IN DARE, NHSEED, HTA
4	#1 OR #2 OR #3
5	((monoamnio* or diamnio* or triamnio* or (amnio* and chorio*))) IN DARE, NHSEED, HTA
6	(((amnio* or membrane* or placenta*) near2 (share* or sharing))) IN DARE, NHSEED, HTA
7	(((foetal or fetal or foetus* or fetus* or gestation*) near3 (age or maturity or mature or immatur* or growth or discordan*))) IN DARE, NHSEED, HTA
8	MeSH DESCRIPTOR gestational age EXPLODE ALL TREES IN DARE,NHSEED,HTA
9	#5 OR #6 OR #7 OR #8
10	#4 AND #9
11	* IN DARE, NHSEED, HTA FROM 2015 TO 2018
12	* IN DARE, NHSEED, HTA WHERE LPD FROM 01/01/2015 TO 13/11/2018
13	#11 OR #12
14	#10 AND #13

Appendix C – Clinical evidence study selection

Clinical evidence study selection for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Figure 1: Flow diagram of clinical article selection for: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and all triplet pregnancies according to chorionicity and amnionicity?



Appendix D – Clinical evidence tables

Clinical evidence tables for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Ref Id
59698

Full citation
Baxi,L.V., Walsh,C.A., Monoamniotic twins in contemporary practice: A single-center study of perinatal outcomes, Journal of Maternal-Fetal and Neonatal Medicine, 23, 506-Fetal, 2010

Country/ies where the study was carried out
USA

Study type
Retrospective cohort study

Study dates
July 2001 - March 2009

Aim of the study</td>
<td>Sample size
n=25 MCMA twin pregnancies (>/=20 weeks GA)
only n=8/25 (16 neonates) with relevant data available: complicated MCMA twin pregnancies

Characteristics
All women were referred from other institutions.
All born by ceasarean section.
Nine women birthed because of non-reassuring fetal heart racing; 3 required emergency C-section.

Inclusion criteria</td>
<td>Outcome Measures (Definition Of)
Gestational age was determined by last menstrual period, embryo transfer date for in vitro fertilisation, or the earliest ultrasonogram for size–dates discrepancies greater than the margin of error.
Neonatal death: death in first 28 days after birth

Monitoring
MCMA pregnancies in study department are managed according to a strict antenatal protocol. First trimester screening for aneuploidy was offered at approx. 12weeks gestation. Second trimester ultrasound was offered at 16 and 19 weeks gestation to allow</td>
<td>Results
All MCMA pregnancies included in cohort study:
Liveborn n=49/50; stillborn (IUFD) n=1/50; Neonatal death n=3/50
Perinatal mortality rate PMR (Stillbirth+Neonatal death) n=4/50
Complicated MCMA twin pregnancies: n=8/25 (16 neonates assessed)
<table>
<tr><th>GA (Weeks)</th><th>Neonates born</th><th>IUFD n</th><th>Neonatal death n</th><th>NEC n</th></tr>
<tr><td>24</td><td>2</td><td>0</td><td>1</td><td>1</td></tr>
<tr><td>25</td><td>2</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>31</td><td>2</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>32</td><td>2</td><td>0</td><td>1</td><td>0</td></tr>
<tr><td>34</td><td>8</td><td>0</td><td>1</td><td>0</td></tr>
<tr><td>total</td><td>16</td><td>1</td><td>3</td><td>1</td></tr>
</table>
</td>
<td>Limitations
Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted):
1 Was the sample frame appropriate to address the target population? Yes - referral for MCMA pregnancy to a tertiary referral university institution
2 Were the study participants sampled in an appropriate way? Unclear - cases were identified on an ongoing basis and confirmed from a computerised perinatal database, but relevant data</td>
</tr>
</table>

Study Details	Participants	Methods	Results	Comments
examined perinatal outcomes among a cohort of MCMA twin gestations, who were managed in a single center using a consistent antenatal protocol	MCMA twin pregnancy referred to study hospital **Exclusion criteria** None reported	detailed fetal anomaly survey and detection of twin–twin transfusion syndrome (TTTS)		only available for 8/25 pregnancies (16 neonates) 3 Were the criteria for inclusion in the sample clearly defined? Yes 4 Were the study subjects and the setting described in detail? No - limited information regarding maternal and neonatal characteristics 5 Was the exposure measured in a valid and reliable way? Yes - used date of last menstrual period to establish gestational age 6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? yes 7 Other limitations - n/a

Study Details	Participants	Methods	Results	Comments
				Other information None **Source of funding** Not reported
Ref Id 743461 **Full citation** Berezowsky, A., Mazkereth, R., Ashwal, E., Mazaki-Tovi, S., Schiff, E., Weisz, B., Lipitz, S., Yinon, Y., Neonatal outcome of late preterm uncomplicated monochorionic twins: what is the optimal time for delivery?, Journal of Maternal-Fetal & Neonatal MedicineJ Matern Fetal Neonatal Med, 29, 1252-6, 2016 **Country/ies where the study was carried out** Israel	**Sample size** 166 **Characteristics** Not reported for overall population but by study group: 34 weeks (n=20) Maternal age, years median 31 (IQR 28-34) Smoking 0 (0) Parity 1 (0-1.75) Hypertensive disorders 6 (30.0%) 35 weeks (n=31) Maternal age, years median 31.5 (IQR 28-35) Smoking 0 (0) Parity 1 (0-2) Hypertensive disorders 10 (32.3%)	**Outcome Measures (Definition Of)** Neonatal Mortality (not reported [NR]) Stillbirth (NR) Neonatal Morbidity: Oxygen requirement (NR) Ventilation (NR) Respiratory distress syndrome (defined as early respiratory distress comprising of cyanosis, grunting, retractions and tachypnea combined with ground glass appearance and air bronchograms on chest X-ray) Intraventricular haemorrhage (NR) Necrotising enterocolitis (NEC) **Monitoring**	**Results** <u>Still birth</u> GA 34 wks (n=166 ongoing pregnancies/n=20 births), n (%): 0 (0) GA 35 wks (n=146 ongoing pregnancies/n=31 births), n (%): 0 (0) GA 36 wks (n=115 ongoing pregnancies/n=87 births), n (%): 0 (0) GA 37 wks (n=28 ongoing pregnancies/n=28 births), n (%): 0 (0) <u>Neonatal mortality</u> GA 34 wks (n=166 ongoing pregnancies/n=20 births), n (%): 0 (0) GA 35 wks (n=146 ongoing pregnancies/n=31 births), n (%): 0 (0) GA 36 wks (n=115 ongoing pregnancies/n=87 births), n (%): 0 (0) GA 37 wks (n=28 ongoing pregnancies/n=28 births), n (%): 0 (0)	**Limitations** Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted): 1 Was the sample frame appropriate to address the target population? Yes (uncomplicated monochorionic bi-amniotic (MCDA) twins born between 34 and 37 weeks' gestation at a single tertiary centre between the years of 2010 and 2012) 2 Were the study participants sampled in an appropriate way? Yes (All

Study type Retrospective Cohort **Study dates** 2010 and 2012 **Aim of the study** To determine the neonatal outcome at late prematurity of uncomplicated monochorionic (MC) twin pregnancies	36 weeks (n=87) Maternal age, years median 32 (IQR 29-35) Smoking 3.5 (3) Parity 1 (0-1) Hypertensive disorders 11 (12.6%) 37 weeks (n=28) Maternal age, years median 32 (IQR 27.5-35) Smoking 3.5 (1) Parity 1 (0-2) Hypertensive disorders 2 (7.1%) **Inclusion criteria** All women with uncomplicated MCDA twin pregnancies who received prenatal care <14 weeks' gestation and gave birth at >34 weeks' gestation **Exclusion criteria** Women with twin to twin transfusion syndrome (TTTS), selective intra-uterine	All women underwent ultrasound evaluation every 2 wks beginning at 16 weeks' gestation until birth. Ultrasound examination included fetal biometry, assessment of amniotic fluid volume in each amniotic sac and Doppler flow measurements (umbilical artery, MCA-PSV and ductus venosus). Non-stress test and ultrasound for biophysical score were done on a weekly basis starting at 32 weeks' gestation and twice per week from 34 weeks onwards	<u>Neonatal morbidities</u> 166 women with uncomplicated MC twin pregnancies GA 34 wks (n=40) Oxygen requirement, n (%): 12 (30.0) Ventilation, n (%): 1 (2.5) RDS, n (%): 4 (10.0) Sepsis, n (%): 1 (2.5) NEC, n (%): 0 (0) IVH, n (%)): 0 (0) GA 35 wks (n=62) Oxygen requirement, n (%): 5 (8.1) Ventilation, n (%): 2 (3.2) RDS, n (%): 1 (1.6) Sepsis, n (%): 2 (3.2) NEC, n (%): 1 (1.6) IVH, n (%): 0 (0) GA 36 wks (n=174) Oxygen requirement, n (%): 15 (8.6) Ventilation, n (%): 4 (2.3) RDS, n (%): 3 (1.7) Sepsis, n (%) 2 (1.1) NEC, n (%): 0 (0) IVH, n (%): 0 (0)	women with uncomplicated MCDA twin pregnancies who received prenatal care before 14 weeks' gestation and gave birth at our centre after 34 weeks' gestation) 3 Were the criteria for inclusion in the sample clearly defined? Yes 4 Were the study subjects and the setting described in detail? Yes 5 Was the exposure measured in a valid and reliable way? yes (ultrasound) 6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? Yes 7 Other limitations No

Study Details	Participants	Methods	Results	Comments
	growth restriction (sour) or twins anemia-polycythemia sequence (TAPS) as well as pregnancies complicated with congenital anomalies or chromosomal abnormalities or intra-uterine fetal death of one or both twin at presentation, and women who gave birth at <34 weeks' gestation		GA 37 wks (n=56) Oxygen requirement, n (%): 3 (5.4) Ventilation, n (%): 0 (0) RDS, n (%): 4 (10.0) Sepsis, n (%): 0 (0) NEC, n (%): 0 (0) IVH, n (%): 0 (0)	**Other information** None **Source of funding** Not reported
Ref Id 922174 **Full citation** Hack, K. E. A., Derks, J. B., Elias, S. G., Van Mameren, F. A., Koopman-Esseboom, C., Mol, B. W. J., Lopriore, E., Schaap, A. H. P., Arabin, B., Duvekot, J. J., Go, A. T. J. I., Wieselmann, E., Eggink, A. J., Willekes, C., Vandenbussche, F. P. H. A., Visser, G. H. A., Perinatal mortality and mode of delivery in monochorionic diamniotic	**Sample size** N=465 twin pregnancies; N=930 twin foetuses **Characteristics** Maternal age, median (range) years = 31 (17–47) Nulliparity, n (%) = 238 (51) Multiparity, n (%) = 227 (49): 1 = 152, 2 = 48, >2 = 27 (Selective) intrauterine growth restriction, n (%) = 59 (13)	**Outcome Measures (Definition Of)** Still birth (defined as an intrauterine fetal death (IUFD) occurring from 32 weeks of gestation). Stillbirths were divided in antepartum deaths, i.e. fetuses in which death was known before onset of labour, and intrapartum fetal deaths, i.e. fetuses that were alive at the start of labour. Perinatal mortality (defined as IUFD or early neonatal death (within 8 days after birth).	**Results** Stillbirth (defined as antepartum deaths, i.e. fetuses in which death was known before onset of labour, and intrapartum fetal deaths, i.e. fetuses that were alive at the start of labour) Stillbirth among MCDA (the majority of the pregnancies in this study were uncomplicated pregnancies) twin gestations from 32 weeks of gestation (n=465 twin pregnancies, n=930 neonates): 32 wks = 1/465 ongoing pregnancies or /66 no of infants born at this GA 33 wks = 2/432 ongoing pregnancies or /70 no of infants born at this GA 34 wks = 0/397 ongoing pregnancies or /80 no of infants born at this GA	**Limitations** Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted): 1. Was the sample frame appropriate to address the target population? Yes 2. Were the study participants sampled in an appropriate way? Yes (all monochorionic twin pregnancies without

Study Details	Participants	Methods	Results	Comments
twin pregnancies >=32 weeks of gestation: A multicentre retrospective cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 118, 1090-1097, 2011 **Country/ies where the study was carried out** the Netherlands **Study type** Retrospective cohort **Study dates** Between January 2000 and December 2005 **Aim of the study** To assess perinatal mortality rates of monochorionic diamniotic (MCDA) twins not complicated by twin-twin transfusion syndrome (TTTS)	**Inclusion criteria** All monochorionic twins without twin-twin transfusion syndrome born at 32 weeks of gestation or later; also only twin pregnancies in which both fetuses were alive at 32 weeks of gestation. **Exclusion criteria** Monoamniotic pregnancies, pregnanci es complicated by TTTS, majorajor lethal chromosomal and congenital malformations and other pregnancies resulting in birth before 32 weeks of gestation.	Early neonatal death (defined as death of an infant during the first 7 days of life). Late neonatal death (defined as death between 8 and 28 days after birth). **Monitoring** All twin pregnancies were monitored according to a standard protocol, which consisted of a 1st trimester determination of chorionicity, a detailed anomaly scan at 20 weeks of gestational age, and regular ultrasound assessment of growth, amniotic fluid volume and Doppler of the umbilical artery at least at 20, 24 and 28 weeks and fortnightly thereafter.	35 wks = 0/357 ongoing pregnancies or /118 no of infants born at this GA 36 wks = 0/298 ongoing pregnancies or /178 no of infants born at this GA 37 wks = 2/209 ongoing pregnancies or /236 no of infants born at this GA 38 wks = 0/91 ongoing pregnancies or /138 no of infants born at this GA 39 wks = 0/22 ongoing pregnancies or /28 no of infants born at this GA >40 wks = 0/8 ongoing pregnancies or /16 no of infants born at this GA Perinatal mortality (defined as IUFD or early neonatal death (within 8 days after birth)) Perinatal mortality among MCDA (the majority of the pregnancies in this study were uncomplicated pregnancies) twin gestations from 32 weeks of gestation (n=465 twin pregnancies, n=930 neonates): 32 wks = 2/465 ongoing pregnancies or /66 no of infants born at this GA 33 wks = 2/432 ongoing pregnancies or /70 no of infants born at this GA 34 wks = 1/397 ongoing pregnancies or /80 no of infants born at this GA 35 wks = 0/357 ongoing pregnancies or /118 no of infants born at this GA 36 wks = 0/298 ongoing pregnancies or /178 no of infants born at this GA	twin-twin transfusion syndrome born at >=32 weeks of gestation between January 2000 and December 2005 in all 10 perinatal referral centres in the Netherlands) 3. Were the criteria for inclusion in the sample clearly defined? Yes 4. Were the study subjects and the setting described in detail? Yes 5. Was the exposure measured in a valid and reliable way? Yes 6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? Yes 7. Other limitations No

Study Details	Participants	Methods	Results	Comments
			37 wks = 2/209 ongoing pregnancies or /236 no of infants born at this GA 38 wks = 0/91 ongoing pregnancies or /138 no of infants born at this GA 39 wks = 0/22 ongoing pregnancies or /28 no of infants born at this GA >40 wks = 1/8 ongoing pregnancies or /16 no of infants born at this GA Early neonatal death (defined as death of an infant during the first 7 days of life) Early neonatal death among MCDA (the majority of the pregnancies in this study were uncomplicated pregnancies) twin gestations from 32 weeks of gestation (n=465 twin pregnancies, n=930 neonates): 32 wks = 1/465 ongoing pregnancies or /66 no of infants born at this GA 33 wks = 0/432 ongoing pregnancies or /70 no of infants born at this GA 34 wks = 1/397 ongoing pregnancies or /80 no of infants born at this GA 35 wks = 0/357 ongoing pregnancies or /118 no of infants born at this GA 36 wks = 0/298 ongoing pregnancies or /178 no of infants born at this GA 37 wks = 0/209 ongoing pregnancies or /236 no of infants born at this GA 38 wks = 0/91 ongoing pregnancies or /138 no of infants born at this GA	**Other information** None **Source of funding** None

Study Details	Participants	Methods	Results	Comments
			39 wks = 0/22 ongoing pregnancies or /28 no of infants born at this GA >40 wks = 1/8 ongoing pregnancies or /16 no of infants born at this GA Late neonatal death (defined as death between 8 and 28 days after birth) Late neonatal death among MCDA (the majority of the pregnancies in this study were uncomplicated pregnancies) twin gestations from 32 weeks of gestation (n=465 twin pregnancies, n=930 neonates): 32 wks = 0/465 ongoing pregnancies or /66 no of infants born at this GA 33 wks = 0/432 ongoing pregnancies or /70 no of infants born at this GA 34 wks = 3/397 ongoing pregnancies or /80 no of infants born at this GA 35 wks = 0/357 ongoing pregnancies or /118 no of infants born at this GA 36 wks = 0/298 ongoing pregnancies or /178 no of infants born at this GA 37 wks = 2/209 ongoing pregnancies or /236 no of infants born at this GA 38 wks = 0/91 ongoing pregnancies or /138 no of infants born at this GA 39 wks = 0/22 ongoing pregnancies or /28 no of infants born at this GA >40 wks = 0/8 ongoing pregnancies or /16 no of infants born at this GA	

Study Details	Participants	Methods	Results	Comments
Ref Id 922220 **Full citation** Lee, H. J., Kim, S. H., Chang, K. H., Sung, J. H., Choi, S. J., Oh, S. Y., Roh, C. R., Kim, J. H., Gestational age at delivery and neonatal outcome in uncomplicated twin pregnancies: what is the optimal gestational age for delivery according to chorionicity?, Obstet Gynecol SciObstetrics & gynecology science, 59, 9-16, 2016 **Country/ies where the study was carried out** South Korea **Study type** Retrospective cohort **Study dates** From January 1995 to December 2013	**Sample size** N=697 twin pregnancies **Characteristics** Monochorionic diamniotic (MCDA) = 25% (171/697); dichorionic diamniotic (DCDA) = 75% (526/697). Maternal age, mean (SD) years: 35 wks = 32.8±4.7; 36 wks = 31.8±3.8; 37 wks = 31.9±3.4; 38 wks = 31.8±3.9; >=39 wks = 30.1±3.2 Multiparity, number (%): 35 wks = 23 (38.3); 36 wks = 59 (25.5); 37 wks = 79 (25.5); 38 wks = 16 (20.3); >=39 wks = 5 (29.4) **Inclusion criteria** All women with uncomplicated monochorionic and dichorionic twin	**Outcome Measures (Definition Of)** Fetal death in utero (not defined). Neonatal mortality (not defined). Perinatal mortality (not defined). Respiratory distress syndrome (RDS) (defined as the presence of respiratory grunting and retracting, an increased oxygen requirement (FiO2 >0.4) combined with ground-glass appearance and air bronchograms on chest X-ray. Mechanical ventilator support (not defined). **Monitoring** Not reported	**Results** Fetal death in utero (not defined) Fetal death among uncomplicated MCDA twin gestations from 35 weeks of gestation (n=171 pregnancies): 35 wks = 1/20 pregnancies 36 wks = 0/61 pregnancies 37 wks = 0/68 pregnancies 38 wks = 0/16 pregnancies >=39 wks = 0/6 pregnancies Fetal death among uncomplicated DCDA twin gestations from 35 weeks of gestation (n=526 pregnancies): 35 wks = 1/40 pregnancies 36 wks = 0/170 pregnancies 37 wks = 2/242 pregnancies 38 wks = 0/63 pregnancies >=39 wks = 0/11 pregnancies Perinatal mortality (not defined) Fetal death among uncomplicated MCDA twin gestations from 35 weeks of gestation (n=171 pregnancies): 35 wks = 1/20 pregnancies 36 wks = 1/61 pregnancies 37 wks = 0/68 pregnancies 38 wks = 0/16 pregnancies >=39 wks = 1/6 pregnancies	**Limitations** Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted): 1. Was the sample frame appropriate to address the target population? Yes 2. Were the study participants sampled in an appropriate way? Yes (all women with uncomplicated monochorionic and dichorionic twin pregnancies who gave birth at a tertiary referral hospital in Seoul, Korea from January 1995 to December 2013 after 35 weeks of gestation) 3. Were the criteria for inclusion in the

