Perinatal mortality, timing of delivery and prenatal management of monoamniotic twin pregnancies: systematic review and meta-analysis

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ABSTRACT

Objective: To quantify the rate of perinatal mortality in monochorionic monoamniotic (MCMA) twin pregnancies according to gestational age and to ascertain the incidence of mortality in pregnancies managed as inpatient compared to outpatient.

Methods: Medline, Embase and Cinahl databases were searched. The primary outcomes explored were the incidence of intrauterine death (IUD), neonatal death (NND) and perinatal (PND) death in MCMA twin pregnancies at different gestational age windows (24-30, 31-32, 33-34, 35-36 and beyond 37 weeks of gestation). The secondary outcomes were the incidence of IUD, NND and PND in MCMA twin pregnancies according to the type of fetal monitoring (inpatient vs outpatient) and that of unscheduled deliveries. Random effect model meta-analyses were used to analyse the data.

Results Twenty-five studies (814 non-anomalous twin pairs reaching 24 weeks of gestation) were included. Single (sIUD) and double (dIUD) occurred in 5.0% (95% CI 3.6-6.6) and 4.6% (95% CI 3.3-6.2) of cases, respectively. IUD occurred in 8.6% (95% CI 50.2-12.2) of cases at 24-30 weeks, 2.3% (95% CI 1.1-3.7) at 31-32 weeks and in 4.4% (95% CI 1.9-7.9) at 33-34 weeks of gestation, while there was no IUD, either single or double, from 35 weeks of gestation. In MCMA twin pregnancies managed mainly as inpatient, the incidence of IUD was 5.9% (95% CI 2.9-9.9) while the corresponding figures for those managed mainly as outpatient, IUD was 14.6% (95% CI 8.6-21.8). Finally, 42% (95% CI 27.8-57.4) of MCMA where delivered before the scheduled time, mainly due to spontaneous preterm labour or abnormal CTG findings.

Conclusions: MCMA twins are at high risk of perinatal loss during the third trimester of pregnancies, with the large majority of such losses occurring as apparently unexpected events. Inpatient management seems to be associated with a low rate of mortality although further studies

are needed in order to establish the appropriate type and timing of prenatal assessment in these pregnancies.

INTRODUCTION

Chorionicity is the main determinant of perinatal outcome in twin pregnancies. Monochorionic (MC) are at higher risk of perinatal mortality and morbidity compared to dichorionic (DC) pregnancies due to the excess risk of preterm birth, growth discordance and complications unique to MC placentas such as twin to twin transfusion syndrome (TTTS), twin reverse arterial perfusion (TRAP) sequence and selective intrauterine growth restriction[1-7]. Prenatal identification of monochorionic monoamniotic (MCMA) twins is fundamental because monoamnionicity carries a further increased risk of adverse pregnancy outcome compared to MC diamniotic pregnancies, thus ideally requiring a tailored approach[8].

Despite this, the optimal type of management of MCMA pregnancies has still to be elucidated. There is no randomised controlled trial addressing the type and frequency of follow-up in MCMA pregnancies and no specific recommendation on how to manage MCMA twins is provided by the different national bodies. MCMA pregnancies are usually delivered between 32 and 34 weeks of gestation in view of the reported high risk of unexpected fetal loss with advancing gestation[9]. The antenatal management protocol of MA twin is also controversial, with some studies advocating an inpatient follow-up of these pregnancies with serial ultrasound and cardiotocographic (CTG) assessment, while others report no difference in the perinatal outcome between cases managed as

inpatient and those as outpatient[9]. However, published studies are likely to be biased by their retrospective design, small sample size and inclusion of cases with fetal anomalies, thus making it difficult to extrapolate a robust evidence of the actual risk of perinatal mortality in these pregnancies.

The primary aim of this systematic review was to quantify the incidence of perinatal mortality in MCMA twin pregnancies according to gestational age. The secondary aim was to ascertain the risk of mortality in pregnancies managed as inpatient compared to those managed as outpatient.

METHODS

Protocol, eligibility criteria, information sources and search

This review was performed according to a priori designed protocol recommended for systematic reviews and meta-analysis[10]. Medline, Embase and Cinahl were searched electronically on the 17.12.2017 and updated on the 17.07.2018 utilizing combinations of the relevant medical subject heading (MeSH) terms, key words, and word variants for "monoamniotic", "twin pregnancies" and "outcome" (Supplementary Table 1). The search and selection criteria were restricted to English language. Reference lists of relevant articles and reviews were hand searched for additional reports. Prisma and MOOSE guidelines were followed[11,12]. The study was registered with the PROSPERO database (Registration number: CRD42016043062).

