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Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes (Review)

Jones LV, Ray A, Moy FM, Buckley BS

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[Intervention Review]

Techniques of monitoring blood glucose during pregnancy for women with pre-existing diabetes

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ABSTRACT

Background

There are a number of ways of monitoring blood glucose in women with diabetes during pregnancy, with self-monitoring of blood glucose (SMBG) recommended as a key component of the management plan. No existing systematic reviews consider the benefits/effectiveness of different techniques of blood glucose monitoring on maternal and infant outcomes among pregnant women with pre-existing diabetes. The effectiveness of the various monitoring techniques is unclear. This review is an update of a review that was first published in 2014 and subsequently updated in 2017.

Objectives

To compare techniques of blood glucose monitoring and their impact on maternal and infant outcomes among pregnant women with pre-existing diabetes.

Search methods

For this update, we searched Cochrane Pregnancy and Childbirth's Trials Register, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP) (1 November 2018), and reference lists of retrieved studies.

Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs comparing techniques of blood glucose monitoring including SMBG, continuous glucose monitoring (CGM), automated telemedicine monitoring or clinic monitoring among pregnant women with pre-existing diabetes mellitus (type 1 or type 2). Trials investigating timing and frequency of monitoring were also eligible for inclusion. RCTs using a cluster-randomised design were eligible for inclusion but none were identified.

Data collection and analysis

Two review authors independently assessed study eligibility, extracted data and assessed the risk of bias of included studies. Data were checked for accuracy. The quality of the evidence was assessed using the GRADE approach.

Main results

This review update includes a total of 12 trials (944) women (type 1 diabetes: 660 women; type 2 diabetes: 113 women; type 1 or type 2 (unspecified): 171 women. The trials took place in Europe, the USA and Canada. Three of the 12 included studies are at low risk of bias, eight

studies are at moderate risk of bias, and one study is at high risk of bias. Four trials reported that they were provided with the continuous glucose monitors free of charge or at a reduced cost by the manufacturer.

Continuous glucose monitoring (CGM) versus intermittent glucose monitoring, (four studies, 609 women)

CGM may reduce hypertensive disorders of pregnancy (pre-eclampsia and pregnancy-induced hypertension) (risk ratio (RR) 0.58, 95% confidence interval (CI) 0.39 to 0.85; 2 studies, 384 women; low-quality evidence), although it should be noted that only two of the four relevant studies reported data for this composite outcome. Conversely, this did not translate into a clear reduction for pre-eclampsia (RR 0.65, 95% CI 0.39 to 1.08; 4 studies, 609 women, moderate-quality evidence). There was also no clear reduction in caesarean section (average RR 0.94, 95% CI 0.75 to 1.18; 3 studies, 427 women; I^2 = 41%; moderate-quality evidence) or large-for-gestational age (average RR 0.84, 95% CI 0.57 to 1.26; 3 studies, 421 women; I^2 = 70%; low-quality evidence) with CGM. There was not enough evidence to assess perinatal mortality (RR 0.82, 95% CI 0.05 to 12.61, 71 infants, 1 study; low-quality evidence), or mortality or morbidity composite (RR 0.80, 95% CI 0.61 to 1.06; 1 study, 200 women) as the evidence was based on single studies of low quality. CGM appears to reduce neonatal hypoglycaemia (RR 0.66, 95% CI 0.48 to 0.93; 3 studies, 428 infants). Neurosensory disability was not reported.

Other methods of glucose monitoring

For the following five comparisons, self-monitoring versus a different type of self-monitoring (two studies, 43 women); self-monitoring at home versus hospitalisation (one study, 100 women), pre-prandial versus post-prandial glucose monitoring (one study, 61 women), automated telemedicine monitoring versus conventional system (three studies, 84 women), and constant CGM versus intermittent CGM (one study, 25 women), it is uncertain whether any of the interventions has any impact on any of our GRADE outcomes (hypertensive disorders of pregnancy, caesarean section, large-for-gestational age) because the quality of the evidence was found to be very low. This was due to evidence largely being derived from single trials, with design limitations and limitations with imprecision (wide CIs, small sample sizes, and few events). There was not enough evidence to assess perinatal mortality and neonatal mortality and morbidity composite. Other important outcomes, such as neurosensory disability, were not reported in any of these comparisons.