Study Details	Participants	Methods	Results	Comments
Aim of the study To analyse the neonatal outcome according to gestational age at birth in uncomplicated twin pregnancies based on the Korean data in order to determine the optimal time for birth in uncomplicated monochorionic and dichorionic twin pregnancies	pregnancies who gave birth at the author's center after 35 weeks of gestation. **Exclusion criteria** Twin pregnancies complicated by twin-to-twin transfusion syndrome, monoamniotic twins, discordant twins, intrauterine fetal growth restriction, preterm labour, preterm premature rupture of membranes, placenta abruption, placenta previa, hypertension (gestational hypertensio n, preeclampsia, eclampsia, superimposed preeclampsia, and chronic hypertension), diabetes (gestational diabetes and overt diabetes), presence of other severe maternal medical diseases, fetal death		Fetal death among uncomplicated DCDA twin gestations from 35 weeks of gestation (n=526 twin pregnancies): 35 wks = 1/40 pregnancies 36 wks = 0/170 pregnancies 37 wks = 2/242 pregnancies 38 wks = 0/63 pregnancies >=39 wks = 0/11 pregnancies Neonatal mortality (not defined) Fetal death among uncomplicated MCDA twin gestations from 35 weeks of gestation (n=171 pregnancies): 35 wks = 0/20 pregnancies 36 wks = 1/61 pregnancies 37 wks = 0/68 pregnancies 38 wks = 0/16 pregnancies >=39 wks = 1/6 pregnancies Fetal death among uncomplicated DCDA twin gestations from 35 weeks of gestation (n=526 pregnancies): 35 wks = 0/40 pregnancies 36 wks = 0/170 pregnancies 37 wks = 0/242 pregnancies 38 wks = 0/63 pregnancies >=39 wks = 0/11 pregnancies Respiratory distress syndrome (RDS) (defined as the presence of respiratory grunting and retracting, an increased oxygen requirement	sample clearly defined? Yes 4. Were the study subjects and the setting described in detail? Yes 5. Was the exposure measured in a valid and reliable way? Unclear (not reported) 6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? No (outcomes not defined) 7. Other limitations No **Other information** None **Source of funding** This study was supported in part by the Korea Health

Study Details	Participants	Methods	Results	Comments
	before 35 weeks of gestation or chromosomal anomalies or major congenital malformations in one or more of twins. Major fetal congenital malformation was defined as that requires medical or surgical treatment after birth. Discordant twin was defined as intertwin weight discordance of > 20%.		(FiO2 >0.4) combined with ground-glass appearance and air bronchograms on chest X-ray) Fetal death among uncomplicated MCDA twin gestations from 35 weeks of gestation (n=171 pregnancies): 35 wks = 2/20 pregnancies 36 wks = 0/61 pregnancies 37 wks = 0/68 pregnancies 38 wks = 0/16 pregnancies >=39 wks = 0/6 pregnancies Fetal death among uncomplicated DCDA twin gestations from 35 weeks of gestation (n=526 pregnancies): 35 wks = 4/40 pregnancies 36 wks = 1/170 pregnancies 37 wks = 0/242 pregnancies 38 wks = 0/63 pregnancies >=39 wks = 0/11 pregnancies Mechanical ventilator support (not defined) Fetal death among uncomplicated MCDA twin gestations from 35 weeks of gestation (n=171 pregnancies): 35 wks = 2/20 pregnancies 36 wks = 2/61 pregnancies 37 wks = 1/68 pregnancies 38 wks = 0/16 pregnancies >=39 wks = 1/6 pregnancies	Technology R&D Project through the Korea Health Industry Development Institute, funded by the Ministry of Health and Welfare, Republic of Korea (grant no. HI14C0306)

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>Fetal death among uncomplicated DCDA twin gestations from 35 weeks of gestation (n=526 pregnancies):
35 wks = 5/40 pregnancies
36 wks = 4/170 pregnancies
37 wks = 2/242 pregnancies
38 wks = 0/63 pregnancies
>=39 wks = 0/11 pregnancies</td><td></td></tr>
<tr><td>Ref Id
922246

Full citation
Masheer, S., Islam, Z., Dileep, D., Munim, S., Twin chorionicity and prospective stillbirth risk: Experience at a tertiary care hospital, Journal of the Pakistan Medical Association, 67, 360-364, 2017

Country/ies where the study was carried out
Pakistan

Study type
Retrospective cohort study</td><td>Sample size
544 cases of multiple pregnancies; 394 (72.4%) twin pregnancies met inclusion criteria:
n=84 MCDA (168 babies) 21.3%
n=310 DCDA (620 babies) 78.7%

Characteristics
Approx. one-third of women giving birth at the facility are high-risk pregnancies, as the unit serves as a referral centre for its four secondary care hospitals.
mean maternal age: MCDA 28.15±4.45</td><td>Outcome Measures (Definition Of)
Stillbirths: intrauterine fetal death between 25 weeks gestation and birth.
Neonatal death: death of liveborn infant within 28 days of life.
Neonatal morbidities: respiratory morbidities (respiratory distress syndrome, transient tachypnoea of newborn, pneumothorax, and intubation/mechanical ventilation), necrotising enterocolitis and sepsis

Monitoring
Chorionicity was determined mainly before 14 weeks and not beyond</td><td>Results
STILLBIRTH (risk as %)<table><tr><td>GA (Weeks)</td><td>MCDA twins</td><td>DCDA twins</td></tr><tr><td>25</td><td>5.9</td><td>1.9</td></tr><tr><td>26</td><td>3.7</td><td>1.0</td></tr><tr><td>27</td><td>3.7</td><td>1.6</td></tr><tr><td>28</td><td>3.7</td><td>1.6</td></tr><tr><td>29</td><td>3.7</td><td>1.7</td></tr><tr><td>30</td><td>3.7</td><td>1.3</td></tr><tr><td>31</td><td>0</td><td>1.4</td></tr><tr><td>32</td><td>0</td><td>1.1</td></tr><tr><td>33</td><td>0</td><td>0.4</td></tr><tr><td>34</td><td>0</td><td>0.4</td></tr><tr><td>35</td><td>0</td><td>0</td></tr></table></td><td>Limitations
Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted):
1 Was the sample frame appropriate to address the target population? yes - from (private-sector) tertiary referral centre with maternal-fetal sub-specialty (high risk: unit serves as a referral centre for its four secondary care hospitals)
2 Were the study participants sampled</td></tr>
</table>

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>Study dates
January 2001 - December 2012

Aim of the study
Assess the adverse perinatal outcomes, in particular the stillbirth and neonatal complications, and their association with gestational age.</td>
<td>years, DCDA 28.51±4.80 years
mean gestational age at birth: MCDA 34.76±2.70 weeks, DCDA 35.43±2.60 weeks
mean birth weight: MCDA 2,047.15±509.8 grams, DCDA 2,204.68±535.1 grams

Inclusion criteria
Twin pregnancies referred to study hospital in study period

Exclusion criteria
gestational age <25 weeks, higher order multiple gestation, monoamniotic twins, referral beyond 20 weeks, major congenital abnormalities compatible with life and those without documentation of</td>
<td>20 weeks by ultrasound assessment.
Gestational age was determined by patient's last menstrual period and confirmed by ultrasound dating scan.
Growth discordance was defined as difference in birth weight of more than 20% discrepancy.
Data was collected on a structured proforma and was retrieved from the hospital medical records, labour room management system and NICU records. The database included the demographic details, obstetric information including parity, caesarean section rates between two groups of twins and caesarean section during labour, and neonatal variables.</td>
<td>
<table>
<tr><td>36</td><td>0</td><td>0</td></tr>
<tr><td>>/=37</td><td>0</td><td>0</td></tr>
</table>
PERINATAL DEATH
<table>
<tr><td>GA (weeks)</td><td>MCDA twins</td><td>DCDA twins</td></tr>
<tr><td>25</td><td>2.3</td><td>0</td></tr>
<tr><td>26</td><td>0</td><td>0.6</td></tr>
<tr><td>27</td><td>0.6</td><td>0.2</td></tr>
<tr><td>28</td><td>0</td><td>0</td></tr>
<tr><td>29</td><td>0</td><td>0.9</td></tr>
<tr><td>30</td><td>1.9</td><td>0.2</td></tr>
<tr><td>31</td><td>0</td><td>0.2</td></tr>
<tr><td>32</td><td>0</td><td>0.5</td></tr>
<tr><td>33</td><td>0</td><td>0.2</td></tr>
<tr><td>34</td><td>0</td><td>0.2</td></tr>
<tr><td>35</td><td>0.9</td><td>0</td></tr>
<tr><td>36</td><td>0</td><td>0</td></tr>
<tr><td>>/=37</td><td>0</td><td>0</td></tr>
</table>
MORBIDITIES
MCDA twins
</td>
<td>in an appropriate way? yes
3 Were the criteria for inclusion in the sample clearly defined? yes - exclusions clearly defined
4 Were the study subjects and the setting described in detail? yes - reported overall maternal characteristics, and by chorionicity
5 Was the exposure measured in a valid and reliable way? yes - Gestational age was determined by patient's last menstrual period and confirmed by ultrasound dating scan
6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across</td>
</tr>
</table>

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td></td>
<td>chorionicity in early pregnancy</td>
<td></td>
<td>
<table>
<tr><th>GA (weeks)</th><th>n (neonates born)</th><th>Respiratory n(%)</th><th>Sepsis n(%)</th><th>NEC n(%)</th></tr>
<tr><td>25</td><td>4</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>26</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>27</td><td>2</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>28</td><td>0</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>29</td><td>2</td><td>2 (100)</td><td>1 (50)</td><td>0</td></tr>
<tr><td>30</td><td>8</td><td>4 (50)</td><td>0</td><td>2 (25)</td></tr>
<tr><td>31</td><td>4</td><td>4 (100)</td><td>3 (75)</td><td>1 (25)</td></tr>
<tr><td>32</td><td>2</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>33</td><td>14</td><td>2 (14.3)</td><td>0</td><td>0</td></tr>
<tr><td>34</td><td>24</td><td>4 (16.7)</td><td>1 (4.2)</td><td>0</td></tr>
<tr><td>35</td><td>32</td><td>3 (9.4)</td><td>1 (2.8)</td><td>1 (2.8)</td></tr>
<tr><td>36</td><td>34</td><td>1 (3)</td><td>0</td><td>0</td></tr>
<tr><td>>/=37</td><td>42</td><td>1 (2.5</td><td>0</td><td>0</td></tr>
</table>
DCDA twins
</td>
<td>all study participants? yes - stillbirth, neonatal mortality, neonatal morbidities clearly defined
7 Other limitations
No

Other information
None

Source of funding
None</td>
</tr>
</table>

Study Details	Participants	Methods	Results	Comments

GA (weeks)	n (neonates born)	Respiratory n(%)	Sepsis n(%)	NEC n(%)
25	0	0	0	0
26	6	5 (83.3)	3 (50)	1 (20)
27	6	5 (83.3)	2 (33.3)	1 (16.7)
28	2	2 (100)	2 (100)	0
29	12	8 (66.7)	4 (33.3)	1 (8.3)
30	14	8 (57.1)	4 (33.3)	1 (7.1)
31	12	6 (50)	0	0
32	30	6 ((20)	0	1 (3.1)
33	26	5 (19.2)	1 (3.8)	1 (3.8)
34	60	3 (5)	1 (1.7)	0
35	72	2 (2.8)	1 (1.4)	0
36	108	0	0	0

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>>/=37</td><td>270</td><td>1 (0.4)</td><td>0</td><td>0</td></tr>
</table>
</td><td></td></tr>
<tr><td>Ref Id
922250

Full citation
Morikawa, M., Yamada, T., Sato, S., Cho, K., Minakami, H., Prospective risk of stillbirth: Monochorionic diamniotic twins vs. dichorionic twins, Journal of Perinatal MedicineJ Perinat Med, 40, 245-249, 2012

Country/ies where the study was carried out
Japan

Study type
Retrospective cohort study

Study dates
2005 – 2008

Aim of the study</td><td>Sample size
MCDA twin pregnancies n=3241
DCDA twin pregnancies n=6581

Characteristics
Maternal age: MCDA 30.5 SD 4.8 years; DCDA 32.3 SD 4.6 years
GA at birth: MCDA 34.6 SD 3.3 weeks; DCDA 35.3 SD 2.8 weeks
Sum of infant weight: MCDA 4052 SD 1083 grams; DCDA 4343 SD 954 grams

Inclusion criteria
Birth occurred at ≥ 22 weeks of gestation

Exclusion criteria
unspecified chorionicity of the placenta,</td><td>Outcome Measures (Definition Of)
live-born/stillborn (SB=stillbirth)
early neonatal death (END) within 7 days of life

Monitoring
Physicians are required to determine chorionicity of the placenta with ultrasound by the end of 10th week of gestation in Japan</td><td>Results
Stillbirth (SB) & Early Neonatal Death (END) & alive
MCDA twins
<table>
<tr><th>GA (weeks)</th><th>SB neonates n</th><th>END neonates n</th><th>alive neonates n</th><th>total neonates n</th></tr>
<tr><td>22</td><td>15</td><td>5</td><td>0</td><td>20</td></tr>
<tr><td>23</td><td>11</td><td>7</td><td>16</td><td>34</td></tr>
<tr><td>24</td><td>13</td><td>5</td><td>28</td><td>46</td></tr>
<tr><td>25</td><td>10</td><td>7</td><td>37</td><td>54</td></tr>
<tr><td>26</td><td>5</td><td>11</td><td>78</td><td>94</td></tr>
<tr><td>27</td><td>7</td><td>5</td><td>88</td><td>100</td></tr>
<tr><td>28</td><td>5</td><td>3</td><td>128</td><td>136</td></tr>
<tr><td>29</td><td>8</td><td>2</td><td>140</td><td>150</td></tr>
<tr><td>30</td><td>5</td><td>1</td><td>150</td><td>156</td></tr>
<tr><td>31</td><td>8</td><td>2</td><td>176</td><td>186</td></tr>
<tr><td>32</td><td>8</td><td>2</td><td>272</td><td>282</td></tr>
<tr><td>33</td><td>4</td><td>6</td><td>316</td><td>326</td></tr>
</table>
</td><td>Limitations
Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted):
1 Was the sample frame appropriate to address the target population? Yes
2 Were the study participants sampled in an appropriate way? Yes - successive births at >/=22weeks GA
3 Were the criteria for inclusion in the sample clearly defined? Yes
4 Were the study subjects and the setting described in detail? Yes
5 Was the exposure measured in a valid and reliable way?</td></tr>
</table>

Study Details	Participants	Methods	Results	Comments
determine reliably the risk of stillbirth among twin pregnancies	MCMA twin pregnancies, MCDA and undetermined sex in one twin or unlike sex (female-male) pairs, DCDA and undetermined sex in one twin			Unclear how gestational age was assessed 6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? yes 7 Other limitations No **Other information** None **Source of funding** Not reported

34	1	2	533	536
35	3	1	768	772
36	3	4	1435	1442
37	4	3	1649	1656
38	1	1	388	390
39	0	1	77	78
40	0	0	24	24
41	0	0	0	0
total n	111	68	6303	6482

DCDA twins

GA (weeks)	SB neonates n	END neonates n	alive neonates	total neonates n
22	4	9	11	24
23	8	14	34	56
24	0	8	64	72
25	1	4	71	76
26	1	4	67	72
27	3	2	113	118
28	3	4	119	126

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>
<table>
<tr><td>29</td><td>5</td><td>5</td><td>178</td><td>188</td></tr>
<tr><td>30</td><td>6</td><td>2</td><td>190</td><td>198</td></tr>
<tr><td>31</td><td>4</td><td>1</td><td>251</td><td>256</td></tr>
<tr><td>32</td><td>5</td><td>2</td><td>383</td><td>390</td></tr>
<tr><td>33</td><td>4</td><td>1</td><td>583</td><td>588</td></tr>
<tr><td>34</td><td>5</td><td>5</td><td>932</td><td>942</td></tr>
<tr><td>35</td><td>7</td><td>3</td><td>1488</td><td>1498</td></tr>
<tr><td>36</td><td>7</td><td>7</td><td>2968</td><td>2982</td></tr>
<tr><td>37</td><td>7</td><td>2</td><td>4171</td><td>4180</td></tr>
<tr><td>38</td><td>5</td><td>1</td><td>1092</td><td>1098</td></tr>
<tr><td>39</td><td>2</td><td>1</td><td>221</td><td>224</td></tr>
<tr><td>40</td><td>1</td><td>1</td><td>68</td><td>70</td></tr>
<tr><td>41</td><td>0</td><td>0</td><td>4</td><td>4</td></tr>
<tr><td>total n</td><td>78</td><td>76</td><td>13008</td><td>13162</td></tr>
</table>
</td><td></td></tr>
<tr><td>Ref Id
744863

Full citation
Wood, S., Tang, S., Ross, S., Sauve, R., Stillbirth in twins, exploring the optimal</td><td>Sample size
n=17,724 twin births (8,862 twin sets); The study authors were unable to obtain placental type on live births (only indirectly estimate the number of</td><td>Outcome Measures (Definition Of)
stillbirth: death in utero at ≥20 weeks of gestation or with a stillborn birthweight of ≥500 grams</td><td colspan="2">Results
Overall incidence:
Stillbirths and neonatal deaths: n=506 (Antepartum stillbirths: n=236; Intrapartum stillbirths: n=26; Neonatal deaths: n=244)
Neonatal death: 14.0/1000 live births
Survived past 28 days: n=17,218</td><td>Limitations
Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted):</td></tr>
</table>

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>gestational age for delivery: a retrospective cohort study, BJOG: An International Journal of Obstetrics & GynaecologyBjog, 121, 1284-90; discussion 1291, 2014

Country/ies where the study was carried out
Canada

Study type
Retrospective cohort study

Study dates
1992 – 2007

Aim of the study
the optimal gestational age at birth for twins</td>
<td>MCDA and DCDA twins), however only data on stillbirths (where chorionicity has been confirmed) has been extracted

Characteristics
live birth n= 17429; antepartum stillbirth n=202
Maternal age >/=35years: live birth 19.4%; stillbirth 20.3%; or 10.5
Weight >91kg: live birth 9%; stillbirth 8.2%; or 0.90
smoking: livebirth 16.3%; stillbirth 18.8%; or 1.19

Inclusion criteria
all twin pregnancies in the years 1992–2007 in which the fetuses survived until ≥23 weeks of gestation

Exclusion criteria</td>
<td>neonatal death: demise following live birth up to 28 days of age
Chorionicity for stillbirths was based on the database placental pathology codes and data from the chart review of the provincial Reproductive Care Committee files. If a discrepancy was found then the Reproductive Care Committee files were considered to be correct. If chorionicity was not documented but the twins were of discordant sexes, then the twins were assumed to be dichorionic, otherwise chorionicity was considered to be unknown

Monitoring
Use of a database: demographic, birth, and pregnancy outcome data for over 600,000 births from 81 hospitals in Alberta, Canada. Perinatal and birth records of all perinatal deaths are</td>
<td>STILLBIRTH (ANTEPARTUM) RISK (Risk of antepartum stillbirth in twins by gestational age per 1000 fetuses at risk, excluding deaths with congenital anomaly)
<table>
<tr><th>GA (weeks) at death</th><th>total</th><th>DCDA n</th><th>MCDA n</th><th>MCMA n</th><th>unknown chorio n</th></tr>
<tr><td><23</td><td>17</td><td>5</td><td>4</td><td>7</td><td>1</td></tr>
<tr><td>23</td><td>16</td><td>4</td><td>9</td><td>0</td><td>3</td></tr>
<tr><td>24</td><td>21</td><td>1</td><td>9</td><td>3</td><td>8</td></tr>
<tr><td>25</td><td>21</td><td>4</td><td>9</td><td>8</td><td>0</td></tr>
<tr><td>26</td><td>19</td><td>6</td><td>10</td><td>3</td><td>0</td></tr>
<tr><td>27</td><td>10</td><td>0</td><td>6</td><td>4</td><td>0</td></tr>
<tr><td>28</td><td>10</td><td>1</td><td>6</td><td>3</td><td>0</td></tr>
<tr><td>29</td><td>8</td><td>2</td><td>3</td><td>1</td><td>2</td></tr>
<tr><td>30</td><td>9</td><td>4</td><td>3</td><td>2</td><td>0</td></tr>
<tr><td>31</td><td>11</td><td>2</td><td>4</td><td>4</td><td>1</td></tr>
<tr><td>32</td><td>10</td><td>5</td><td>1</td><td>2</td><td>2</td></tr>
<tr><td>33</td><td>10</td><td>6</td><td>3</td><td>1</td><td>0</td></tr>
<tr><td>34</td><td>7</td><td>4</td><td>3</td><td>0</td><td>0</td></tr>
<tr><td>35</td><td>3</td><td>0</td><td>3</td><td>0</td><td>0</td></tr>
</table>
</td>
<td>1 Was the sample frame appropriate to address the target population? Yes
2 Were the study participants sampled in an appropriate way? Yes
3 Were the criteria for inclusion in the sample clearly defined? Yes
4 Were the study subjects and the setting described in detail? Yes - the study authors were unable to obtain placental type on live births. Therefore, they could only indirectly estimate the number of MCDA and DCDA twins. However, only data for stillbirths has been used
5 Was the exposure measured in a valid and reliable way? Unclear - gestational</td>
</tr>
</table>