Study selection, data collection and data items

The primary outcome explored in the present systematic review was the incidence of intra-uterine death (IUD), neonatal death (NND) and perinatal (PND) death in MCMA twin pregnancies in the following gestational age windows:

- 24-30 weeks
- 31-32-weeks
- 33-34 weeks
- 35-36 weeks
- more than 37 weeks

IUD was defined as the incidence of fetal demise from 24 weeks of gestation and was divided into single (sIUD) or double (dIUD) according to the death of one or both twins. NND was defined as the death of at least one of the new-borns up to 28 days of life, while PND as the incidence of IUD and NND. We also aimed to categorize the cause of IUD into those related to the presence of TTTS or growth restriction and those sudden or unexpected, defined as IUD occurring in MCMA twins without a prior recognizable chronic condition such as transfusion events or growth abnormalities.

The secondary outcomes were the incidence of IUD, NND and PND in twin pregnancies according to the type of fetal monitoring. For the purpose of this analysis, twin pregnancies were divided into those electively admitted to the hospital for fetal monitoring (inpatients) and those followed as outpatients. Finally, we explored the incidence of unscheduled deliveries in MCMA twin pregnancies scheduled for elective delivery at 32 and between 32 and 34 weeks of gestation.

Only studies reporting the number of MCMA twin pregnancies in each gestational age window and the relative number of deaths were considered suitable for the inclusion. Studies including cases with fetal anomalies were excluded in view of the higher risk of mortality in twins affected by structural or chromosomal anomalies. Only full text articles were considered eligible for the inclusion. Case reports, conference abstracts and case series with fewer than 3 cases were excluded to avoid publication bias. Furthermore, studies published before 2000 were not included as advances in management of twin pregnancies make them less relevant.

Two authors (FD, DB) reviewed all abstracts independently. Agreement regarding potential relevance was reached by consensus; full text copies of those papers were obtained and the same two reviewers independently extracted relevant data regarding study characteristics and pregnancy outcome. Inconsistencies were discussed by the reviewers and consensus reached or by discussion with a third author. If more than one study was published on the same cohort with identical endpoints, the report containing the most comprehensive information on the population was included to avoid overlapping populations. For those articles in which information was not reported but the methodology was such that this information would have been recorded initially, the authors were contacted.

Quality assessment of the included studies was performed using the Newcastle-Ottawa Scale (NOS) for case-control studies. According to NOS, each study is judged on three broad perspectives: the selection of the study groups; the comparability of the groups; and the ascertainment of the outcome of interest[13]. Assessment of the selection of a study includes the evaluation of the representativeness of the exposed cohort, selection of the non-exposed cohort, ascertainment of exposure and the demonstration that the outcome of interest was not present at the start of study. Assessment of the

comparability of the study includes the evaluation of the comparability of cohorts based on the design or analysis. Finally, the ascertainment of the outcome of interest includes the evaluation of the type of the assessment of the outcome of interest, length and adequacy of follow-up. According to NOS a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability[13].

Statistical analysis

Overall, we evaluated the prevalence of each of the explored outcomes in MCMA twin pregnancies. Proportion meta-analyses using a random-effect model to account for the inter-study heterogeneity was used to analyse the data. The potential publication bias was assessed either graphically, displaying the odds ratios of individual studies vs the logarithm of their standard errors (funnel plots), and formally, using Egger's regression asymmetry test[14]. Tests for publication bias were not performed when the overall number of included studies was less than 10 in view of their low power. (Supplementary Material 2)[15].

All analyses were carried out using STATA, version 13.1 (Stata Corp., College Station, TX, 2013).

RESULTS

General characteristics

A total of 607 articles were identified and assessed with respect to their eligibility for inclusion (Supplementary Table 2, Excluded studies). Of those 25 studies were included in the systematic review (Table 1, Figure 1)[16-40]. These 25 studies included 1068 MCMA twin pregnancies; information on the perinatal mortality according to the gestational age at loss was provided for 814 non-anomalous twin pairs reaching 24 weeks of gestation, which represent the population analysed in this systematic review.

The results of quality assessment of the included studies using the Newcastle-Ottawa Scale (NOS) are presented in Table 2. Most of the included studies showed an overall good score regarding the selection and comparability of the study groups, and for ascertainment of the outcome of interest. The main weaknesses of these studies were their retrospective design, small sample size, different gestational ages at ultrasound and lack of information on prenatal management of twins affected by weight discordance.