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr>
<td></td>
<td>Triplet pregnancies, twin pregnancies for which siblings could not be matched, and those with unknown gestational age</td>
<td>reviewed by the hospital Perinatal Mortality Committees and then forwarded for further review to the provincial Reproductive Care Committee
Data was available on the gestational age at diagnosis of stillbirth (GA at death, not GA at birth), though there is often a delay between when a death occurs and when clinicians or women recognise it; however, as women are usually being seen frequently at term the study authors state that the inaccuracies would be limited during this critical period of time</td>
<td>
<table>
<tr><td>36</td><td>5</td><td>4</td><td>1</td><td>0</td><td>0</td></tr>
<tr><td>37</td><td>5</td><td>1</td><td>3</td><td>0</td><td>1</td></tr>
<tr><td>38</td><td>17</td><td>7</td><td>10</td><td>0</td><td>0</td></tr>
<tr><td>39</td><td>3</td><td>1</td><td>1</td><td>0</td><td>1</td></tr>
<tr><td>40</td><td>0</td><td></td><td></td><td></td><td></td></tr>
<tr><td>41</td><td>0</td><td></td><td></td><td></td><td></td></tr>
<tr><td>42</td><td>0</td><td></td><td></td><td></td><td></td></tr>
</table>
ESTIMATED STILLBIRTH RATE
<table>
<tr><th>GA at death (completed weeks)</th><th>MCDA stillbirth n fetuses at risk (n/1000)</th><th>DCDA stillbirth n fetuses at risk (n/1000)</th></tr>
<tr><td>36</td><td>2076 (0.48/1000)</td><td>7359 (0.54/1000)</td></tr>
<tr><td>37</td><td>1299 (2.3/1000)</td><td>4605 (0.22/1000)</td></tr>
<tr><td>38</td><td>540 (17.4/1000)</td><td>1914 (3.7/1000)</td></tr>
</table>
</td>
<td>age not always measurable in cases of stillbirth: in cases where a clear determination of the gestational age at diagnosis of stillbirth could not be made, the gestational age at birth was used
6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? No - data for stillbirth clearly reported, data for neonatal death unclear whether refers to MCDA, DCDA, or all twin-type combined result.
7 Other limitations No

Other information
No</td>
</tr>
</table>

Study Details	Participants	Methods	Results	Comments
				Source of funding The authors' research group (Partnership for Research and Education in Mothers and Infants) is supported by an unrestricted grant from Abbott Nutrition
Ref Id 236682 **Full citation** Breathnach,F.M., McAuliffe,F.M., Geary,M., Daly,S., Higgins,J.R., Dornan,J., Morrison,J.J., Burke,G., Higgins,S., Dicker,P., Manning,F., Carroll,S., Malone,F.D., Optimum timing for planned delivery of uncomplicated monochorionic and dichorionic twin pregnancies, Obstetrics and Gynecology, 119, 50-59, 2012 **Country/ies where the study was carried out**	**Sample size** N=1001 twin pregnancies Relevant data presented only for uncomplicated pregnancies: 66% (131/200) of monochorionic twins (who attained a gestational age of 34 weeks with an uncomplicated pregnancy at that point) and 71% (565/801) of dichorionic twins (who were uncomplicated at 36 weeks) **Characteristics**	**Outcome Measures (Definition Of)** Perinatal mortality (defined as death of a fetus/neonate weighing at least 500 g or who attained a gestational age of at least 24 completed weeks, occurring either in utero or within the first 7 days of life). Monitoring All women meeting inclusion criteria underwent intensive fetal surveillance carried out by dedicated trained research ultrasonographers using standardised ultrasound equipment which included biometry, placental	**Results** Perinatal mortality (defined as death of a fetus/neonate weighing at least 500 g or who attained a gestational age of at least 24 completed weeks, occurring either in utero or within the first 7 days of life). Perinatal mortality among apparently uncomplicated MCDA twin gestations from 34 weeks of gestation (n=131 twin pregnancies): 34^{+0}–34^{+6} wks = 2/131 pregnancies 35^{+0}–35^{+6} wks = 2/118 pregnancies 36^{+0}–36^{+6} wks = 1/96 pregnancies 37^{+0}–37^{+6} wks = 0/49 pregnancies 38 or more wks = 0/11 pregnancies Perinatal mortality among apparently uncomplicated DCDA twin gestations from 36 weeks of gestation (n=565 twin pregnancies): 36^{+0}–36^{+6} wks = 0/not reported 37^{+0}–37^{+6} wks = 0/not reported	**Limitations** Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted): 1. Was the sample frame appropriate to address the target population? Yes 2. Were the study participants sampled in an appropriate way? Yes (all twin pregnancies presenting to 8 study centers between 11 and 22 completed

Study Details	Participants	Methods	Results	Comments
Ireland **Study type** Prospective cohort **Study dates** May 2007 to October 2009 **Aim of the study** To identify the optimum gestational age for elective birth of apparently uncomplicated monochorionic and dichorionic twin pregnancies by determining the neonatal risk associated with elective birth at each gestational age in the late-third trimester, and to ascertain the prospective risk of death or severe perinatal morbidity in ongoing pregnancies	Monochorionic diamniotic (MCDA) = 20% (200/1001); dichorionic diamniotic (DCDA) = 80% (801/1001). MCDA: Maternal age, mean years = 31.3 Parity, 1 or more births = 93 (47%) Twin–twin transfusion syndrome = 20 (10%) DCDA: Maternal age, mean years = 33.0 Parity, 1 or more births = 405 (51%) Twin–twin transfusion syndrome = not applicable **Inclusion criteria** All twin pregnancies presenting to the study centers between 11 and 22 completed weeks of gestation, with both fetuses being alive at the time of	location and number, fetal Doppler measurements, and cord insertion site. 2 wk growth scans were performed from 16 wks of gestation until birth for monochorionic twin pairs and from 24 wks of gestation in dichorionic pregnancies. Umbilical arterial and middle cerebral arterial Doppler waveforms were recorded in addition to standard biometry (abdominal circumference, biparietal diameter, head circumference, femur length) and documentation of the deepest vertical pocket of amniotic fluid in each sac.	38 or more wk = 0/not reported	weeks of gestation) 3. Were the criteria for inclusion in the sample clearly defined? Yes 4. Were the study subjects and the setting described in detail? Yes 5. Was the exposure measured in a valid and reliable way? Unclear (not reported) 6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? Yes 7. Other limitations No **Other information** None **Source of funding**

Study Details	Participants	Methods	Results	Comments
	enrolment, with intact membranes. Apparently uncomplicated twin pregnancies - pregnancies were considered uncomplicated in the setting of fetal growth that was appropriate for gestational age (>10th centile), with normal amniotic fluid volume/umbilical artery Doppler evaluation in both twins on pre-labour ultrasonography and in the absence of a maternal or fetal indication for labour **Exclusion criteria** Monoamniotic twins; cases of prenatally identified twin–twin transfusion syndrome were excluded from the analysis. Also confirmed or suspected major fetal			Supported by a grant from Health Research Board of Ireland (Grant Code IMA/2005/3)

Study Details	Participants	Methods	Results	Comments
	abnormality, rupture of membranes or fetal demise recognized at the time of consideration for enrolment			
Ref Id 924422 **Full citation** Burgess, Jennifer L, Unal, Elizabeth R, Nietert, Paul J, Newman, Roger B, Risk of late-preterm stillbirth and neonatal morbidity for monochorionic and dichorionic twins, American Journal of Obstetrics and Gynecology, 210, 578. e1-578. e9, 2014 **Country/ies where the study was carried out** USA **Study type** Retrospective cohort **Study dates** From 1987 to 2010	**Sample size** N=768 twin pregnancies; N=1536 fetuses Characteristics Monochorionic diamniotic (MCDA) = 22% (167/768); dichorionic diamniotic (DCDA) = 78% (601/768). MCDA: Maternal age, median (range) years = 25 (16-44) Parity, median (range) = 1 (0-7) DCDA: Maternal age, median (range) years = 28 (15-47) Parity, median (range) = 1 (0-9)	**Outcome Measures (Definition Of)** Stillbirth (defined as an intrauterine fetal death (IUFD) between 34 weeks' gestation and birth). Neonatal death (defined as the death of a live-born infant by 28 days of life). Respiratory morbidity (includes use of any respiratory support device or supplemental oxygen outside the labour room and those babies with a stated diagnosis of transient tachypnea of the newborn infant or respiratory distress syndrome). Sepsis or sepsis work up (not defined).	**Results** Stillbirth (defined as an intrauterine fetal death (IUFD) between 34 weeks' gestation and birth). Perinatal mortality among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=167 twin pregnancies): 34^{+0}-34^{+6} wks = 0/167 ongoing pregnancies 35^{+0}-35^{+6} wks = 0/136 ongoing pregnancies 36^{+0}-36^{+6} wks = 0/94 ongoing pregnancies 37^{+0}-37^{+6} wks = 0/58 ongoing pregnancies 38^{+0}-38^{+6} wks = 0/20 ongoing pregnancies >39 wks = 0/3 ongoing pregnancies Perinatal mortality among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=601 twin pregnancies): 34^{+0}-34^{+6} wks = 1/601 ongoing pregnancies 35^{+0}-35^{+6} wks = 0/491 ongoing pregnancies 36^{+0}-36^{+6} wks = 0/358 ongoing pregnancies 37^{+0}-37^{+6}wks = 0/240 ongoing pregnancies 38^{+0}-38^{+6} wks = 0/99 ongoing pregnancies >39 wks = 0/22 ongoing pregnancies	**Limitations** Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted): 1. Was the sample frame appropriate to address the target population? Yes 2. Were the study participants sampled in an appropriate way? Yes (all dichorionic and monochorionic twins at >=34 weeks' gestation who were born at the Medical University of South Carolina (MUSC) from 1987-2010)

Study Details	Participants	Methods	Results	Comments
Aim of the study To determine the prospective risk for stillbirth among continuing monochorionic and dichorionic twin gestations in the late preterm and early term gestational age time periods	**Inclusion criteria** All dichorionic and monochorionic twins at >=34 weeks' gestation who were born at the Medical University of South Carolina from 1987-2010 **Exclusion criteria** Gestational age <34 weeks, monoamnionicity, aneuploidy, fetal anomalies that require prolonged hospitalisation or immediate surgery, co-twin death at <34 weeks' gestation, or unknown chorionicity	Necrotising enterocolitis (not defined). Intraventricular haemorrhage defined as any grade only) **Monitoring** Twin gestations were managed in a standardised fashion following protocols that were established by the supervising Maternal-Fetal Medicine specialist. Since the inception of the Twin Clinic, 3rd trimester fetal surveillance has included ultrasonographic surveillance of fetal growth, growth discordance, and amniotic fluid volumes at least every 4 weeks. Since 2005, monochorionic twins have undergone ultrasound surveillance at least every 3 weeks. Umbilical artery Doppler assessment was not used routinely for ultrasonographic fetal assessment.	Neonatal death (defined as the death of a live-born infant by 28 days of life). Neonatal death among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=167 twin pregnancies): 34^{+0}-34^{+6} wks = 0/167 ongoing pregnancies 35^{+0}-35^{+6} wks = 0/136 ongoing pregnancies 36^{+0}-36^{+6} wks = 0/94 ongoing pregnancies 37^{+0}-37^{+6} wks = 0/58 ongoing pregnancies 38^{+0}-38^{+6} wks = 0/20 ongoing pregnancies >39 wks = 0/3 ongoing pregnancies Neonatal death among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=167 twin pregnancies): 34^{+0}-34^{+6} wks = 1/601 ongoing pregnancies 35^{+0}-35^{+6} wks = 2/491 ongoing pregnancies 36^{+0}-36^{+6} wks = 1/358 ongoing pregnancies 37^{+0}-37^{+6} wks = 0/240 ongoing pregnancies 38^{+0}-38^{+6} wks = 0/99 ongoing pregnancies >39 wks = 0/22 ongoing pregnancies Respiratory morbidity (includes use of any respiratory support device or supplemental oxygen outside the labour room and those babies with a stated diagnosis of transient tachypnea of the newborn infant or respiratory distress syndrome).	3. Were the criteria for inclusion in the sample clearly defined? Yes 4. Were the study subjects and the setting described in detail? Yes 5. Was the exposure measured in a valid and reliable way? Yes 6. Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? Yes 7. Other limitations No **Other information** No **Source of funding** Supported by grant number UL1TR000062 from the National Center

Study Details	Participants	Methods	Results	Comments
		Weekly non-stress testing has been initiated routinely at 32 weeks' gestation for monochorionic twins and 34 weeks' gestation for dichorionic twins, unless earlier surveillance was indicated. All twins were seen on a weekly basis after 34 weeks' gestation.	Respiratory morbidity among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=334 neonates): 34^{+0}-34^{+6} wks = 13/62 neonates born 35^{+0}-35^{+6} wks = 13/84 neonates born 36^{+0}-36^{+6} wks = 4/72 neonates born 37^{+0}-37^{+6} wks = 5/76 neonates born 38^{+0}-38^{+6} wks = 2/34 neonates born >39 wks = 0/6 neonates born Respiratory morbidity among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=1202 neonates): 34^{+0}-34^{+6} wks = 71/220 neonates born 35^{+0}0-35^{+6} wks = 47/266 neonates born 36^{+0}-36^{+6} wks = 37/236 neonates born 37^{+0}-37^{+6} wks = 21/282 neonates born 38^{+0}-38^{+6} wks = 11/154 neonates born >39 wks = 3/44 neonates born Sepsis or sepsis work-up among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=334 neonates): 34^{+0}-34^{+6} wks = 23/62 neonates born 35^{+0}-35^{+6} wks = 25/84 neonates born 36^{+0}-36^{+6} wks = 7/72 neonates born 37^{+0}-37^{+6} wks = 5/76 neonates born 38^{+0}-38^{+6} wks = 4/34 neonates born >39 wks = 1/6 neonates born	for Advancing Translational Scienc es

Study Details	Participants	Methods	Results	Comments
			Sepsis or sepsis work-up among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=1202 neonates): 34^{+0}-34^{+6} wks = 123/220 neonates born 35^{+0}-35^{+6} wks = 71/266 neonates born 36^{+0}-36^{+6} wks = 38/236 neonates born 37^{+0}-37^{+6} wks = 19/282 neonates born 38^{+0}-38^{+6} wks = 12/154 neonates born >39 wks = 7/44 neonates born Necrotising enterocolitis (not defined) among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=334 neonates): 34^{+0}-34^{+6} wks = 1/62 neonates born 35^{+0}-35^{+6} wks = 0/84 neonates born 36^{+0}-36^{+6} wks = 0/72 neonates born 37^{+0}-37^{+6} wks = 0/76 neonates born 38^{+0}-38^{+6} wks = 0/34 neonates born >39 wks = 0/6 neonates born Necrotising enterocolitis (not defined) among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=1202 neonates): 34^{+0}-34^{+6} wks = 2/220 neonates born 35^{+0}-35^{+6} wks = 0/266 neonates born 36^{+0}-36^{+6} wks = 0/236 neonates born 37^{+0}-376 wks = 0/282 neonates born 38^{+0}-38^{+6} wks = 0/154 neonates born >39 wks = 0/44 neonates born	

<table>
<tr><th>Study Details</th><th>Participants</th><th>Methods</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>Intraventricular haemorrhage (any grade) among uncomplicated MCDA twin gestations from 34 weeks of gestation (n=334 neonates):
34^{+0}-34^{+6} wks = 1/62 neonates born
35^{+0}-35^{+6} wks = 0/84 neonates born
36^{+0}-36^{+6} wks = 0/72 neonates born
37^{+0}-37^{+6} wks = 0/76 neonates born
38^{+0}-38^{+6} wks = 0/34 neonates born
>39 wks = 0/6 neonates born
Intraventricular haemorrhage (any grade) among uncomplicated DCDA twin gestations from 34 weeks of gestation (n=1202 neonates):
34^{+0}-34^{+6} wks = 3/220 neonates born
35^{+0}-35^{+6} wks = 2/266 neonates born
36^{+0}-36^{+6} wks = 3/236 neonates born
37^{+0}-37^{+6} wks = 1/282 neonates born
38^{+0}-38^{+6} wks = 0/154 neonates born
>39 wks = 0/44 neonates born</td><td></td></tr>
<tr><td>Ref Id
744694

Full citation
Sung, J. H., Kim, S. H., Kim, Y. M., Kim, M. N., Lee, H. R., Lee, H. J., Lee, E. J., Choi, S. J., Oh, S. Y., Roh, C. R., Kim, J. H., Neonatal outcomes of twin</td><td>Sample size
n=1198 twin pregnancies included in final study:
MCDA n=302; DCDA n=896

Characteristics
Maternal age (years):</td><td>Outcome Measures (Definition Of)
Gestational age was calculated by the woman's last menstrual period or date of fertilization in those undergoing assisted reproduction techniques (ART). When the menstrual date was</td><td>Results
Number of twin births<table><tr><td>GA (weeks)</td><td>MCDA n</td><td>DCDA n</td></tr><tr><td>34</td><td>34</td><td>114</td></tr><tr><td>35</td><td>63</td><td>119</td></tr><tr><td>36</td><td>93</td><td>256</td></tr><tr><td>37</td><td>87</td><td>313</td></tr></table></td><td>Limitations
Risk of bias was assessed using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies (Adapted):
1 Was the sample frame appropriate to</td></tr>
</table>

<table>
<tr>
<th>Study Details</th>
<th>Participants</th>
<th>Methods</th>
<th>Results</th>
<th>Comments</th>
</tr>
<tr>
<td>pregnancies delivered at late-preterm versus term gestation based on chorionicity and indication for delivery, Journal of Perinatal Medicine, 44, 903-911, 2016

Country/ies where the study was carried out
South Korea

Study type
Retrospective cohort study

Study dates
1994 – 2014

Aim of the study
compare the neonatal outcomes of twin pregnancies delivered at late-preterm
to those delivered at term gestation based on chorionicity and indication for birth</td>
<td>MCDA (34-37wks) 30.9 SD 4 (n=190); MCDA (37+wks) 30.4 SD 3.1 (n=112);
DCDA (34-37wks) 32.4 SD 4 (n=489); DCDA (37+wks) 32.4 SD 3.5 (n=407)
GA at birth (weeks):
MCDA (34-37wks) 35.7 SD 0.8 (n=190); MCDA (37+wks) 37.6 SD 0.7 (n=112);
DCDA (34-37wks) 35.7 SD 0.9 (n=489); DCDA (37+wks) 37.6 SD 0.6 (n=407)

Inclusion criteria
twin pregnancies having both twin fetuses alive at 34 weeks of gestation and born at or beyond 34 weeks of gestation

Exclusion criteria
pregnancies complicated by twin-to-twin transfusion syndrome (TTTS),</td>
<td>unreliable or discordant with the first-trimester ultrasound measurements, ultrasound-based dating criteria were used.
Neonatal outcome measures included sex, birthweight, the Apgar scores, necessity of admission to neonatal intensive care unit (NICU), necessity of mechanical ventilator treatment, respiratory distress syndrome (RDS), transient tachypnea of newborn (TTN), hypoglycaemia, hyperbilirubinemia, hypothermia and neonatal mortality.
RDS was diagnosed as the presence of respiratory grunting and retracting, an increased oxygen requirement (FiO2 > 0.4) combined with ground-glass appearance, and air bronchograms on chest radiographs

Monitoring</td>
<td>
<table>
<tr><td>38</td><td>19</td><td>78</td></tr>
<tr><td>>/=39</td><td>6</td><td>16</td></tr>
</table>
Fetal, neonatal, perinatal death
MCDA
<table>
<tr><td>GA (weeks)</td><td>ongoing pregnancies n</td><td>fetal death n (%)</td><td>neonatal death n (%)</td><td>perinatal death n (%)</td></tr>
<tr><td>34</td><td>302</td><td>1 (0.33)</td><td>0</td><td>1 (0.33)</td></tr>
<tr><td>35</td><td>268</td><td>3 (1.12)</td><td>0</td><td>3 (1.12)</td></tr>
<tr><td>36</td><td>205</td><td>0</td><td>1 (0.49)</td><td>1 (0.49)</td></tr>
<tr><td>37</td><td>112</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>38</td><td>25</td><td>0</td><td>0</td><td>0</td></tr>
<tr><td>>/=39</td><td>6</td><td>0</td><td>1 (16.67)</td><td>1 (16.67)</td></tr>
<tr><td>total</td><td>302</td><td>4 (1.32)</td><td>2 (0.66)</td><td>6 (1.99)</td></tr>
</table>
DCDA
<table>
<tr><td>GA (weeks)</td><td>ongoing pregnancies n</td><td>fetal death n (%)</td><td>neonatal death n (%)</td><td>perinatal death n (%)</td></tr>
<tr><td>34</td><td>896</td><td>0</td><td>1 (0.11)</td><td>1 (0.11)</td></tr>
</table>
</td>
<td>address the target population? Yes
2 Were the study participants sampled in an appropriate way? Yes - consecutive twin pregnancies in study hospital
3 Were the criteria for inclusion in the sample clearly defined? Yes
4 Were the study subjects and the setting described in detail? Yes
5 Was the exposure measured in a valid and reliable way? Yes
6 Were the outcome measures clearly defined, valid, reliable, and implemented consistently across all study participants? yes
7 Other limitations No</td>
</tr>
</table>

Study Details	Participants	Methods	Results	Comments
	monoamniotic twins, fetal death before 34 weeks of gestation or chromosomal anomalies or major congenital malformation in one or both twins, and unknown chorionicity	Chorionicity was determined by early ultrasonographic findings such as gestational sac number, placental number, the presence of either “twin-peak” or “T” sign, and fetal sex, which was later confirmed through pathologic examination of the placenta.	35 / 782 / 1 (0.13) / 0 / 1 (1.13) 36 / 663 / 0 / 1 (0.15) / 1 (0.15) 37 / 407 / 2 (0.49) / 0 / 2 (0.49) 38 / 94 / 0 / 0 / 0 >/=39 / 16 / 0 / 0 / 0 total / 896 / 3 (0.33) / 2 (0.22) / 5 (0.56)	**Other information** None **Source of funding** Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI14C0306)

Appendix E – Forest plots

Forest plots for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

No meta-analysis was undertaken for this review and so there are no forest plots. Available data were plotted graphically and these graphs are presented in appendix M.

Appendix F – GRADE tables

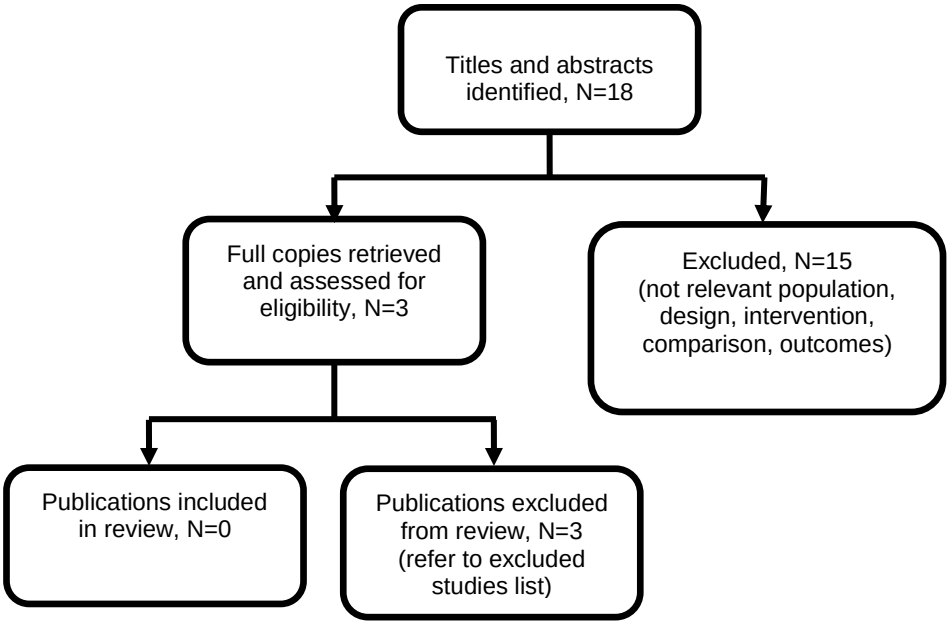
GRADE tables for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Not applicable. Risk of bias was assessed using an adapted an adapted version of the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (Munn 2015) for incidence studies.

Appendix G – Economic evidence study selection

Economic evidence study selection for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Figure 2: Flow diagram of economic article selection for the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and all triplet pregnancies according to chorionicity and amniocity



Appendix H – Economic evidence tables

Economic evidence tables for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Table 23: Health economic evidence tables for interventions that are effective in preventing spontaneous preterm birth in twin and triplet pregnancy

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
CG129 England, Wales and Northern Ireland Cost utility analysis Conflict of interest: none Funding: This work was undertaken by the now defunct National Collaborating Centre for Women's and Children's Health (subsumed within the	Elective birth was assumed to occur at a gestational age of 37+0 weeks versus expectant management	Women with a multiple pregnancy Modelling: "What-if" economic evaluation Source of clinical effectiveness data: Minakami (1996) for stillbirth rates by gestational age and Suzuki (2000) for respiratory morbidity by gestational age costs: N/A – the "what-if" model considered the incremental costs of the intervention that would be	Incremental QALY gain of elective birth: • 0.278 QALYs	Elective birth cost-effective if incremental costs ≤ £5,560 Sensitivity analysis: A probabilistic sensitivity analysis suggested there was a 89.6% probability that elective birth would generate a QALY gain compared to expectant management	Perspective: NHS Currency: GBP Cost year: 2011 Time horizon: Lifetime Discounting: QALYs discounted at 3.5% Applicability: directly applicable Quality: potentially serious limitations

Study Country Study type	Intervention details	Study population Study design Data sources	Costs: description and values Outcomes: description and values	Results: Cost-effectiveness	Comments
National Guideline Alliance from 1 April 2016), which received funding from the National Institute for Health and Care Excellence (NICE).		consistent with cost effectiveness			

Appendix I – Economic evidence profiles

Economic evidence profiles for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Table 24: Health economic evidence profile for interventions that are effective in preventing spontaneous preterm birth in twin and triplet pregnancy

Study	Limitations	Applicability	Other comments	Costs	Effects	Incremental cost effectiveness	Uncertainty
CG 129 England, Wales and Northern Ireland	Potentially serious limitations[1,2,3]	Directly applicable	Cost utility analysis Outcome measure: QALYs derived from stillbirth and respiratory morbidity rates	N/A	0.278 QALY gain per birth	Elective birth at a gestational age of 37+0 weeks was cost effective compared to expectant management for incremental costs ≤ £5,560	Estimates of effect from non-randomised studies have a high risk of bias and therefore point estimates and confidence intervals may not capture an accurate estimate of true effect. However, the bias is likely to favour the comparator as birth is more likely to be expedited if there are complications or concerns

1. Clinical evidence based on observational population-based studies
2. Study population was mainly women with dichorionic twin pregnancies and therefore sub-group analysis was not possible for monochorionic twin pregnancies or triplets
3. Model did not explicitly cost different strategies

Appendix J – Economic analysis

Economic analysis for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

No economic analysis was conducted for this review.

Appendix K – Excluded studies

Excluded studies for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

Clinical studies

Study	Reason for Exclusion
Prospective risk of late stillbirth in monochorionic twins: a regional cohort study, Ultrasound in Obstetrics & GynecologyUltrasound Obstet Gynecol, 39, 500-4, 2012	Data not reported by weekly gestational age
Aboulghar,M.M., Aboulghar,M.A., Amin,Y.M., Al-Inany,H.G., Mansour,R.T., Serour,G.I., The use of vaginal natural progesterone for prevention of preterm birth in IVF/ICSI pregnancies, Reproductive Biomedicine Online, 25, 133-138, 2012	Randomised controlled trial (RCT) intervention examining effect of progesterone in singleton and twin pregnancies
Adegbite,A.L., Ward,S.B., Bajoria,R., Perinatal outcome of spontaneously conceived triplet pregnancies in relation to chorionicity, American Journal of Obstetrics and Gynecology, 193, 1463-1471, 2005	No relevant data by gestational age
Al-Riyami, N., Al-Rusheidi, A., Al-Khabori, M., Perinatal outcome of monochorionic in comparison to dichorionic twin pregnancies, Oman Medical Journal, 28, 173-177, 2013	Outcomes reported fortnightly for gestational age, not weekly
Anselem, O., Mephon, A., Le Ray, C., Marcellin, L., Cabrol, D., Goffinet, F., Continued pregnancy and vaginal delivery after 32 weeks of gestation for monoamniotic twins, European Journal of Obstetrics, Gynecology, & Reproductive BiologyEur J Obstet Gynecol Reprod Biol, 194, 194-8, 2015	Presents relevant outcomes by weekly gestational age in graphical annotation only
Argoti, P. S., Papanna, R., Bebbington, M. W., Kahlek, N., Baschat, A., Johnson, A., Moise, K. J., Jr., Outcome of fetoscopic laser ablation for twin-to-twin transfusion syndrome in dichorionic-triamniotic triplets compared with monochorionic-diamniotic twins, Ultrasound in Obstetrics & Gynecology, 44, 545-9, 2014	No relevant outcomes by gestational age
Assuncao, R. A., Liao, A. W., Brizot Mde, L., Krebs, V. L., Zugaib, M., Perinatal outcome of twin pregnancies delivered in a teaching hospital, Revista Da Associacao Medica Brasileira, 56, 447-51, 2010	Data not reported by weekly gestational age
Awwad,J., Usta,I.M., Ghazeeri,G., Yacoub,N., Succar,J., Hayek,S., Saasouh,W., Nassar,A.H., A randomised controlled double-blind clinical trial of 17-hydroxyprogesterone caproate for the prevention of preterm birth in twin gestation (PROGESTWIN): evidence for reduced neonatal morbidity, BJOG: An International Journal of Obstetrics and Gynaecology, 122, 71-79, 2015	Not a study design outlined in the protocol
Bajoria,R., Ward,S.B., Adegbite,A.L., Comparative study of perinatal outcome of dichorionic and trichorionic iatrogenic triplets, American Journal of Obstetrics and Gynecology, 194, 415-424, 2006	Data not reported by weekly gestational age
Bardin, R., Oron, G., Levy, Y., Sapir, O., Meizner, I., Fisch, B., Wiznitzer, A., Hadar, E., First-trimester inter- and intrafetal	No relevant data by gestational age

Study	Reason for Exclusion
size discrepancies in bichorionic twins conceived by in vitro fertilization: can it predict pregnancy outcome?, Fertility and Sterility, 108, 296-301, 2017	
Barigye, O., Pasquini, L., Galea, P., Chambers, H., Chappell, L., Fisk, N. M., High risk of unexpected late fetal death in monochorionic twins despite intensive ultrasound surveillance: a cohort study, PLoS Medicine / Public Library of Science, 2, e172, 2005	Data not reported by weekly gestational age
Barrett, J. F., Hannah, M. E., Hutton, E. K., Willan, A. R., Allen, A. C., Armson, B. A., Gafni, A., Joseph, K. S., Mason, D., Ohlsson, A., Ross, S., Sanchez, J. J., Asztalos, E. V., A randomized trial of planned cesarean or vaginal delivery for twin pregnancy, N Engl J MedThe New England journal of medicine, 369, 1295-305, 2013	RCT assessing outcomes related to mode of birth. Not possible to extract data relating gestational age to different subgroup (twin type) and other outcomes
Beasley,E., Megerian,G., Gerson,A., Roberts,N.S., Monoamniotic twins: case series and proposal for antenatal management, Obstetrics and Gynecology, 93, 130-134, 1999	Case series, not cohort. Unclear which cases are confirmed monochorionic monoamniotic (reports on 8 suspected, but only 6 confirmed)
Bensdorp, A. J., Hukkelhoven, C. W., van der Veen, F., Mol, B. W. J., Lambalk, C. B., van Wely, M., Dizygotic twin pregnancies after medically assisted reproduction and after natural conception: maternal and perinatal outcomes, Fertility and Sterility, 106, 371-377.e2, 2016	No relevant data by gestational age
Blitz, M. J., Benja-Athonsirikul, N., Rochelson, B., Greenberg, M., Bracero, L. A., Association of chorionicity with umbilical arterial cord ph in twin pregnancies, Reproductive Sciences, 25 (1), 231A, 2018	Conference abstract
Bricelj, K., Tul, N., Lasic, M., Bregar, A. T., Verdenik, I., Lucovnik, M., Blickstein, I., Respiratory morbidity in twins by birth order, gestational age and mode of delivery, Journal of Perinatal Medicine, 44, 899-902, 2016	No data by chorionicity/amnionicity
Briery,C.M., Veillon,E.W., Klauser,C.K., Martin,R.W., Chauhan,S.P., Magann,E.F., Morrison,J.C., Progesterone does not prevent preterm births in women with twins, Southern Medical Journal, 102, 900-904, 2009	Not a study design outlined in the protocol
Brincat, M. R., Sant, M., Calleja, N., Optimal gestational age for delivery in uncomplicated dichorionic twin pregnancies: A Population-Based study, Malta Medical Journal, 29, 20-28, 2017	No usable data
Carr, S. R., Aronson, M. P., Coustan, D. R., Survival rates of monoamniotic twins do not decrease after 30 weeks' gestation, American Journal of Obstetrics and Gynecology, 163, 719-722, 1990	Presents relevant outcomes by weekly gestational age in graphical annotation only
Carter, E. B., Bishop, K. C., Goetzinger, K. R., Tuuli, M. G., Cahill, A. G., The impact of chorionicity on maternal pregnancy outcomes, American Journal of Obstetrics & Gynecology, 213, 390.e1-7, 2015	No relevant data by gestational age
Cheong-See, F., Schuit, E., Arroyo-Manzano, D., Khalil, A., Barrett, J., Joseph, K. S., Asztalos, E., Hack, K., Lewi, L., Lim, A., Liem, S., Norman, J. E., Morrison, J., Combs, C. A.,	Systematic review with meta-analysis. Unclear which studies contributed to the pooled

Study	Reason for Exclusion
Garite, T. J., Maurel, K., Serra, V., Perales, A., Rode, L., Worda, K., Nassar, A., Aboulghar, M., Rouse, D., Thom, E., Breathnach, F., Nakayama, S., Maria Russo, F., Robinson, J. N., Dodd, J. M., Newman, R. B., Bhattacharya, S., Tang, S., Mol, B. W. J., Zamora, J., Thilaganathan, B., Thangaratinam, S., Prospective risk of stillbirth and neonatal complications in twin pregnancies: Systematic review and meta-analysis, BMJ (Online), 354 (no pagination), 2016	estimates. All studies identified and assessed individually for inclusion
Cheong-See F,, Schuit E, , Arroyo-Manzano D, , et al., Optimal timing of delivery in women with twin pregnancies: A meta-analysis of evidence, CRD42014007538	A full-text copy of the article could not be obtained
Cheung, Yin Bun, Yip, Paul, Karlberg, Johan, Mortality of twins and singletons by gestational age: a varying-coefficient approach, American Journal of Epidemiology, 152, 1107-1116, 2000	No data by chorionicity/amnionicity (combines all twin types)
Chitrit, Y., Filidori, M., Pons, J. C., Duyme, M., Papiernik, E., Perinatal mortality in twin pregnancies: A 3-year analysis in Seine Saint-Denis (France), European Journal of Obstetrics Gynecology and Reproductive Biology, 86, 23-28, 1999	No data by amnionicity
Chmait, R. H., Kontopoulos, E., Bornick, P. W., Maitino, T., Quintero, R. A., Triplets with feto-fetal transfusion syndrome treated with laser ablation: the USFetus experience, Journal of Maternal-Fetal & Neonatal Medicine, 23, 361-5, 2010	No relevant data by gestational age
Cleary-Goldman, Jane, Dâ€ ™Alton, Mary E., Prospective risk of intrauterine death of monochorionic-diamniotic twins, American Journal of Obstetrics and Gynecology, 196, e11, 2007	Letter to the editor
Combs, C. A., Garite, T., Maurel, K., Das, A., Porto, M., Failure of 17-hydroxyprogesterone to reduce neonatal morbidity or prolong triplet pregnancy: A double-blind, randomized clinical trial, American Journal of Obstetrics and Gynecology, 203, 248.e1-248.e9, 2010	Not a study design outlined in the protocol
Combs,C.A., Garite,T., Maurel,K., Das,A., Porto,M., 17-Hydroxyprogesterone caproate for twin pregnancy: A double-blind, randomized clinical trial, Obstetrical and Gynecological Survey, 66, 393-394, 2011	RCT intervention assessing progesterone on preterm birth
Cordero,L., Franco,A., Joy,S.D., Monochorionic monoamniotic twins: neonatal outcome, Journal of Perinatology, 26, 170-175, 2006	No relevant data by gestational age
Cordero,L., Franco,A., Joy,S.D., O'shaughnessy,R.W., Monochorionic diamniotic infants without twin-to-twin transfusion syndrome, Journal of Perinatology, 25, 753-758, 2005	No relevant data by gestational age
Coutinho Nunes, F., Domingues, A. P., Vide Tavares, M., Belo, A., Ferreira, C., Fonseca, E., Moura, P., Monochorionic versus dichorionic twins: Are obstetric outcomes always different?, Journal of Obstetrics and Gynaecology, 36, 598-601, 2016	No relevant data by gestational age
Danon, D., Sekar, R., Hack, K. E. A., Fisk, N. M., Increased stillbirth in uncomplicated monochorionic twin pregnancies: A	There is a more recent systematic review by Cheong-See et al. BMJ review 2016