Synthesis of the results

Twenty-four studies including 814 non-anomalous MCMA twin pregnancies reaching 24 weeks of gestations explored the incidence of mortality according to gestational age. Overall IUD, including either sIUD or dIUD, occurred in 11.8% (95% CI 7.9-16.4) of cases, while the corresponding figures for sIUD and dIUD were 5.2% (95% CI 3.6-6.6) and 4.6% (95% CI 3.3-6.2), respectively. The incidence of NND was 5.1% (95% CI 3.7-6.7) (Table 3, Figure 2).

The incidence of mortality varied according to the different gestational age windows explored. IUD occurred in 8.6% (95% CI 5.2-12.2) of cases at 24-30 weeks, 2.3% (95% CI 1.1-3.7) at 31-32 weeks and in 4.4% (95% CI 1.9-7.9) at 33-34 weeks of gestation, while there was no IUD, either single or double, from 35 weeks of gestation, although the sample size was small (Figure 3).

sIUD and dIUD occurred in 4.0% (95% CI 2.7-5.4) and 3.7% (95% CI 2.6-5.1) at 24-30 weeks, 1.2% (95% CI 0.5-2.1) and 1.1% (95% CI 0.5-2.2) at 31-32 weeks, and 2.0% (95% CI 0.7-3.8) and 2.0% (95% CI 0.7-3.8) of cases at 33-34 weeks of gestation. Finally, NND occurred in 4.9% (95% CI 3.5-6.4) at 24-30 weeks, while there was no death later in gestation (Table 3)

When analysing those studies reporting the aetiology of IUD, 29.5% (95% CI 22.4-45.8; I^2: 55.2%) of the overall losses were due to TTTS or growth restriction, while 49.4% (95% CI 29.1-69.8; I^2: 59.6%) were unexpected IUD. Furthermore, from 31 weeks of gestation all IUDs included in the present systematic review were reported to be unexpected and not the consequence of chronic conditions which can be potentially identified in utero.

Twenty studies reported the incidence of mortality in pregnancies managed mainly as inpatient compared to those followed up as outpatient. In MCMA twin pregnancies managed mainly as inpatient, the incidence of IUD was 5.9% (95% CI 2.9-9.9) while the corresponding figures for sIUD and dIUD were 3.6% (95% CI 1.9-6.0) and 2.1 (95% CI 0.8-4.0), respectively (Table 4). Conversely, in MCMA twin pregnancies managed mainly as outpatient, IUD occurred in 14.6% (95% CI 8.6-21.8), while sIUD and dIUD in 4.7% (95% CI 2.4-7.8) and 6.5 (95% CI 4.1-9.1), respectively (Figure 4).

In pregnancies managed mainly as inpatients, 29.9% (95% CI 11.4-52.7; I^2: 0%) of the IUD were due to TTTS/or growth restriction, while 60.9% (33.2-85.2; I^2: 21.4%) were unexpected, while the

corresponding figures for cases managed mainly as outpatients were 12.2% (95% CI 4.1-23.2; I^2: 0%) and 74.4% (95% CI 55.0-89.8; I^2: 38.3%), respectively.

Finally, we explored the rate of unscheduled deliveries; 37.8% (95% CI 28.0-48.2) of MCMA where delivered before the scheduled time, mainly due to spontaneous preterm labour or abnormal CTG findings. In MCMA twin pregnancies scheduled for delivery at 32 weeks of gestation, the rate of unscheduled deliveries was 18.5% (95% CI 6.5-34.8), while the corresponding figure for those scheduled between 32 and 34 weeks was 34.7.4% (95% CI 26.6-43.2) (Table 5). When stratifying the analysis according to the type of prenatal management adopted, the risk of unexpected delivery was 44.9 (95% CI 28.7-61.6) and 42.3 (95% CI 26.4-59.4) in pregnancies managed mainly as in and outpatient respectively. In pregnancies managed mainly as inpatients, 22.7% (95% CI 10.3-38.2) and 44.9% (95% CI 28.7-61.6) of the unexpected deliveries were due to PTB and CTG abnormalities, while the corresponding figures for pregnancies managed mainly as outpatients were 16.4% (95% CI 10.4-23.4) and 16.7% (95% CI 5.9-31.4) respectively (Supplementary Table 3).

DISCUSSION

Main findings

The findings from this systematic review show that the overall incidence of fetal loss in MCA twin pregnancies is approximately 12%. The large majority of fetal losses occurred before 30 weeks of gestation; while the risk of demise at 31-32 and 33-34 weeks of gestation was 2% and 4% respectively Most IUDs were unexpected, thus questioning the optimal type of assessment in these pregnancies. Finally, the incidence of fetal loss in pregnancies managed mainly as inpatient was 6% as compared to 15% in those follow-up as outpatient. Despite this, the large heterogeneity in the type of prenatal assessment among the included studies highlights the need for developing an adequate protocol of prenatal management of MCMA twin pregnancies focusing on the type and frequency of follow-up rather than admission or not to the hospital.

Strengths and limitations

The small number of cases in some of the included studies, their retrospective non-randomized design, dissimilarity of the populations (due to various inclusion criteria), lack of standardized criteria for the antenatal management of MCMA twin pregnancies represent the major limitations of this systematic review. Assessment of the potential publication bias was also problematic because of the nature of the outcome evaluated (outcome rates, with the left-side limited to a value of zero), which limits the reliability of funnel plots, and because of the scarce number of individual studies, which strongly limits the reliability of formal tests.

Another major limitation of this systematic review is represented by the differences in the antenatal management of MCMA, in terms of type and frequency of assessment.

Despite these limitations, the present review represents the most comprehensive published estimate of the investigated outcomes in MCMA twin pregnancies.

Implications for clinical practice

Management of MCMA twin pregnancies is challenging. As there are no randomized trials assessing the optimal prenatal management of MCMA in terms of type and frequency of follow-up and gestational age at delivery, it is not possible to provide specific recommendation on how to

manage these pregnancies. It is true that MCMA twins are rare; however, prenatal identification of those pregnancies is fundamental in their risk stratification and tailoring their antenatal care[4].

In the present systematic review, only 30% of IUD were due to recognisable conditions such as TTTS or growth abnormalities, while the large majority of them occurred unexpectedly. However, prenatal diagnosis of TTTS in MCMA twin pregnancies is challenging and not based upon classical ultrasound features observed in MCDA pregnancies. Polyhydramnios and non-visualization of the bladder in one of the twins are usually the first signs of TTTS in MCMA twin pregnancies. In this scenario, it may be entirely possible that some of the fetal losses labelled as unexpected were the results of undiagnosed TTTS. This highlights the need of a thorough regular examination of MCMA twins in order to look for signs of TTTS, such as the amniotic fluid volume, visualization of the bladder and fetal Doppler.

Timing of delivery of apparently uncomplicated MCMA twins is still debated. It is common practice to deliver MCMA twins between 32 and 34 weeks of gestation, in view of the reported high risk of IUD in the third trimester of pregnancy. However, most of the previously published studies included fetuses with anomalies, who are at higher risk of fetal loss and come from an era in which the natural history of TTTS had not been systematically elucidated, thus explaining the high rate of deaths labelled as unexpected in otherwise apparently uncomplicated MCMA twins.
The findings from this review showed that fetal loss occur in 2% of pregnancies at 31-32 and 4% at 33-34 weeks of gestation; furthermore, about 2% of losses at 33-34 weeks of gestation were double fetal demises thus highlight the need for a thorough follow-up if pregnancies is continued beyond 32 weeks. A policy of elective delivery at 32 weeks of gestation may look appropriate in view of the apparently higher risk of fetal demise occurring later on in gestation but should be balanced against the potentially higher risk of neonatal morbidity. However, a large proportion of MCMA twins will be delivered before the scheduled time especially as a consequence of spontaneous preterm labour.

The type of prenatal follow-up of MCMA twin pregnancies is also controversial. Some studies claimed that elective admission to the hospital in the third trimester may improve the outcome of

MCMA pregnancies, while others have shown no difference. Furthermore, there is no consensus yet on when to start intensive follow-up and monitoring.

In the present systematic review, the incidence of fetal loss was 6% in pregnancies managed mainly as inpatients compared to 15% in those follow-up as outpatient. However, there was a significant heterogeneity in the management protocols among the included studies, which might have biased the results.

The perinatal outcome of MC pregnancies is not only dependent on the degree of placental sharing between the twins but also by the direction and the magnitude of blood flow through the inter-twin anastomoses. The MCMA twins have a lower risk of developing TTTS compared to MCDA pregnancies due to their peculiar vascular arrangement with nearby placental insertions of the umbilical cords and the large arterio-arterial anastomoses. However, acute unpredictable transfusion events can still occur[3].