Study	Reason for Exclusion
Systematic Review and Meta-Analysis, Obstetrics and Gynecology, 121, 1318-1326, 2013	
D'Antonio, F., Khalil, A., Dias, T., Thilaganathan, B., Early fetal loss in monochorionic and dichorionic twin pregnancies: analysis of the Southwest Thames Obstetric Research Collaborative (STORK) multiple pregnancy cohort, Ultrasound in obstetrics & gynecology : the official journal of the International Society of Ultrasound in Obstetrics and Gynecology, 41, 632-636, 2013	Data not reported by weekly gestational age
D'Antonio, F., Thilaganathan, B., Laoreti, A., Khalil, A., Southwest Thames Obstetric Research, Collaborative, Birth-weight discordance and neonatal morbidity in twin pregnancy: analysis of STORK multiple pregnancy cohort, Ultrasound in Obstetrics & GynecologyUltrasound Obstet Gynecol, 52, 586-592, 2018	Study examines the association between weight discordance and neonatal morbidity in twin pregnancy progressing to at least 34 weeks of gestation
D'Antonio, F., Thilaganathan, B., Toms, J., Manzoli, L., Bhide, A., Papageorghiou, A., Khalil, A., Perinatal outcome after fetoscopic laser surgery for twin-to-twin transfusion syndrome in triplet pregnancies, BJOG: An International Journal of Obstetrics and Gynaecology, 123, 328-336, 2016	Specific population group (triplet pregnancies affected by twin-twin transfusion syndrome treated with fetoscopic laser surgery)
DeFalco,L.M., Sciscione,A.C., Megerian,G., Tolosa,J., Macones,G., O'Shea,A., Pollock,M.A., Inpatient versus outpatient management of monoamniotic twins and outcomes, American Journal of Perinatology, 23, 205-212, 2006	Does not report outcomes by weekly gestational age
Demaria,F., Goffinet,F., Kayem,G., Tsatsaris,V., Hessabi,M., Cabrol,D., Monoamniotic twin pregnancies: antenatal management and perinatal results of 19 consecutive cases, BJOG: An International Journal of Obstetrics and Gynaecology, 111, 22-26, 2004	Does not report outcomes by weekly gestational age
Dias, T., Contro, E., Thilaganathan, B., Khan, H., Zanardini, C., Mahsud-Dornan, S., Bhide, A., Pregnancy outcome of monochorionic twins: does amnionicity matter?, Twin Research & Human Genetics: the Official Journal of the International Society for Twin Studies, 14, 586-92, 2011	No usable data
Diemert, A., Diehl, W., Huber, A., Glosemeyer, P., Hecher, K., Laser therapy of twin-to-twin transfusion syndrome in triplet pregnancies, Ultrasound in Obstetrics & Gynecology, 35, 71-4, 2010	Specific population (triplets: dichorionic triamniotic and monochorionic monoamniotic after laser procedure)
Dodd, J. M., Crowther, C. A., Haslam, R. R., Robinson, J. S., Elective birth at 37 weeks of gestation versus standard care for women with an uncomplicated twin pregnancy at term: The Twins Timing of Birth Randomised Trial, Obstetrical and Gynecological Survey, 67, 675-676, 2012	Data not available based on amniocity. Limited data based on chorionicity. Gestational age only presented as mean/median in elective compared to standard care birth
Dodd, J. M., Deussen, A. R., Grivell, R. M., Crowther, C. A., Elective birth at 37 weeksâ€ ™ gestation for women with an uncomplicated twin pregnancy, Cochrane Database of Systematic Reviews, 2014	Study examines the risks and benefits of an elective caesarean section in uncomplicated twin pregnancies

Study	Reason for Exclusion
Domingues, A. P., Fonseca, E., Belo, A., Moura, P., Twins prematurity-the influence of prenatal surveillance, Journal of Maternal-Fetal and Neonatal Medicine, 28, 1108-1111, 2015	No data by amnionicity
Domingues, A. P., Fonseca, E., Vasco, E., Moura, P., Should apparently uncomplicated monochorionic twins be delivered electively at 32 weeks, Journal of Maternal-Fetal and Neonatal Medicine, 22, 1077-1080, 2009	No usable data
Dong, Y., Luo, Z. C., Yang, Z. J., Chen, L., Guo, Y. N., Branch, W., Zhang, J., Huang, H., Is Cesarean Delivery Preferable in Twin Pregnancies at >=36 Weeks Gestation?, PLoS ONE [Electronic Resource], 11, e0155692, 2016	No data by amnionicity
Duyos Mateo, I., de la Calle, M., Revello, R., Salas, P., Zapardiel, I., Gonzalez, A., Fetal and early neonatal outcomes in 147 triplet pregnancies, Ginecologia y Obstetricia de Mexico, 81, 86-91, 2013	Not in English language
Ezra,Y., Shveiky,D., Ophir,E., Nadjari,M., Eisenberg,V.H., Samueloff,A., Rojansky,N., Intensive management and early delivery reduce antenatal mortality in monoamniotic twin pregnancies, Acta Obstetricia et Gynecologica Scandinavica, 84, 432-435, 2005	Does not report outcomes by weekly gestational age
Farah, N., Hogan, J., Johnson, S., Stuart, B., Daly, S., Prospective risk of fetal death in uncomplicated monochorionic twins, Acta Obstetricia et Gynecologica Scandinavica, 91, 382-5, 2012	Data not reported by weekly gestational age (weekly gestational age information only noted in some cases for mortality outcomes, inconsistent)
Feng, B., Zhai, J., Cai, Y., Effect of twin pregnancy chorionic properties on maternal and fetal outcomes, Taiwanese Journal of Obstetrics and Gynecology, 57, 351-354, 2018	No relevant data by gestational age
Fennessy, K. M., Doyle, L. W., Naud, K., Reidy, K., Umstad, M. P., Triplet pregnancy: is the mode of conception related to perinatal outcomes?, Twin Research & Human Genetics: the Official Journal of the International Society for Twin StudiesTwin Res Hum Genet, 18, 321-7, 2015	No relevant data by gestational age
Fichera, A., Prefumo, F., Stagnati, V., Marella, D., Valcamonico, A., Frusca, T., Outcome of monochorionic diamniotic twin pregnancies followed at a single center, Prenatal Diagnosis, 35, 1057-64, 2015	Outcomes reported for fortnightly gestational age, not weekly gestational age at birth
Fichera,A., Zambolo,C., Accorsi,P., Martelli,P., Ambrosi,C., Frusca,T., Perinatal outcome and neurological follow up of the cotwins in twin pregnancies complicated by single intrauterine death, European Journal of Obstetrics, Gynecology, and Reproductive Biology, 147, 37-40, 2009	Study examines the outcome of the surviving co-twin in pregnancies complicated by single intrauterine death
Geisler, M. E., O'Mahony, A., Meaney, S., Waterstone, J. J., O'Donoghue, K., Obstetric and perinatal outcomes of twin pregnancies conceived following IVF/ICSI treatment compared with spontaneously conceived twin pregnancies, European Journal of Obstetrics Gynecology and Reproductive Biology, 181, 78-83, 2014	No relevant data by gestational age
Ghalili, A., McLennan, A., Pedersen, L., Kesby, G., Hyett, J., Outcomes of monochorionic diamniotic twin pregnancies: a comparison of assisted and spontaneous conceptions,	No relevant data by gestational age

Study	Reason for Exclusion
Australian & New Zealand Journal of Obstetrics & Gynaecology, 53, 437-42, 2013	
Giancotti, A., Muto, B., Diambrosio, V., Bevilacqua, E., Pasquali, G., Squarcella, A., La Torre, R., Ultrasound management and clinical outcome of twin pregnancies, Journal of Obstetrics and Gynaecology, 33, 675-677, 2013	No relevant data by gestational age
Gluck, O., Mizrachi, Y., Bar, J., Barda, G., The impact of advanced maternal age on the outcome of twin pregnancies, Archives of Gynecology and Obstetrics, 297, 891-895, 2018	Study compares obstetrical and neonatal outcomes between women with dichorionic-diamniotic twin pregnancies older than 35 years of age with women younger than 35 years of age
Gomes, C., Soares, P., Edral, A., Gadelha, M., Silva, A. P., An overview of twin pregnancy complications: The experience of a differentiated perinatal center, Twin Research and Human Genetics, 20, 631-632, 2017	Conference abstract
Goossens, S. M. T. A., Ensing, S., van der Hoeven, M. A. H. B. M., Roumen, F. J. M. E., Nijhuis, J. G., Mol, B. W., Comparison of planned caesarean delivery and planned vaginal delivery in women with a twin pregnancy: A nation wide cohort study, European Journal of Obstetrics Gynecology and Reproductive Biology, 221, 97-104, 2018	No data by chorionicity/amnionicity
Gupta, S., Fox, N. S., Feinberg, J., Klauser, C. K., Rebarber, A., Outcomes in twin pregnancies reduced to singleton pregnancies compared with ongoing twin pregnancies, American Journal of Obstetrics & Gynecology, 213, 580.e1-5, 2015	Study compares the risks of adverse pregnancy outcomes between ongoing twin pregnancies and twin pregnancies reduced to singleton pregnancies
Hack, K. E. A., Derks, J. B., De Visser, V. L., Elias, S. G., Visser, G. H. A., The natural course of monochorionic and dichorionic twin pregnancies: A historical cohort, Twin Research and Human Genetics, 9, 450-455, 2006	No data by amnionicity
Hack, K. E. A., Derks, J. B., Elias, S. G., Franx, A., Roos, E. J., Voerman, S. K., Bode, C. L., Koopman-Esseboom, C., Visser, G. H. A., Increased perinatal mortality and morbidity in monochorionic versus dichorionic twin pregnancies: Clinical implications of a large Dutch cohort study, BJOG: An International Journal of Obstetrics and Gynaecology, 115, 58-67, 2008	Data not reported by weekly gestational age
Hack, K. E. A., Koopman-Esseboom, C., Derks, J. B., Elias, S. G., de Kleine, M. J. K., Baerts, W., Go, A. T. J. I., Schaap, A. H. P., van der Hoeven, M. A. H. B. M., Eggink, A. J., Sollie, K. M., Weisglas-Kuperus, N., Visser, G. H. A., Long-term neurodevelopmental outcome of monochorionic and matched dichorionic twins, PLoS ONE, 4 (8) (no pagination), 2009	No relevant outcomes reported
Hack, K. E. A., Vereycken, M. E. M. S., Torrance, H. L., Koopman-Esseboom, C., Derks, J. B., Perinatal outcome of monochorionic and dichorionic twins after spontaneous and assisted conception: a retrospective cohort study, Acta Obstetricia et Gynecologica Scandinavica, 97, 717-726, 2018	No relevant data by gestational age
Hack, K. E., Derks, J. B., Schaap, A. H., Lopriore, E., Elias, S. G., Arabin, B., Eggink, A. J., Sollie, K. M., Mol, B. W. J.,	Does not report outcomes by weekly gestational age

Study	Reason for Exclusion
Duvekot, H. J., Willekes, C., Go, A. T., Koopman-Esseboom, C., Vandenbussche, F. P., Visser, G. H., Perinatal outcome of monoamniotic twin pregnancies, Obstetrics and Gynecology, 113, 353-360, 2009	
Halling, C., Malone, F. D., Breathnach, F. M., Stewart, M. C., McAuliffe, F. M., Morrison, J. J., Dicker, P., Manning, F., Corcoran, J. D., Neuro-developmental outcome of a large cohort of growth discordant twins, European Journal of Pediatrics, 175, 381-389, 2016	No relevant data by gestational age
Hartley, R. S., Emanuel, I., Hitti, J., Perinatal mortality and neonatal morbidity rates among twin pairs at different gestational ages: optimal delivery timing at 37 to 38 weeks' gestation, American Journal of Obstetrics & GynecologyAm J Obstet Gynecol, 184, 451-8, 2001	No data by chorionicity/amnionicity
Heazell, A. E., Whitworth, M. K., Whitcombe, J., Glover, S. W., Bevan, C., Brewin, J., Calderwood, C., Canter, A., Jessop, F., Johnson, G., Martin, I., Metcalf, L., Research priorities for stillbirth: process overview and results from UK Stillbirth Priority Setting Partnership, Ultrasound in Obstetrics & GynecologyUltrasound Obstet Gynecol, 46, 641-7, 2015	Editorial
Hehir, M. P., McTiernan, A., Martin, A., Carroll, S., Gleeson, R., Malone, F. D., Improved Perinatal Mortality in Twins--Changing Practice and Technologies, American Journal of Perinatology, 33, 84-9, 2016	No data by amnionicity
Helmerhorst, Frans M, Perquin, Denise AM, Donker, Diane, Keirse, Marc JNC, Perinatal outcome of singletons and twins after assisted conception: a systematic review of controlled studies, Bmj, 328, 261, 2004	No data by chorionicity/amnionicity
Henningsen, A. A., Gissler, M., Skjaerven, R., Bergh, C., Tiitinen, A., Romundstad, L. B., Wennerholm, U. B., Lidegaard, O., Nyboe Andersen, A., Forman, J. L., Pinborg, A., Trends in perinatal health after assisted reproduction: A Nordic study from the CoNARTaS group, Human Reproduction, 30, 710-716, 2015	No data for chorionicity/amnionicity
Henry, A., Lees, N., Bein, K. J., Hall, B., Lim, V., Chen, K. Q., Welsh, A. W., Hui, L., Shand, A. W., Pregnancy outcomes before and after institution of a specialised twins clinic: A retrospective cohort study, BMC Pregnancy and Childbirth, 15 (1) (no pagination), 2015	No relevant data by gestational age
Heyborne, K. D., Porreco, R. P., Garite, T. J., Phair, K., Abril, D., Improved perinatal survival of monoamniotic twins with intensive inpatient monitoring, American Journal of Obstetrics and Gynecology, 192, 96-101, 2005	Presents relevant outcomes by weekly gestational age in graphical annotation only
Hiersch, L., Eitan, M., Ashwal, E., Weisz, B., Chayen, B., Lipitz, S., Yinon, Y., Amniotic fluid discordance in monochorionic diamniotic twin pregnancies is associated with increased risk for twin anemia-polycythemia sequence, Prenatal Diagnosis, 36, 1099-1103, 2016	No relevant data by gestational age
Hirst, J. E., Villar, J., Victora, C. G., Papageorghiou, A. T., Finkton, D., Barros, F. C., Gravett, M. G., Giuliani, F., Purwar, M., Frederick, I. O., Pang, R., Cheikh Ismail, L., Lambert, A.,	Study examines risk factors specific for antepartum stillbirth

Study	Reason for Exclusion
Stones, W., Jaffer, Y. A., Altman, D. G., Noble, J. A., Ohuma, E. O., Kennedy, S. H., Bhutta, Z. A., The antepartum stillbirth syndrome: risk factors and pregnancy conditions identified from the INTERGROWTH-21st Project, BJOG: An International Journal of Obstetrics and Gynaecology, 125, 1145-1153, 2018	
Hoffman, M., Habli, M., Donepudi, R., Boring, N., Johnson, A., Moise, K. J., Papanna, R., Perinatal outcomes of single fetal survivor after fetal intervention for complicated monochorionic twins, Prenatal Diagnosis, 38, 511-516, 2018	No relevant data by gestational age
Hofmeyr, G. J., Barrett, J. F., Crowther, C. A., Planned caesarean section for women with a twin pregnancy, Cochrane Database of Systematic Reviews, 12, CD006553, 2015	Study examines the effects of a policy of planned caesarean section versus planned vaginal birth for twin pregnancy on maternal and neonatal mortality and morbidity
Huber,A., Diehl,W., Zikulnig,L., Bregenzer,T., Hackeloer,B.J., Hecher,K., Perinatal outcome in monochorionic twin pregnancies complicated by amniotic fluid discordance without severe twin-twin transfusion syndrome, Ultrasound in Obstetrics and Gynecology, 27, 48-52, 2006	No relevant data by gestational age
Imamura, T., Maeda, H., Kinoshita, H., Kin, S., Monochorionic diamniotic twins with centrally located and closely spaced umbilical cord insertions in the placenta, Clin Case RepClinical case reports, 6, 342-345, 2018	Not a study design outlined in the protocol
Ishii, K., Prenatal diagnosis and management of monoamniotic twins, Current Opinion in Obstetrics & Gynecology, 27, 159-64, 2015	Not a study design outlined in the protocol
Ishii, K., Nakata, M., Wada, S., Hayashi, S., Murakoshi, T., Sago, H., Perinatal outcome after laser surgery for triplet gestations with feto-fetal transfusion syndrome, Prenatal Diagnosis, 34, 734-8, 2014	Specific population (triplets: dichorionic triamniotic and monochorionic monoamniotic after laser procedure)
Jahanfar, S., Lim, K., Oviedo-Joekes, E., Optimal threshold for birth weight discordance: Does knowledge of chorionicity matter?, Journal of Perinatology, 36, 704-12, 2016	Study examined the optimal threshold of birth weight discordance for prediction of stillbirth, perinatal mortality and morbidity in twins with or without chorionicity
Kahn, B., Lumey, L. H., Zybert, P. A., Lorenz, J. M., Cleary-Goldman, J., D'Alton, M. E., Robinson, J. N., Prospective risk of fetal death in singleton, twin, and triplet gestations: implications for practice, Obstetrics & GynecologyObstet Gynecol, 102, 685-92, 2003	No data by chorionicity/amnionicity
Kaveh, M., Ghajarzadeh, M., Tanha, F. D., Nayeri, F., Keramati, Z., Shariat, M., Ghaheri, A., Pregnancy complications and neonatal outcomes in multiple pregnancies: A comparison between assisted reproductive techniques and spontaneous conception, International Journal of Fertility and Sterility, 8, 367-372, 2015	No data by chorionicity/amnionicity
Kawaguchi,H., Ishii,K., Yamamoto,R., Hayashi,S., Mitsuda,N., Perinatal death of triplet pregnancies by chorionicity,	No relevant data by gestational age

Study	Reason for Exclusion
American Journal of Obstetrics and Gynecology, 209, 36e1-36e7, 2013	
Ko, H. S., Choi, S. K., Wie, J. H., Park, I. Y., Park, Y. G., Shin, J. C., Optimal Timing of Delivery Based on the Risk of Stillbirth and Infant Death Associated with Each Additional Week of Expectant Management in Multiple Pregnancies: a National Cohort Study of Koreans, Journal of Korean Medical ScienceJ Korean Med Sci, 33, e80, 2018	No data by chorionicity/amnionicity
Kosinska-Kaczynska, K., Szymusik, I., Kaczynski, B., Wielgos, M., Observational study of associations between gestational weight gain and perinatal outcomes in dichorionic twin pregnancies, International Journal of Gynaecology & Obstetrics, 138, 94-99, 2017	No relevant data by gestational age
Kramer, Michael S, Liu, Shiliang, Luo, Zhongcheng, Yuan, Hongbo, Platt, Robert W, Joseph, KS, Analysis of perinatal mortality and its components: time for a change?, American Journal of Epidemiology, 156, 493-497, 2002	Article examines the differences between stillbirths and early neonatal deaths
Kristiansen, M. K., Joensen, B. S., Ekelund, C. K., Petersen, O. B., Sandager, P., Perinatal outcome after first-trimester risk assessment in monochorionic and dichorionic twin pregnancies: A population-based register study, BJOG: An International Journal of Obstetrics and Gynaecology, 122, 1362-1369, 2015	No relevant data by gestational age
Lachowska, M., Lachowski, K., Krolak-Olejnik, B., Respiratory disorders and neonatal outcomes of triplet pregnancies - our ten year experience, Signa Vitae, 13, 76-78, 2017	No data by chorionicity/amnionicity
Lappen, J. R., Hackney, D. N., Bailit, J. L., Maternal and neonatal outcomes of attempted vaginal compared with planned cesarean delivery in triplet gestations, American Journal of Obstetrics and Gynecology, 215, 493.e1-493.e6, 2016	No data by chorionicity/amnionicity
Leduc,L., Takser,L., Rinfret,D., Persistance of adverse obstetric and neonatal outcomes in monochorionic twins after exclusion of disorders unique to monochorionic placentation, American Journal of Obstetrics and Gynecology, 193, 1670-1675, 2005	No relevant data by gestational age
Lee, Y. M., Wylie, B. J., Simpson, L. L., D'Alton, M. E., Twin chorionicity and the risk of stillbirth, Obstetrics and Gynecology, 111, 301-308, 2008	Data not reported by weekly gestational age (weekly gestational age information only noted in some cases for mortality outcomes, inconsistent)
Lewi, L., Jani, J., Blickstein, I., Huber, A., Gucciardo, L., Van Mieghem, T., Done, E., Boes, A. S., Hecher, K., Gratacos, E., Lewi, P., Deprest, J., The outcome of monochorionic diamniotic twin gestations in the era of invasive fetal therapy: a prospective cohort study, American Journal of Obstetrics and Gynecology, 199, 514.e1-514.e8, 2008	Data not reported by weekly gestational age (weekly gestational age information only noted in some cases for mortality outcomes, inconsistent)
Lia,J.E.D., Worthington,D., Carr,M.H., Graupe,M.H., Melone,P.J., Placental laser surgery for severe previable feto-fetal transfusion syndrome In triplet gestation, American Journal of Perinatology, 26, 559-564, 2009	Specific population (triplets: dichorionic triamniotic and monochorionic monoamniotic after laser procedure)