An adequate prenatal management of MA twins should include serial assessment of the amniotic fluid, fetal urinary bladders and Doppler studies to rule out signs of TTTS. It is unclear whether systematic evaluation of umbilical cords to diagnose entanglement may reduce the risk of fetal loss as many of them are acute events which may not be easily predicted. Regarding the frequency of fetal monitoring, a twice weekly scan starting from 24-26 weeks of gestation has been proposed in view of the high rate of perinatal loss occurring at 24-30 weeks of gestation. Despite this, parental counselling should stress the fact that a normal scan cannot completely rule out adverse events, as they may occur acutely.

Further large studies are needed in order to develop objective protocols for antenatal surveillance of MCMA twins aiming at reducing the risk of perinatal mortality and morbidity in these pregnancies. Considering the occurrence of IUD in the sub-groups of MCMA pregnancies managed as in- and outpatients (5.9% and 14.6% respectively), a minimum 298 (149 per group) pregnancies per group would be needed to find a different in mortality according to the two management options, with a power of 80% and an alpha error of 0.05.

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Table 1. General characteristics of the studies included.

Author	Year	Country	Study design	Period analysed	Antenatal management	GA at delivery (w)	Pregnancies (n)
Saccone[16]	2018	Italy, Spain, United Kingdom, United States	Retrospective	2010-2017	Inpatient/outpatient	32-34	185
Chinnaia[17]	2018	United Kingdom	Retrospective	2000-2013	Inpatient/outpatient	32-35	55
Kristiansen[18]	2015	Denmark	Retrospective	2008-2011	Outpatient	34	24
Prefumo[19]	2013	Italy	Retrospective	2004-2013	Inpatient	32	20
Anselem[20]	2012	France	Retrospective	1993-2014	Outpatient	36	38
Van Mieghem[21]	2012	Canada, Belgium, The Netherlands, Austria, Switzerland, United States	Retrospective	2003-2012	Inpatient/outpatient	32-34	193
Murata[22]	2012	Japan	Retrospective	2001-2011	Inpatient	32-34	38
Suzuki[23]	2012	Japan	Retrospective	NS	NS	Up to 39	18
Arriola-Garibay[24]	2011	United States	Retrospective	2007-2013	Inpatient	32	6
Dias[25]	2011	United Kingdom	Retrospective	1997-2008	Outpatient	34	30
Quinn[26]	2011	United States	Retrospective	2000-2009	Inpatient	34	13
De Assuncao[27]	2010	Brazil	Retrospective	2003-2006	Inpatient/Outpatient	34	38
Baxi[28]	2010	United States	Retrospective	2001-2009	Inpatient	34	25
Hack[29]	2010	Netherlands	Retrospective	2000-2007	Inpatient or Outpatient	32-34	98
Arabin[30]	2010	Netherlands	Retrospective	NS	Outpatient	NS	17
Heinl[31]	2009	United States	Retrospective	NS	Outpatient	33-34	3
Cordero[32]	2007	United States	Retrospective	1990-2005	Inpatient or Outpatient	32-34	36
Pasquini[33]	2007	United Kingdom	Retrospective	1994-2005	Outpatient	32	20

De Falco[34]	2007	United States	Retrospective	1991-2001	Inpatient or Outpatient	NS	23
Heyborne[35]	2005	United states	Retrospective	1993-2003	Inpatient or Outpatient	32-34	96
Ezra[36]	2005	Israel	Retrospective	1986-2002	Inpatient or Outpatient	NS	33
De Maria[37]	2004	France	Retrospective	1993-2001	Outpatient	36	19
Sau[38]	2002	United Kingdom	Retrospective	1994-2000	Outpatient	32	7
Allen[39]	2001	Canada	Retrospective	1993-2000	Inpatient or Outpatient	32-35	25
Sabire[40]	2000	United Kingdom	Retrospective	1992-1998	Inpatient or Outpatient	34	8