Study	Reason for Exclusion
Liem, S., Schuit, E., Hegeman, M., Bais, J., de Boer, K., Bloemenkamp, K., Brons, J., Duvekot, H., Bijvank, B. N., Franssen, M., Gaugler, I., de Graaf, I., Oudijk, M., Papatsonis, D., Pernet, P., Porath, M., Scheepers, L., Sikkema, M., Sporken, J., Visser, H., van Wijngaarden, W., Woiski, M., van Pampus, M., Mol, B. W., Bekedam, D., Cervical pessaries for prevention of preterm birth in women with a multiple pregnancy (ProTWIN): a multicentre, open-label randomised controlled trial, Lancet, 382, 1341-9, 2013	Intervention using pessary for prevention of preterm birth in twins
Lim, A. C., Schuit, E., Bloemenkamp, K., Bernardus, R. E., Duvekot, J. J., Erwich, J. J., van Eyck, J., Groenwold, R. H., Hasaart, T. H., Hummel, P., Kars, M. M., Kwee, A., van Oirschot, C. M., van Pampus, M. G., Papatsonis, D., Porath, M. M., Spaanderman, M. E., Willekes, C., Wilpshaar, J., Mol, B. W., Bruinse, H. W., 17alpha-hydroxyprogesterone caproate for the prevention of adverse neonatal outcome in multiple pregnancies: a randomized controlled trial, Obstetrics & Gynecology, 118, 513-20, 2011	RCT intervention of progesterone. Some stratification by chorionicity but relevant outcomes unavailable relating to gestational age
Liu,A.L., Yung,W.K., Yeung,H.N., Lai,S.F., Lam,M.T., Lai,F.K., Lo,T.K., Lau,W.L., Leung,W.C., Factors influencing the mode of delivery and associated pregnancy outcomes for twins: a retrospective cohort study in a public hospital, Hong Kong Medical Journal, 18, 99-107, 2012	No data by chorionicity/amnionicity
Lopes Perdigao, J., Straub, H., Zhou, Y., Gonzalez, A., Ismail, M., Ouyang, D. W., Perinatal and obstetric outcomes of dichorionic vs trichorionic triplet pregnancies, American Journal of Obstetrics & Gynecology, 214, 659.e1-5, 2016	No relevant data by gestational age
Luke, B., Reducing fetal deaths in multiple births: optimal birthweights and gestational ages for infants of twin and triplet births, Acta Geneticae Medicae et GemellologiaeActa Genet Med Gemellol (Roma), 45, 333-48, 1996	No data by chorionicity/amnionicity
Lumme,R.H., Saarikoski,S.V., Monoamniotic twin pregnancy, Acta Geneticae Medicae et Gemellologiae, 35, 99-105, 1986	No relevant data by gestational age
Luo, Q., Han, X., Clinical characteristics and outcome of twin pregnancies complicated by single intrauterine death, Journal of Perinatal Medicine, 46, 75-79, 2018	Data not reported by weekly gestational age
Lynch, A., McDuffie, R., Jr., Lyons, E., Chase, M., Orleans, M., Perinatal loss among twins, Permanente JournalPerm, 11, 7-12, 2007	No relevant data by gestational age
Mahony, R., Mulcahy, C., McAuliffe, F., Herlihy, C. O., Carroll, S., Foley, M. E., Fetal death in twins, Acta Obstetricia et Gynecologica Scandinavica, 90, 1274-80, 2011	Data not reported by weekly gestational age (weekly gestational age information only noted in some cases for mortality outcomes, inconsistent)
Maia, C. B., Liao, A. W., Brizot, M. L., Francisco, R. P. V., Zugaib, M., Prediction of perinatal mortality in triplet pregnancies, Archives of Gynecology and Obstetrics, 294, 473-477, 2016	Data presented for all triplets combined, not subgrouped by chorionicity type
Manso, P., Vaz, A., Taborda, A., Silva, I. S., Chorionicity and perinatal complications in twin pregnancy a 10 years case series, Acta Medica Portuguesa, 24, 695-698, 2011	Not in English language

Study	Reason for Exclusion
Marques, M., Nascimento, S., Fetal and maternal complications of multiple pregnancy, Journal of Perinatal Medicine, 43, no pagination, 2015	Conference abstract
Mascarenhas, M., Kamath, M. S., Muthukumar, K., Mangalaraj, A. M., Chandy, A., Aleyamma, T. K., Obstetric outcomes of monochorionic pregnancies conceived following assisted reproductive technology: A retrospective study, Journal of Human Reproductive Sciences, 7, 119-124, 2014	No relevant data by gestational age
Masheer, S., Maheen, H., Munim, S., Perinatal outcome of twin pregnancies according to chorionicity: an observational study from tertiary care hospital, Journal of Maternal-Fetal & Neonatal Medicine, 28, 23-5, 2015	Outcomes presented as monochorionic compared to dichorionic twinsets, no information on monochorionic amnionicity. Outcomes not presented as related to gestational age at birth (exposure)
Matsui, M., Takahashi, Y., Iwagaki, S., Chiaki, R., Asai, K., Kawabata, I., Preliminary preventive protocol from first trimester of pregnancy to reduce preterm birth rate for dichorionic-diamniotic twins, Taiwanese Journal of Obstetrics & Gynecology, 56, 23-26, 2017	Study compares two different management strategies (management initiated before 14 or after 14 weeks of gestation) in terms of preterm birth rates in twin pregnancies
McLennan, A. A., Ananth, C. V., Wright, J. D., Siddiq, Z., D'Alton, M. E., Friedman, A. M., Twin pregnancy in the setting of advanced maternal age: Risk of prematurity, neonatal morbidity, and stillbirth, Reproductive Sciences, 23, 266A, 2016	Conference abstract
McLennan, A. S., Gyamfi-Bannerman, C., Ananth, C. V., Wright, J. D., Siddiq, Z., D'Alton, M. E., Friedman, A. M., The role of maternal age in twin pregnancy outcomes, American Journal of Obstetrics & Gynecology, 217, 80.e1-80.e8, 2017	No information regarding chorionicity and amnionicity
McPherson, J. A., Odibo, A. O., Shanks, A. L., Roehl, K. A., Macones, G. A., Cahill, A. G., Impact of chorionicity on risk and timing of intrauterine fetal demise in twin pregnancies, American Journal of Obstetrics & GynecologyAm J Obstet Gynecol, 207, 190.e1-6, 2012	Data presented fortnightly not weekly (gestational age 20-21 weeks, 22-23 weeks, 24-25 weeks...)
Morency, A. M., Shah, P. S., Seaward, P. G. R., Whittle, W., Murphy, K. E., Obstetrical and neonatal outcomes of triplet births-spontaneous versus assisted reproductive technology conception, Journal of Maternal-Fetal and Neonatal Medicine, 29, 938-943, 2016	Relevant outcomes reported for combined triplets, not for chorionicity subgroup
Morikawa, M., Yamada, T., Sato, S., Minakami, H., Prospective risk of intrauterine fetal death in monoamniotic twin pregnancies, Twin Research and Human Genetics, 15, 522-526, 2012	Presents relevant outcomes by weekly gestational age in graphical annotation only
Murata, M., Ishii, K., Kamitomo, M., Murakoshi, T., Takahashi, Y., Sekino, M., Kiyoshi, K., Sago, H., Yamamoto, R., Kawaguchi, H., Mitsuda, N., Perinatal outcome and clinical features of monochorionic monoamniotic twin gestation, Journal of Obstetrics & Gynaecology ResearchJ Obstet Gynaecol Res, 39, 922-5, 2013	No relevant data by gestational age

Study	Reason for Exclusion
Nakayama, S., Ishii, K., Kawaguchi, H., Hayashi, S., Hidaka, N., Murakoshi, T., Mitsuda, N., Perinatal outcome of monochorionic diamniotic twin pregnancies managed from early gestation at a single center, Journal of Obstetrics & Gynaecology Research, 38, 692-7, 2012	Unable to relate outcomes to gestational age (exposure) at birth. Outcomes presented as overall incidence only for monochorionic diamniotic twins
Newman,R.B., Unal,E.R., Multiple gestations: timing of indicated late preterm and early-term births in uncomplicated dichorionic, monochorionic, and monoamniotic twins, Seminars in Perinatology, 35, 277-285, 2011	Included studies were assessed for inclusion
Norman,J.E., MacKenzie,F., Owen,P., Mactier,H., Hanretty,K., Cooper,S., Calder,A., Mires,G., Danielian,P., Sturgiss,S., MacLennan,G., Tydeman,G., Thornton,S., Martin,B., Thornton,J.G., Neilson,J.P., Norrie,J., Progesterone for the prevention of preterm birth in twin pregnancy (STOPPIT): a randomised, double-blind, placebo-controlled study and meta-analysis, The Lancet, 373, -2040, 2009	RCT examining intervention of progesterone
Oldenburg, A., Rode, L., Bodker, B., Ersbak, V., Holmskov, A., Jorgensen, F. S., Larsen, H., Larsen, T., Laursen, L., Mogensen, H., Petersen, O. B., Rasmussen, S., Skibsted, L., Sperling, L., Stornes, I., Zingenberg, H., Tabor, A., Influence of chorionicity on perinatal outcome in a large cohort of Danish twin pregnancies, Ultrasound in Obstetrics & Gynecology, 39, 69-74, 2012	No relevant data by gestational age
Ortibus, E., Lopriore, E., Deprest, J., Vandenbussche, F. P., Walther, F. J., Diemert, A., Hecher, K., Lagae, L., De Cock, P., Lewi, P. J., Lewi, L., The pregnancy and long-term neurodevelopmental outcome of monochorionic diamniotic twin gestations: a multicenter prospective cohort study from the first trimester onward, American Journal of Obstetrics & Gynecology, 200, 494.e1-8, 2009	Data presented as overall incidence for relevant outcomes in cohort study. Some outcomes for some cases present data for gestational age (case-series)
Page, J. M., Pilliod, R. A., Snowden, J. M., Caughey, A. B., The risk of stillbirth and infant death by each additional week of expectant management in twin pregnancies, American Journal of Obstetrics and Gynecology, 212, 630.e1-630.e7, 2015	No information regarding chorionicity and amnionicity
Page, J. M., Thorsten, V., Reddy, U. M., Dudley, D. J., Hogue, C. J. R., Saade, G. R., Pinar, H., Parker, C. B., Conway, D., Stoll, B. J., Coustan, D., Bukowski, R., Varner, M. W., Goldenberg, R. L., Gibbins, K., Silver, R. M., Potentially Preventable Stillbirth in a Diverse U.S. Cohort, Obstetrics & Gynecology, 131, 336-343, 2018	No information regarding chorionicity and amnionicity
Peeters, S. H., Middeldorp, J. M., Lopriore, E., Klumper, F. J., Oepkes, D., Monochorionic triplets complicated by fetofetal transfusion syndrome: a case series and review of the literature, Fetal Diagnosis & TherapyFetal Diagn Ther, 32, 239-45, 2012	Specific population (monochorionic triplets with twin-twin transfusion syndrome versus dichorionic triplets with twin-twin transfusion syndrome comparison of treatment strategies)
Peress, D. A., Peaceman, A. M., Yee, L. M., Evaluation of Trichorionic versus Dichorionic Triplet Gestations from 2005 to 2016 in a Large, Referral Maternity Center, American Journal of Perinatology, 34, 599-605, 2017	No information relating gestational age to relevant outcomes

Study	Reason for Exclusion
Peter, C. , Wenzlaff, P. , Kruempelmann, J., Alzen, G., Bueltmann, E., Perinatal morbidity and early neonatal mortality in twin pregnancies, Open J Obstet Gynecol, 3, 78-89, 2013	Gestational age presented as mean and standard deviation per group, and not related to relevant outcomes
Pharoah, P. O., Adi, Y., Consequences of in-utero death in a twin pregnancy, Lancet, 355, 1597-602, 2000	No information regarding chorionicity and amnionicity
Porta, R., Capdevila, E., Botet, F., Verd, S., Ginovart, G., Moliner, E., Nicolas, M., Rios, J., Morbidity and mortality of very low birth weight multiples compared with singletons, Journal of Maternal-Fetal and Neonatal Medicine, 1-9, 2017	No information regarding chorionicity and amnionicity
Pourali, L., Ayati, S., Jelodar, S., Zarifian, A., Andalibi, M. S. S., Obstetrics and perinatal outcomes of dichorionic twin pregnancy following art compared with spontaneous pregnancy, International Journal of Reproductive BioMedicine, 14, 317-322, 2016	Outcomes reported based on mode of conception, not gestational age at birth
Qin, J. B., Sheng, X. Q., Wang, H., Chen, G. C., Yang, J., Yu, H., Yang, T. B., Worldwide prevalence of adverse pregnancy outcomes associated with in vitro fertilization/intracytoplasmic sperm injection among multiple births: a systematic review and meta-analysis based on cohort studies, Archives of Gynecology & ObstetricsArch Gynecol Obstet, 295, 577-597, 2017	No information on chorionicity or amnionicity
Ravangard, S. F., Ozhand, A., Haeri, S., Shamshirsaz, A. A., Hussain, N., Spiel, M., Ogunleye, O., Billstrom, R., Sadowski, A., Turner, G., Timms, D., Egan, J. F. X., Campbell, W. A., Short-term neonatal outcomes in diamniotic twin pregnancies delivered after 32 weeks and indications of late preterm deliveries, American Journal of Perinatology, 31, 365-371, 2014	Data not reported by weekly gestational age
Razaz, N., Avitan, T., Ting, J., Pressey, T., Joseph, K. S., Perinatal outcomes in multifetal pregnancy following fetal reduction, CMAJ Canadian Medical Association JournalCmaj, 189, E652-E658, 2017	No information on chorionicity or amnionicity
Robinson, B. K., Miller, R. S., D'Alton, M. E., Grobman, W. A., Effectiveness of timing strategies for delivery of monochorionic diamniotic twins, American Journal of Obstetrics & Gynecology, 207, 53.e1-7, 2012	Study design (decision analytic model)
Rode, L., Klein, K., Nicolaides, K. H., Krampl-Bettelheim, E., Tabor, A., Prevention of preterm delivery in twin gestations (PREDICT): a multicenter, randomized, placebo-controlled trial on the effect of vaginal micronized progesterone, Ultrasound in Obstetrics & GynecologyUltrasound Obstet Gynecol, 38, 272-80, 2011	RCT intervention study examining progesterone in twins
Rodis,J.F., McIlveen,P.F., Egan,J.F.X., Borgida,A.F., Turner,G.W., Campbell,W.A., Monoamniotic twins: Improved perinatal survival with accurate prenatal diagnosis and antenatal fetal surveillance, American Journal of Obstetrics and Gynecology, 177, 1046-1049, 1997	Presents relevant outcomes by fortnightly gestational age in graphical annotation only
Roque, H., Gillen-Goldstein, J., Funai, E., Young, B. K., Lockwood, C. J., Perinatal outcomes in monoamniotic	Presents relevant outcomes by fortnightly gestational age in graphical annotation only

Study	Reason for Exclusion
gestations, Journal of Maternal-Fetal and Neonatal Medicine, 13, 414-421, 2003	
Rouse, D. J., Caritis, S. N., Peaceman, A. M., Sciscione, A., Thom, E. A., Spong, C. Y., Varner, M., Malone, F., Iams, J. D., Mercer, B. M., Thorp, J., Sorokin, Y., Carpenter, M., Lo, J., Ramin, S., Harper, M., Anderson, G., A trial of 17 alpha-hydroxyprogesterone caproate to prevent prematurity in twins, New England Journal of Medicine, 357, 454-461, 2007	RCT intervention study examining progesterone in twins
Royal Australian and New Zealand Colleges of Obstetricians and Gynaecologists,., Management of monochorionic twin pregnancy., 1-11, 2014	Guideline/ recommendations for management of complications related to Monochorionic twin pregnancies
Russo, F. M., Pozzi, E., Pelizzoni, F., Todyrenchuk, L., Bernasconi, D. P., Cozzolino, S., Vergani, P., Stillbirths in singletons, dichorionic and monochorionic twins: a comparison of risks and causes, European Journal of Obstetrics, Gynecology, & Reproductive Biology, 170, 131-6, 2013	Data not reported by weekly gestational age
Rzyska, E., Ajay, B., Chandraharan, E., Safety of vaginal delivery among dichorionic diamniotic twins over 10 years in a UK teaching hospital, International Journal of Gynaecology & ObstetricsInt J Gynaecol Obstet, 136, 98-101, 2017	Study examines mode of birth, and causes of non vaginal birth in dichorionic diamniotic twins
Sairam, S., Costeloe, K., Thilaganathan, B., Prospective risk of stillbirth in multiple-gestation pregnancies: a population-based analysis, Obstetrics & GynecologyObstet Gynecol, 100, 638-41, 2002	No information regarding chorionicity and amnionicity
Sela,H.Y., Flood,K., Timing of planned delivery in uncomplicated monochorionic diamniotic twin pregnancies: A review of the literature, Expert Review of Obstetrics and Gynecology, 7, 483-491, 2012	Included studies were assessed for inclusion
Serra, V., Perales, A., Meseguer, J., Parrilla, J. J., Lara, C., Bellver, J., Grifol, R., Alcover, I., Sala, M., Martínez-Escoriza, J. C., et al.,, Increased doses of vaginal progesterone for the prevention of preterm birth in twin pregnancies: a randomised controlled double-blind multicentre trial, BjogBJOG : an international journal of obstetrics and gynaecology, 120, 50â€• 57, 2013	RCT intervention examining progesterone for prevention of preterm birth
Shrim, A., Weisz, B., Gindes, L., Gagnon, R., Parameters Associated With Outcome in Third Trimester Monochorionic Diamniotic Twin Pregnancies, Journal of Obstetrics and Gynaecology Canada, 32, 429-434, 2010	Relevant outcomes not reported related to gestational age at birth (exposure)
Shub, A., Walker, S. P., Planned early delivery versus expectant management for monoamniotic twins, Cochrane Database of Systematic ReviewsCochrane Database Syst Rev, CD008820, 2015	Systematic review - no included studies
Simoes, T., Queiros, A., Goncalves, M. R., Periquito, I., Silva, P., Blickstein, I., Perinatal outcome of dichorionic-triamniotic as compared to trichorionic triplets, Journal of Perinatal Medicine, 44, 875-879, 2016	Data not reported by weekly gestational age
Simoes, T., Queiros, A., Marujo, A. T., Valdoleiros, S., Silva, P., Blickstein, I., Outcome of monochorionic twins conceived	Relevant outcomes not linked to gestational age at birth (exposure).

Study	Reason for Exclusion
by assisted reproduction, Fertility & Sterility, 104, 629-32, 2015	Presented as difference based on mode of conception and chorionicity
Skiadas,C.C., Missmer,S.A., Benson,C.B., Acker,D., Racowsky,C., Spontaneous reduction before 12 weeks' gestation and selective reduction similarly extend time to delivery in in vitro fertilization of trichorionic-triamniotic triplets, Fertility and Sterility, 95, 596-599, 2011	Study examines impact of selective reduction compared to fetal loss
Smith,N.A., Wilkins-Haug,L., Santolaya-Forgas,J., Acker,D., Economy,K.E., Benson,C.B., Robinson,J.N., Contemporary management of monochorionic diamniotic twins: outcomes and delivery recommendations revisited, American Journal of Obstetrics and Gynecology, 203, 133-136, 2010	Data not reported by weekly gestational age
Soong, S., Greer, R. M., Gardener, G., Flenady, V., Kumar, S., Impact of mode of delivery after 32 weeks' gestation on neonatal outcome in dichorionic diamniotic twins, Journal of Obstetrics & Gynaecology ResearchJ Obstet Gynaecol Res, 42, 392-8, 2016	Study examines mode of birth for dichorionic diamniotic twins
Spencer, J. V., Ingardia, C. J., Nold, C. J., Borgida, A. F., Herson, V. C., Egan, J. F. X., Perinatal and neonatal outcomes of triplet gestations based on placental chorionicity, American Journal of Perinatology, 26, 587-590, 2009	No relevant data by gestational age
Stern, E., Cohen, N., Odom, E., Stroustrup, A., Gupta, S., Saltzman, D. H., Rebarber, A., Fox, N. S., Long-term outcomes of twins based on gestational age at delivery, Journal of Maternal-Fetal and Neonatal Medicine, 31, 3102-3107, 2018	Relevant outcomes presented for combined monochorionic diamniotic and dichorionic diamniotic, not separately
Stringer, E. M., Chibwesha, C., Stoner, M., Vwalika, B., Joseph, J., Chi, B. H., Kaunda, E., Goodnight, W., Stringer, J. S., A population-based cohort study of stillbirth among twins in Lusaka, Zambia, International Journal of Gynaecology & ObstetricsInt J Gynaecol Obstet, 130, 74-8, 2015	No information regarding chorionicity or amnionicity
Su, R. N., Zhu, W. W., Wei, Y. M., Wang, C., Feng, H., Lin, L., Yang, H. X., Maternal and neonatal outcomes in multiple pregnancy: A multicentre study in the Beijing population, Chronic Diseases and Translational Medicine, 1, 197-202, 2015	No information regarding chorionicity or amnionicity
Sullivan, A. E., Hopkins, P. N., Weng, H. Y., Henry, E., Lo, J. O., Varner, M. W., Esplin, M. S., Delivery of monochorionic twins in the absence of complications: analysis of neonatal outcomes and costs, American Journal of Obstetrics & GynecologyAm J Obstet Gynecol, 206, 257.e1-7, 2012	No usable data (data by weekly gestational age only reported in figures)
Sullivan, A., Hopkins, P. N., Weng, H. Y., Henry, E., Lo, J. O. T., Varner, M. W., Esplin, M. S., Delivery of monochorionic twins in the absence of complications: analysis of neonatal outcomes and costs, American Journal of Obstetrics and Gynecology., 2018	Duplicate - publication date 2012 (not 2018 as noted)
Sun, L., Zou, G., Wei, X., Chen, Y., Zhang, J., Okun, N., Duan, T., Clinical outcomes after assisted reproductive technology in twin pregnancies: chorionicity-based comparison, Scientific ReportsSci, 6, 26869, 2016	Unable to relate outcomes to gestational age at birth (exposure). Relevant outcomes only reported

Study	Reason for Exclusion
	as overall incidence, for twin type, and for mode of conception
Sun, L., Zou, G., Zhou, F., Yang, Y., Oepkes, D., Duan, T., Outcome of dichorionic triamniotic triplet: the experience from an emerging fetal therapy center, Journal of Maternal-Fetal and Neonatal Medicine, 31, 3075-3079, 2018	Data not reported by weekly gestational age
Suzuki,S., Inde,Y., Miyake,H., Comparison of short-term outcomes of late pre-term singletons and dichorionic twins and optimal timing of delivery, Journal of Obstetrics and Gynaecology, 30, 574-577, 2010	No data by amnionicity
Tessen,J.A., Zlatnik,F.J., Monoamniotic twins: a retrospective controlled study, Obstetrics and Gynecology, 77, 832-834, 1991	No usable data (only reported for monochorionic monoamniotic in a figure)
Trojner Bregar, A., Blickstein, I., Verdenik, I., Lucovnik, M., Tul, N., Outcome of monochorionic-biamniotic twins conceived by assisted reproduction: A population-based study, Journal of Perinatal MedicineJ Perinat Med, 44, 881-885, 2016	Outcomes reported as overall incidence by mode of conception. Cannot extract relevant data associated with gestational age at birth (exposure)
Tul, N., Verdenik, I., Novak, Z., Srsen, T. P., Blickstein, I., Prospective risk of stillbirth in monochorionic-diamniotic twin gestations: A population based study, Journal of Perinatal Medicine, 39, 51-54, 2011	Data not reported by weekly gestational age
Valsecchi,L., Serafini,A., Maniscalsco,L., Frontino,G., Cardani,A., Cavoretto,P., Actual controversies in twin delivery: from the analysis of the case histories to a reasoned protocol, Minerva Ginecologica, 61, 23-33, 2009	No relevant data by gestational age
Van De Mheen, L., Everwijn, S. M. P., Haak, M. C., Manten, G. T. R., Zondervan, H. A., Knapen, M. F. C. M., Engels, M. A. J., Erwich, J. J. H. M., Coumans, A. B., Van Vugt, J. M. G., Bilardo, C. M., Van Pampus, M. G., De Groot, C. J. M., Mol, B. W. J., Pajkrt, E., Outcome of Multifetal Pregnancy Reduction in Women with a Dichorionic Triamniotic Triplet Pregnancy to a Singleton Pregnancy: A Retrospective Nationwide Cohort Study, Fetal Diagnosis and Therapy, 40, 94-99, 2016	Relevant outcomes could not be extracted for different gestational age at birth (exposure)
Van De Mheen, L., Everwijn, S. M. P., Knapen, M. F. C. M., Haak, M. C., Engels, M. A. J., Manten, G. T. R., Zondervan, H. A., Wirjosoekarto, S. A. M., Van Vugt, J. M. G., Erwich, J. J. H. M., Bilardo, C. M., Van Pampus, M. G., De Groot, C. J. M., Mol, B. W. J., Pajkrt, E., Pregnancy outcome after fetal reduction in women with a dichorionic twin pregnancy, Human Reproduction, 30, 1807-1812, 2015	Relevant outcomes not reported as linked to gestational age at birth (exposure)
van de Mheen, L., Ravelli, A. C., Oudijk, M. A., Bijvank, S. N., Porath, M. M., Duvekot, J. J., Scholtenhuis, M. A., Bloemenkamp, K. W., Scheepers, H. C., Woiski, M., van Pampus, M. G., Groot, C. J., Pajkrt, E., Mol, B. W., Prediction of Time to Delivery Week-by-Week in Women with a Triplet Pregnancy, American Journal of Perinatology, 33, 1394-1400, 2016	No information regarding amnionicity
van Mieghem, T, De Heus, R., Lewi, L., Klaritsch, P., Kollmann, M., Baud, D., Vial, Y., Shah, P. S., Ranzini, A. C.,	No relevant data by gestational age

Study	Reason for Exclusion
Mason, L., Raio, L., Lachat, R., Barrett, J., Khorsand, V., Windrim, R., Ryan, G., Prenatal management of monoamniotic twin pregnancies, Obstetrics and Gynecology, 124, 498-506, 2014	
Vasak, B., Verhagen, J. J., Koenen, S. V., Koster, M. P. H., de Reu, P. A. O. M., Franx, A., Nijhuis, J. G., Bonsel, G. J., Visser, G. H. A., Lower perinatal mortality in preterm born twins than in singletons: a nationwide study from The Netherlands, American Journal of Obstetrics and Gynecology, 216, 161.e1-161.e9, 2017	No information on chorionicity or amnionicity
Vedel, C., Oldenburg, A., Worda, K., Larsen, H., Holmskov, A., Andreasen, K. R., Uldbjerg, N., Ramb, J., Bodker, B., Skibsted, L., Sperling, L., Hinterberger, S., Krebs, L., Zingenberg, H., Weiss, E. C., Strobl, I., Laursen, L., Christensen, J. T., Ersbak, V., Stornes, I., Krampl-Bettelheim, E., Tabor, A., Rode, L., Short- and long-term perinatal outcome in twin pregnancies affected by weight discordance, Acta Obstetricia et Gynecologica Scandinavica, 96, 233-242, 2017	No information on outcomes by gestational age at birth (exposure)
Wagner, P., Sonek, J., Mayr, S., Abele, H., Goelz, R., Hoopmann, M., Kagan, K. O., Outcome of dichorionic diamniotic twin pregnancies with spontaneous PPROM before 24 weeks' gestation, Journal of Maternal-Fetal and Neonatal Medicine, 30, 1750-1754, 2017	Data not reported by weekly gestational age
Wang, A. Y., Safi, N., Ali, F., Lui, K., Li, Z., Umstad, M. P., Sullivan, E. A., Neonatal outcomes among twins following assisted reproductive technology: An Australian population-based retrospective cohort study, BMC Pregnancy and Childbirth, 18 (1) (no pagination), 2018	No information on chorionicity or amnionicity
Wang, Y. A., Safi, N., Ali, F., Lui, K., Li, Z., Umstad, M., Sullivan, E., Increased rate of inferior neonatal outcomes among twins following assisted reproductive technology, Human Reproduction, 32, 2017	Conference abstract
Zdanowicz Jarmila, A., Eliane, S., Luigi, R., Mathias, N., Roland, G., Do late preterm twins face an increased neonatal morbidity compared with singletons?, Swiss Medical Weekly, 148 (1-2) (no pagination), 2018	No information on chorionicity or amnionicity

Economic studies

Study	Reason for Exclusion
Hickok, R. A., Walker, A. R., Caughey, A. B., Optimal delivery timing for momo twin gestations undergoing continuous fetal monitoring-cost-effective analysis, Obstetrics and Gynecology, 131 (Supplement 1), 118S, 2018	Conference abstract
Hickok, R. A., Walker, A. R., Caughey, A. B., When to deliver monochorionic-monoamniotic twins	Conference abstract

Study	Reason for Exclusion
undergoing inpatient continuous fetal monitoring-A decision analysis, American Journal of Obstetrics and Gynecology, 218 (1 Supplement 1), S153-S154, 2018	
Sullivan, A., Hopkins, P. N., Weng, H. Y., Henry, E., Lo, J. O. T., Varner, M. W., Esplin, M. S., Delivery of monochorionic twins in the absence of complications: analysis of neonatal outcomes and costs, American Journal of Obstetrics and Gynecology., 2018	Not a full economic evaluation with very limited reporting of costs based on hospital charges.

Appendix L – Research recommendations

Research recommendations for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

No research recommendations were made for this review.

Appendix M – Pooled incidence graphs

Graphs for review question: What is the incidence of stillbirth and neonatal death and morbidity by gestational age in twin and triplet pregnancies according to chorionicity and amnionicity?

The following graphs show estimated crude risk of stillbirth per 1000 ongoing pregnancies, estimated crude risk of neonatal mortality and neonatal morbidities per 1000 neonates born by weeks' gestation in monochorionic/dichorionic twin pregnancies according to amnionicity. Error bars show variability. Studies for which data could not be pooled are not included in the graphical summaries.

Dichorionic diamniotic

Figure 3: Incidence of stillbirth per 1000 ongoing pregnancies by gestational age in dichorionic diamniotic twin pregnancies

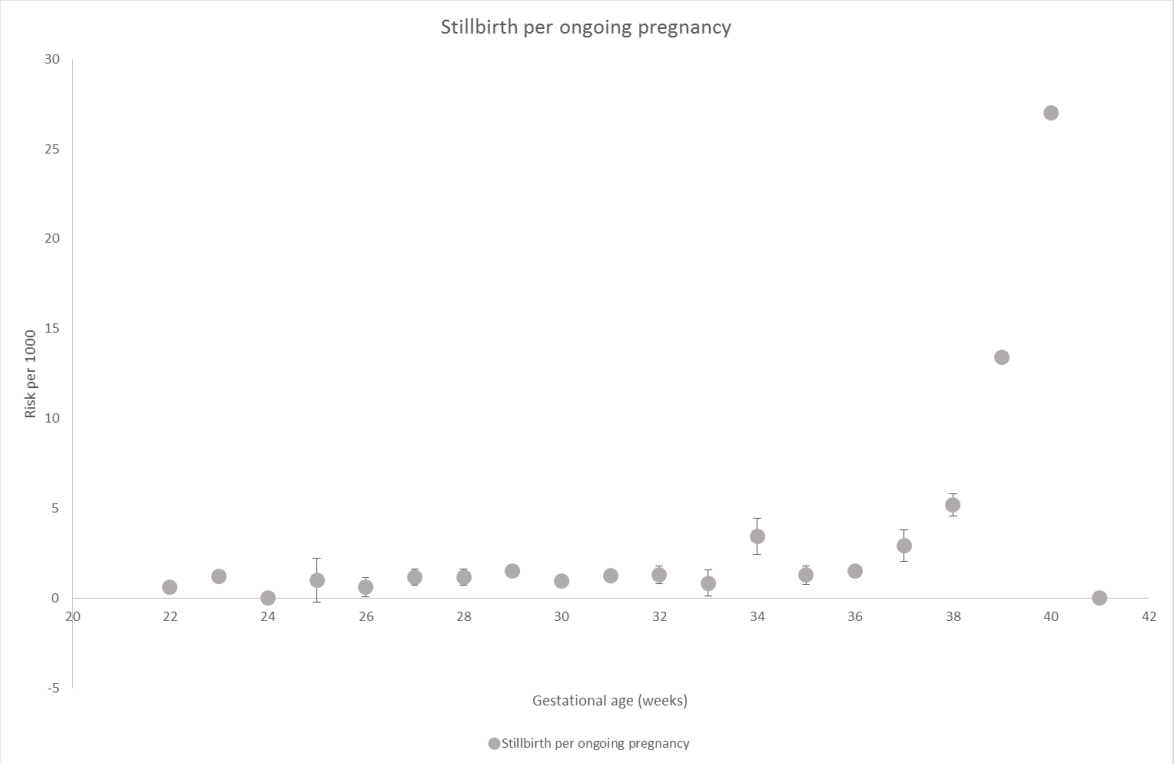


Figure 4: Incidence of neonatal mortality per 1000 neonates born by gestational age in dichorionic diamniotic twin pregnancies

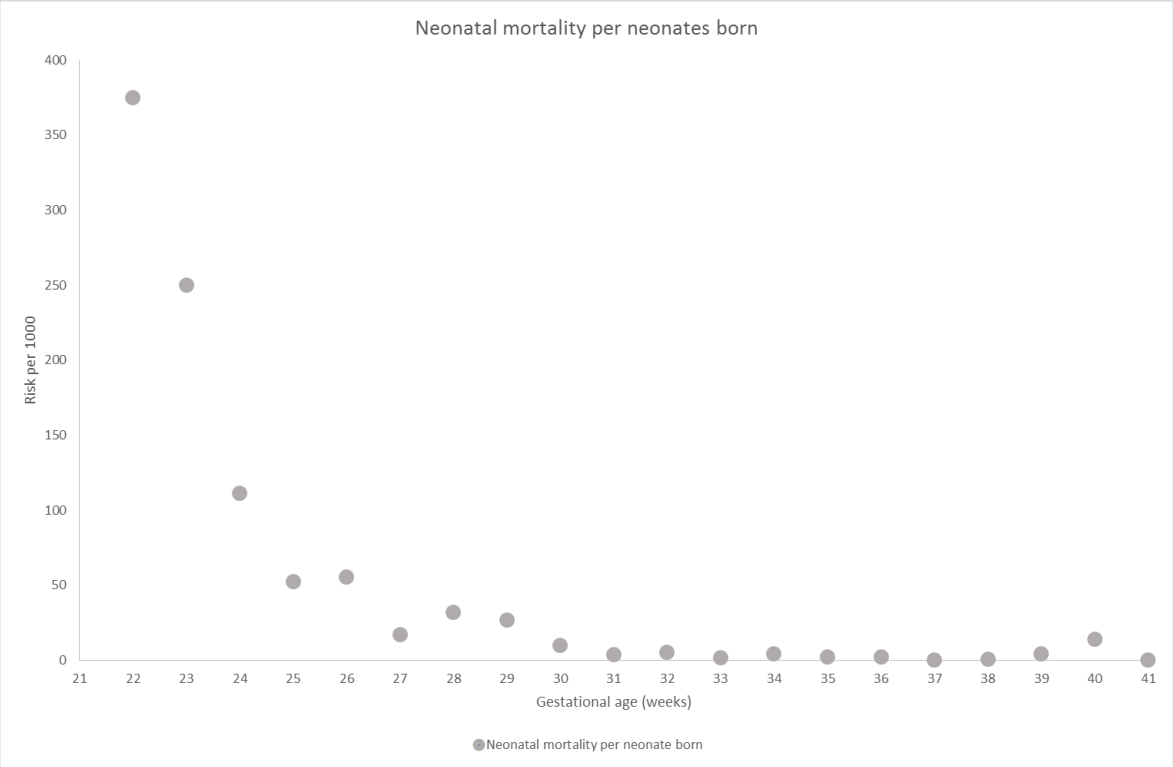


Figure 5: Incidence of neonatal morbidities per 1000 neonates born by gestational age in dichorionic diamniotic twin pregnancies

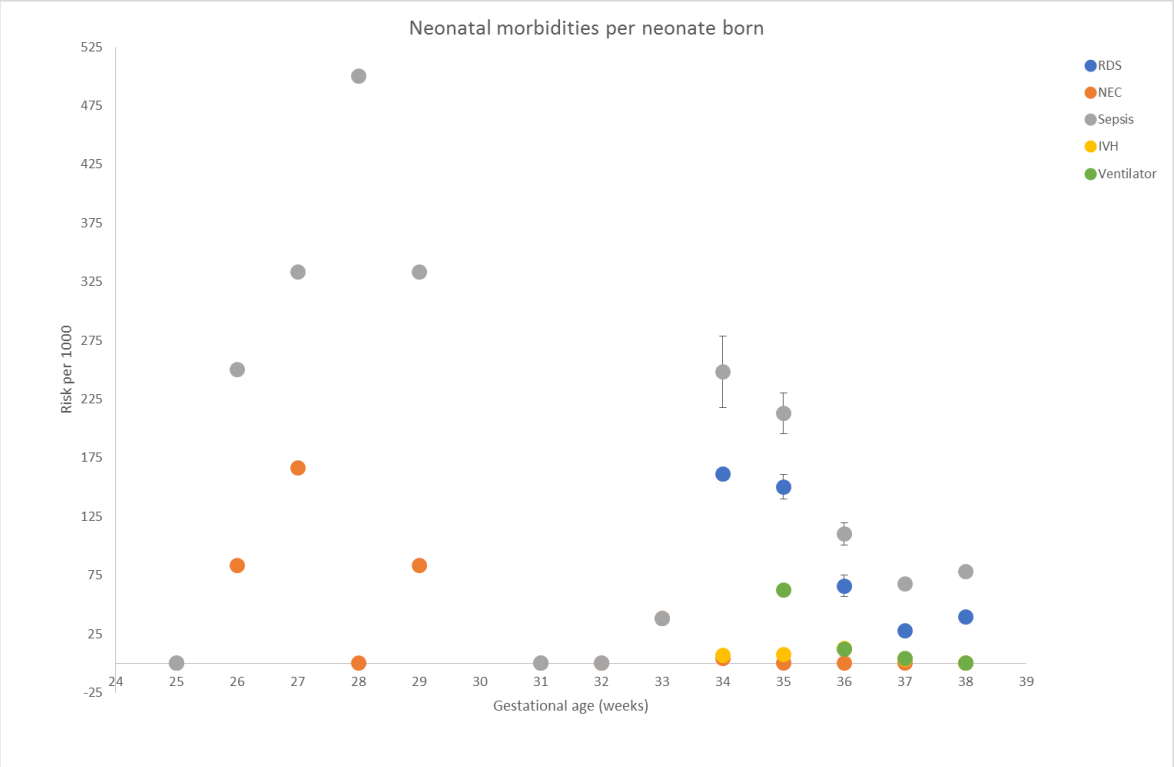
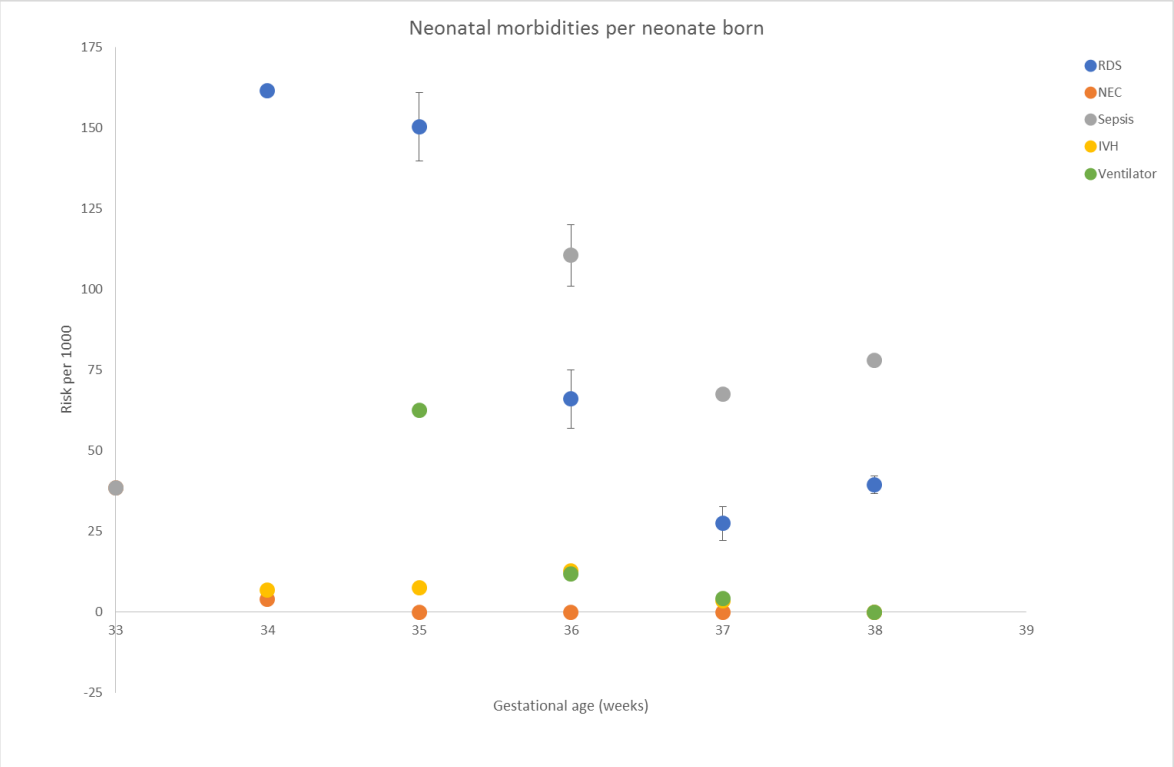