NS: Not stated

Table 2. Quality assessment of the included studies according to Newcastle-Ottawa Scale (NOS) a study can be awarded a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Author	Year	Selection	Comparability	Outcome
Saccone[16]	2018	★★★	★★	★★
Glinianaia[17]	2018	★★★	★★	★★
Kristiansen[18]	2015	★★★	★	★★
Prefumo[19]	2013	★★	★	★★
Anselem[20]	2012	★★	★	★★
Van Mieghem[21]	2012	★★★	★	★★
Murata[22]	2012	★★	★	★★
Suzuki[23]	2012	★★	★	★
Aurioles-Garibay[24]	2011	★★	★	★
Dias[25]	2011	★★	★	★
Quinn[26]	2011	★★	★★	★★
De Assuncao[27]	2010	★★	★	★
Baxi[28]	2010	★★	★	★★
Hack[29]	2010	★★	★	★
Arabin[30]	2010	★	★	★
Heflin[31]	2009	★★	★	★★
Cordero[32]	2007	★★	★	★★
Pasquini[33]	2007	★★★	★	★★
De Falco[34]	2007	★★	★	★★
Heyborne[35]	2005	★★★	★	★★
Ezra[36]	2005	★★	★	★
De Maria[37]	2004	★★	★	★★
Sau[38]	2002	★★	★	★
Allen[39]	2001	★★	★	★★
Sebire[40]	2000	★	★	★

Table 3. Pooled proportions for the occurrence of overall, single (sIUD), double (dIUD) intra-uterine (IUD), neonatal (NND) and perinatal (PND) death in monoamniotic twin pregnancies through gestation.

Outcome	Studies (n)	Fetuses (n/N)	Pooled proportions	I^2 (%)
	Overall mortality			
Overall IUD	24	106/814	11.81 (7.9-16.4)	64.1
sIUD	24	38/814	5.02 (3.6-6.6)	0.8
dIUD*	24	34/814	4.62 (3.3-6.2)	0
NND	24	37/814	5.07 (3.7-6.7)	0
PND	24	143/814	15.80 (11.6-20.6)	58.8
	Mortality between 24 and 30 weeks of gestation			
Overall IUD	24	84/814	8.55 (5.2-12.2)	56
sIUD	24	30/814	3.96 (2.7-5.4)	0
dIUD*	24	27/814	3.74 (2.6-5.1)	0
NND	24	35/814	4.85 (3.5-6.4)	0
PND	24	119/814	12.23 (8.7-16.3)	54.2
	Mortality between 31 and 32 weeks of gestation			
Overall IUD	24	11/633	2.25 (1.1-3.7)	9.7
sIUD	24	5/633	1.17 (0.5-2.1)	0
dIUD*	24	3/633	1.14 (0.5-2.1)	0
NND	24	2/633	1.17 (0.5-2.1)	0
PND	24	13/633	2.59 (1.5-3.9)	0
	Mortality between 33 and 34 weeks of gestation			
Overall IUD	18	11/303	4.41 (1.9-7.9)	34.1
sIUD	18	3/303	1.97 (0.7-3.8)	0
dIUD*	18	4/303	1.96 (0.7-3.8)	0
NND	18	0/303	0 (0-2.7)	0
PND	18	11/303	4.41 (1.9-7.9)	34.1
	Mortality between 35 and 36 weeks of gestation			
Overall IUD	11	0/75	0 (0-7.5)	0
sIUD	11	0/75	0 (0-7.5)	0
dIUD*	11	0/75	0 (0-7.5)	0
NND	11	0/75	0 (0-7.5)	0
PND	11	0/75	0 (0-7.5)	0

*: double IUD was counted as a single event in this category.

Table 4. Pooled proportions for the occurrence of overall, single (sIUD), double (dIUD) intra-uterine (IUD), neonatal (NND) and perinatal (PND) death in monoamniotic twin pregnancies treated mainly as in-and outpatients.

	Inpatient management					Outpatient management			
Outcome	**Studies (n)**	**Fetuses (n/N)**	**Pooled Proportions (95 %)**	**I^2 (%)**		**Studies (n)**	**Fetuses (n/N)**	**Pooled proportions (95%)**	**I^2 (%)**
Overall IUD	12	19/305	5.93 (2.9-9.9)	36.5		14	67/415	14.61 (8.6-21.8)	65.6
sIUD	12	9/305	3.64 (1.9-6.0)	0		14	17/415	4.72 (2.4-7.8)	30.1
dIUD	12	5/305	2.09 (0.8-4.0)	0		14	25/415	6.53 (4.1-9.1)	0
NND	12	8/305	3.0 (1.4-5.2)	0		14	21/415	5.23 (3.2-7.8)	7.9
PND	12	27/305	6.99 (2.8-12.9)	64.0		14	88/415	18.77 (11.7-27.1)	69.7

Table 5. Pooled proportions for the occurrence of unscheduled deliveries in monoamniotic twin pregnancies (PTB: preterm birth; CTG: cardiotocography).

Outcome	Studies	Fetuses (n/N)	Pooled proportions (95% CI)	I^2 (%)
	Overall			
Unscheduled deliveries (overall)	15	216/606	37.81 (28.0-48.2)	79.7
Due to PTB	13	65/178	35.73 (29.0-51.6)	72.2
Due to CTG anomalies	13	80/178	39.15 (23.6-55.9)	73.6
Due to Other reasons	13	33/178	23.85 (12.0-38.52)	68.9
	Delivery scheduled at 32 weeks of gestation			
Unscheduled deliveries (overall)	5	6/39	18.46 (6.5-34.8)	24.8
Due to PTB	4	1/6	22.05 (20.1-55.0)	0
Due to CTG anomalies	4	1/6	22.64 (13.4.59.0)	15.8
Due to Other reasons	4	4/6	64.37 (28.2-93.0)	12.3
	Delivery scheduled at 32-34 weeks of gestation			
Unscheduled deliveries (overall)	7	154/474	34.70 (26.6-43.2)	65.2
Due to PTB	5	52/112	39.96 (21.0-60.6)	75.1
Due to CTG anomalies	5	38/112	35.40 (17.2-56.1)	75.4
Due to Other reasons	5	22/112	22.90 (7.1-44.2)	79.5

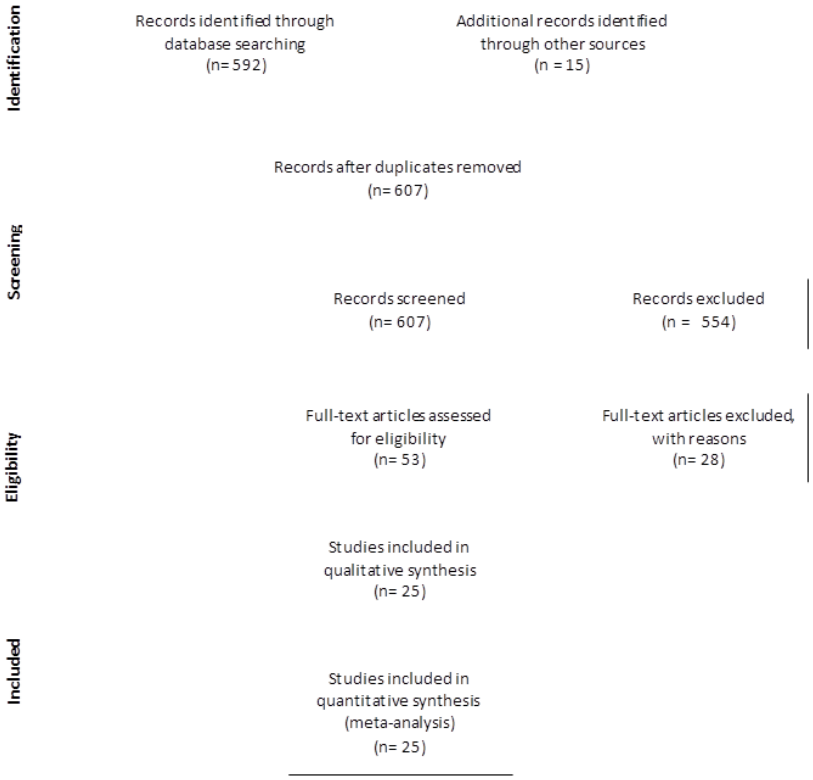
Figure legend

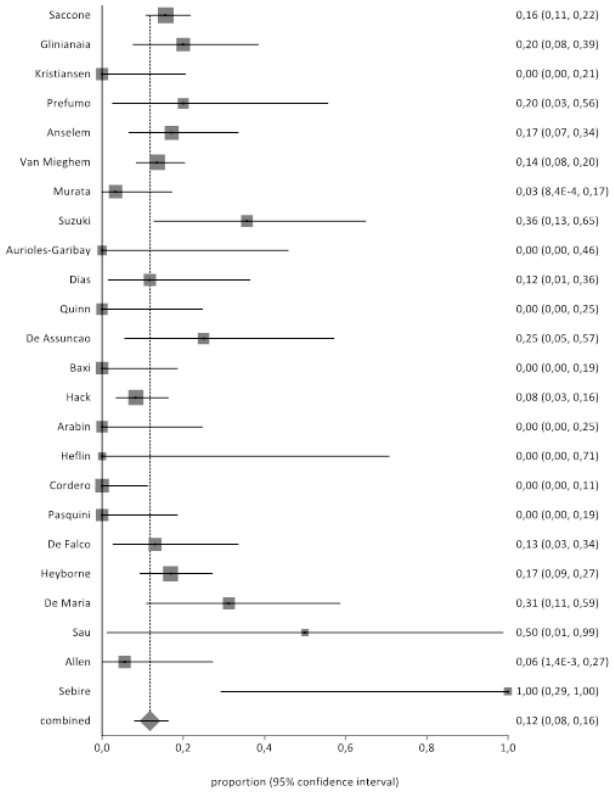
Figure 1. Systematic review flowchart.