Figure 6: Incidence of neonatal morbidities per 1000 neonates born by gestational age in dichorionic diamniotic twin pregnancies: 33 to 39 weeks' gestation



Monochorionic diamniotic

Figure 7: Incidence of stillbirth per 1000 ongoing pregnancies by gestational age in monochorionic diamniotic twin pregnancies

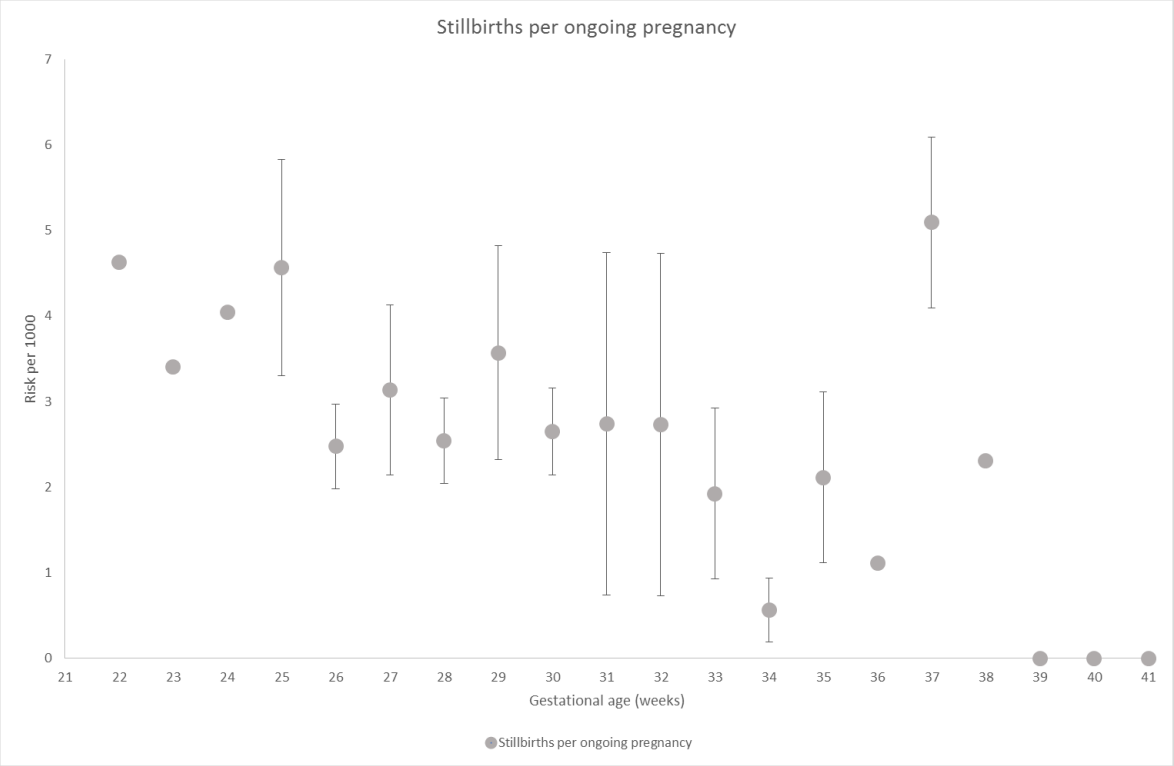


Figure 8: Incidence of neonatal mortality per 1000 neonates born by gestational age in monochorionic diamniotic twin pregnancies

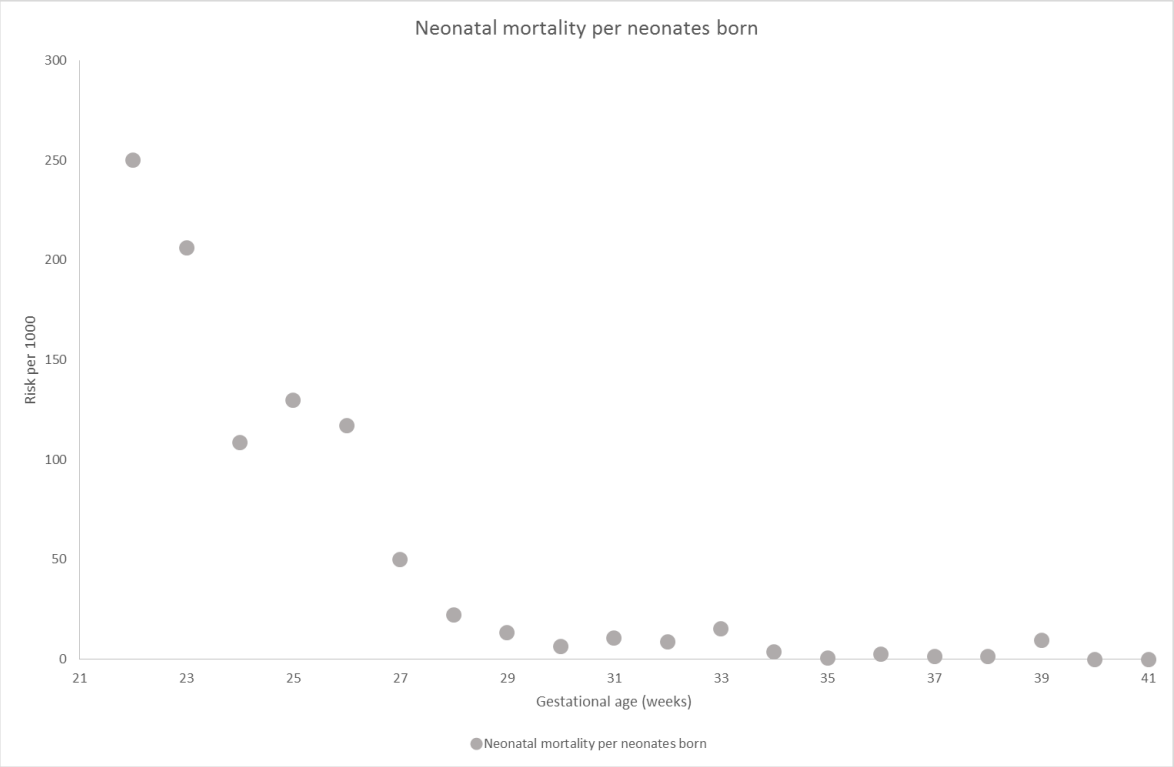


Figure 9: Incidence of neonatal morbidities per 1000 neonates born by gestational age in monochorionic diamniotic twin pregnancies

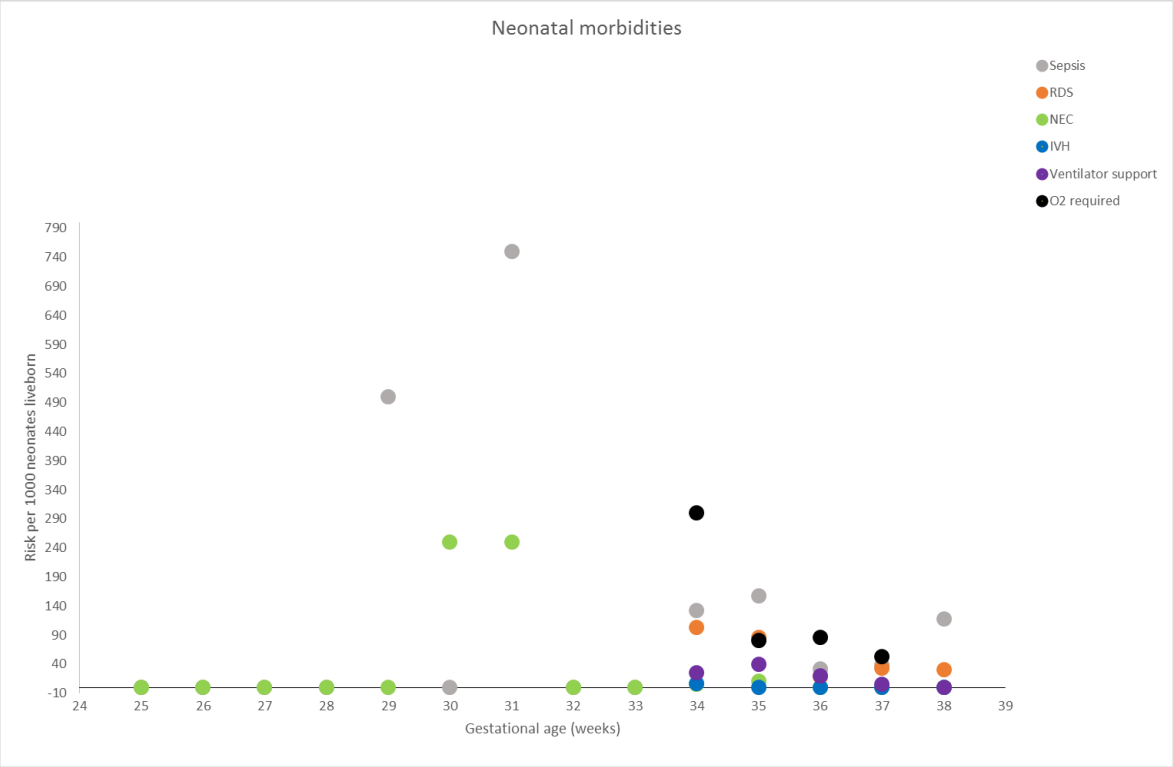
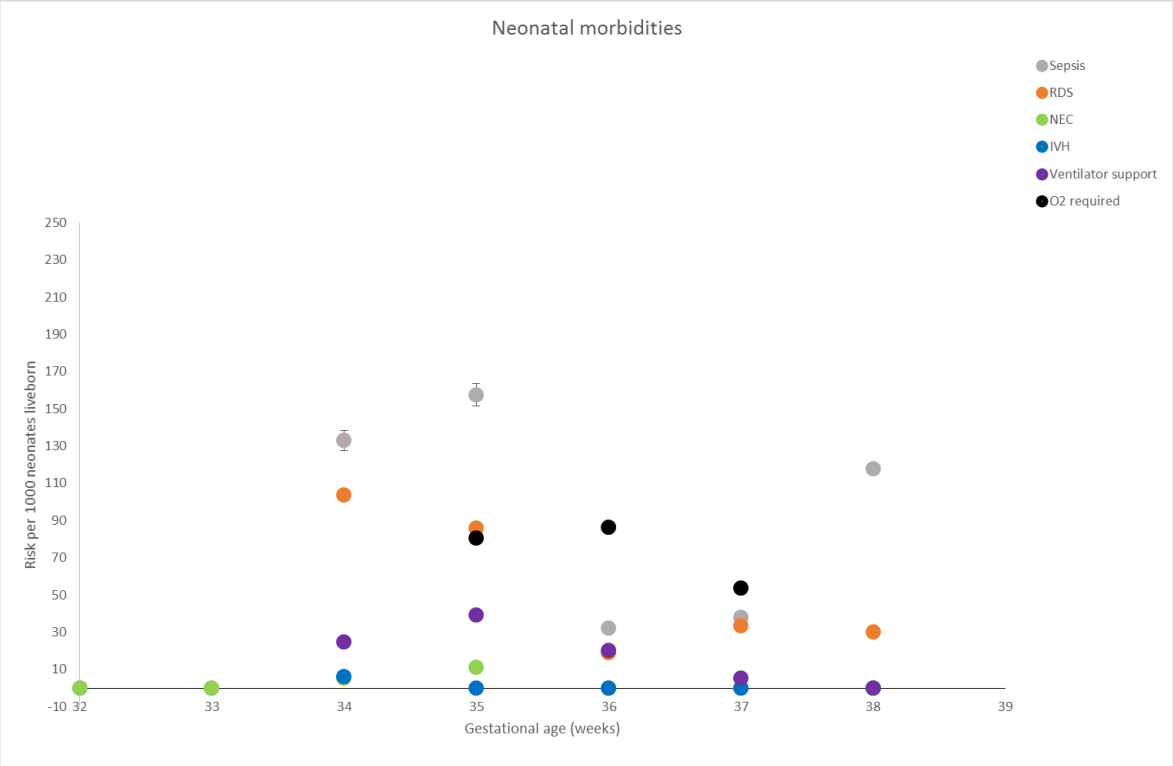


Figure 10: Incidence of neonatal morbidities per 1000 neonates born by gestational age in monochorionic diamniotic twin pregnancies: 32 to 39 weeks' gestation



Monochorionic monoamniotic

Figure 11: Incidence of stillbirths per 1000 ongoing pregnancies by gestational age in monochorionic monoamniotic twin pregnancies

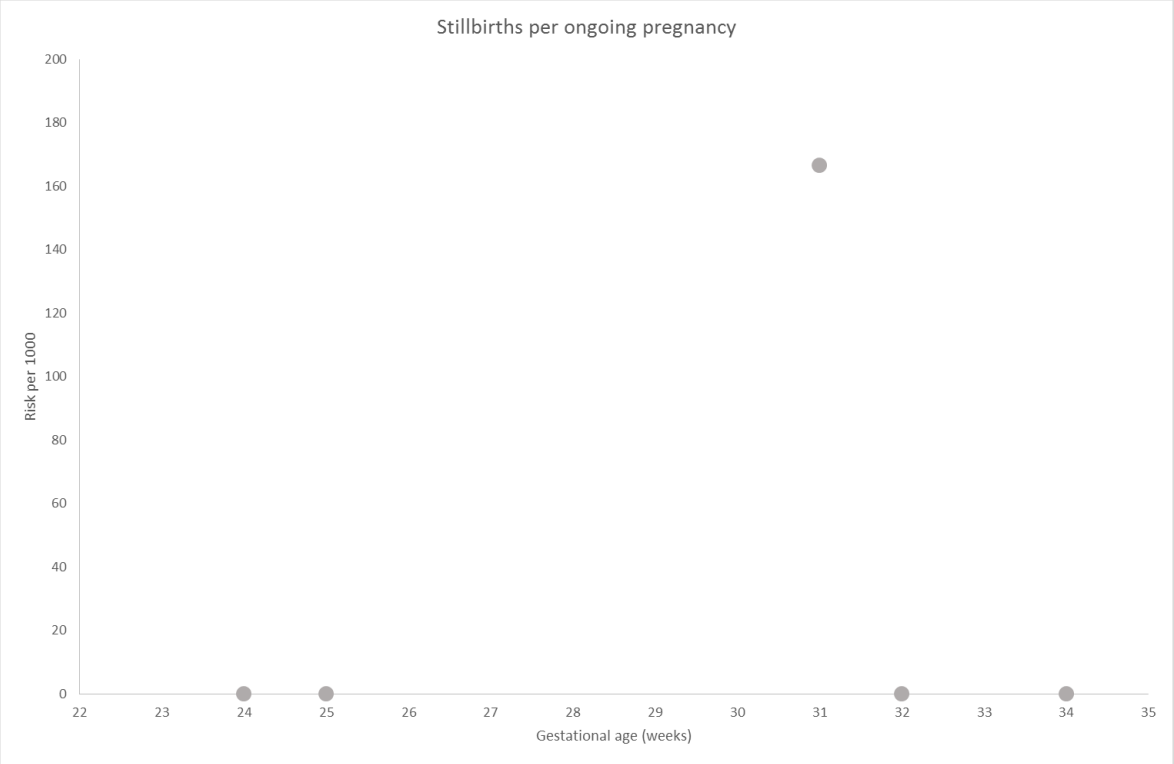


Figure 12: Incidence of neonatal mortality per 1000 neonates born by gestational age in monochorionic monoamniotic twin pregnancies

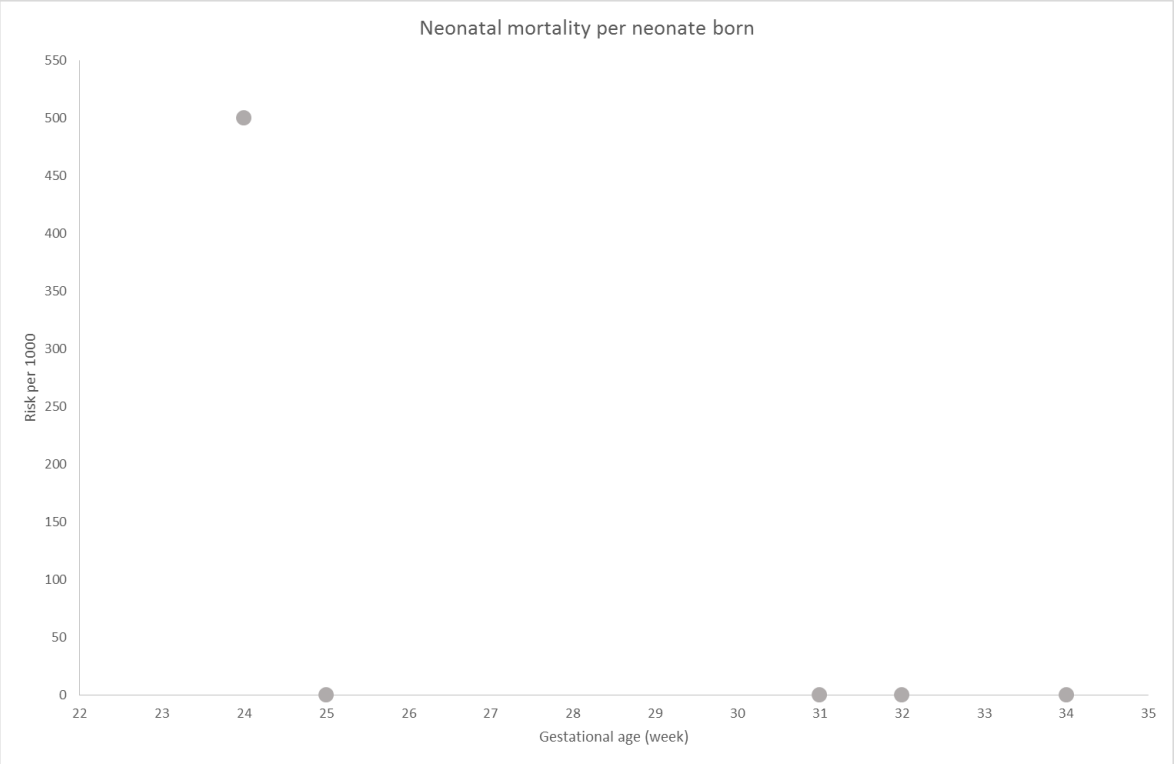


Figure 13: Incidence of necrotising enterocolitis per 1000 neonatea born by gestational age in monochorionic monoamniotic twin pregnancies