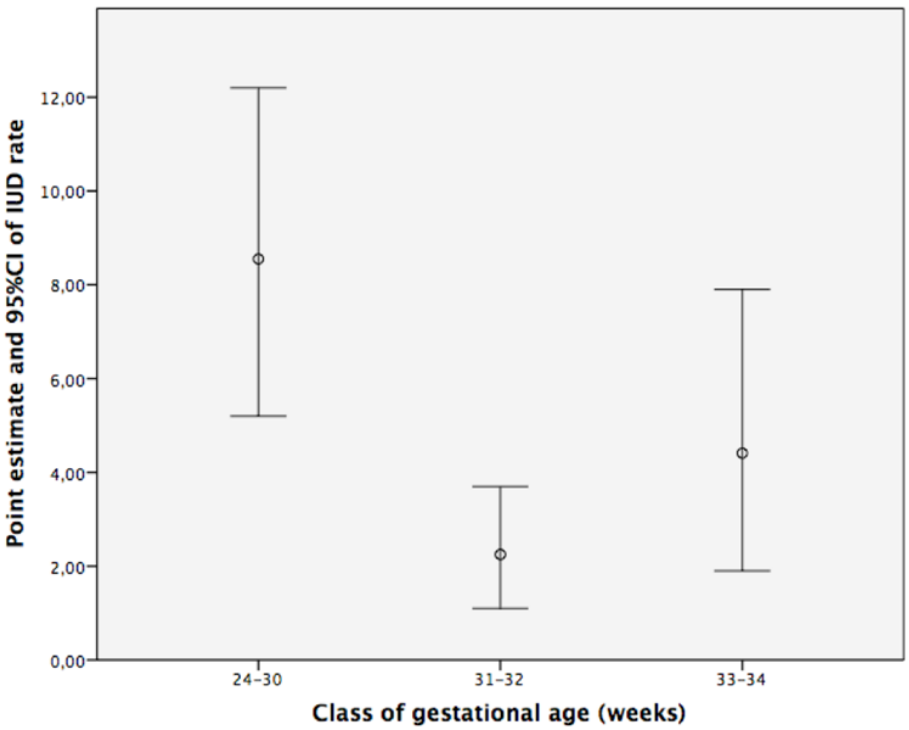
Figure 2. Pooled proportions (95% CI) of the occurrence of overall IUD in MCMA pregnancies.

Figure 3. Point estimates (95% CI) of overall IUD rates according to different gestational age windows.

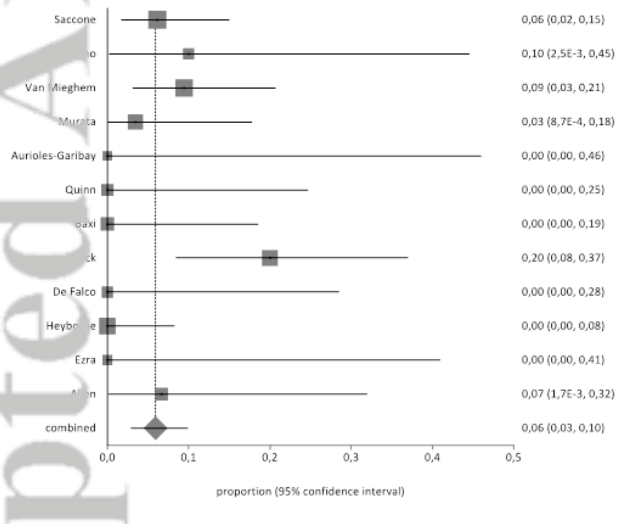
Figure 4. Pooled proportions (95% CI) of the occurrence of overall IUD in MCMA pregnancies manged mainly as in- and outpatient.







Inpatient management



Outpatient management