Authors' conclusions

Two new studies (406 women) have been incorporated to one of the comparisons for this update. Although the evidence suggests that CGM in comparison to intermittent glucose monitoring may reduce hypertensive disorders of pregnancy, this did not translate into a clear reduction for pre-eclampsia, and so this result should be viewed with caution. There was no evidence of a difference for other primary outcomes for this comparison. The evidence base for the effectiveness of other monitoring techniques analysed in the other five comparisons is weak and based on mainly single studies with very low-quality evidence. Additional evidence from large well-designed randomised trials is required to inform choices of other glucose monitoring techniques and to confirm the effectiveness of CGM.

PLAIN LANGUAGE SUMMARY

Methods for monitoring blood glucose in pregnant women with diabetes to improve outcomes

What is the issue and why is this important?

If a mother already has diabetes when she becomes pregnant, she and her baby are at higher risk of various problems. Women with existing diabetes that is not well-controlled at conception and in the first three months of pregnancy are at increased risk of miscarriage, having a baby with developmental problems or stillbirth. The baby is also at increased risk of developing diabetes in childhood. Problems for mothers include developing high blood pressure and associated ill-health, early births, large babies, difficult births and the need for caesarean section. During labour the baby is at increased risk of a shoulder becoming stuck (shoulder dystocia) and of bleeding in the brain (intracranial haemorrhage). After birth the baby is more likely to have low blood sugar levels (hypoglycaemia), jaundice and breathing problems. This means they are more likely to be admitted to intensive care. During pregnancy, the mother will have her blood glucose (sugar) levels monitored so appropriate steps can be taken to control her blood sugar.

Several methods of monitoring blood glucose are used, including regular testing at antenatal clinics and self-monitoring by women at home. The timing varies, such as monitoring before meals versus monitoring after meals, and how often levels are measured. For continuous glucose monitoring (CGM), technologies are used to transfer information directly from the woman to her clinician and include telemedicine (telephone and video systems, information technology) and digital technologies (mobile phones, tablets). The aim of these methods is to provide a more accurate measure of blood sugar levels so that they can be more effectively controlled, in order to reduce potential problems.

What evidence did we find?

This is an update of a review first published in 2014, updated in 2017. We searched for evidence from randomised controlled studies in November 2018. We identified 12 studies involving 944 women (type 1 diabetes: 660 women; type 2 diabetes: 113 women; in two trials (171 women) there was a mix of type 1 and type 2 diabetes. The trials were from Europe, USA and Canada.

There were six comparisons. These were: continuous versus intermittent monitoring of blood glucose (four studies, 609 women); two different ways of self-monitoring (two studies, 43 women); self-monitoring at home versus hospitalisation to control blood glucose levels

(one study, 100 women); blood glucose monitoring before a meal (pre-prandial) versus blood glucose monitoring after a meal (post-prandial) (one study, 61 women); automated telemedicine monitoring versus conventional care (three studies, 84 women); and constant continuous monitoring versus intermittent continuous monitoring (one study, 25 women),

Continuous versus intermittent monitoring may reduce overall high blood pressure problems during pregnancy (two studies, 384 women, low-quality evidence). However, it should be noted that only two of four relevant studies reported data for this outcome. There was more evidence on high blood pressure and protein in their urine (pre-eclampsia), which showed no clear difference (four studies, 609 women). We also found no difference in the number of women having a caesarean section (three studies, 427 women; moderate-quality evidence). There was not enough evidence to assess infant deaths or the combined outcome of infant deaths and ill-health as these outcomes were based on single studies. Four studies received some support from commercial partners.

The other comparisons of different ways of monitoring blood glucose levels were based on very small studies or single studies with very low-quality evidence that did not show any clear differences in outcomes.

What does this mean?

Although the evidence from randomised controlled studies suggests that continuous monitoring of blood glucose levels may be more effective in reducing high blood pressure problems during pregnancy, only two studies reported on this. There was no clear reduction for pre-eclampsia based on evidence from four studies. For other methods of glucose monitoring, the review showed that there is not enough evidence to say with any certainty which monitoring method for blood glucose is best. More research is needed to find out which other monitoring method is best at reducing the risk of complications for pregnant women with pre-existing diabetes and to confirm the effectiveness of continuous glucose monitoring.

SUMMARY OF FINDINGS

Summary of findings for the main comparison. Continuous glucose monitoring compared to intermittent glucose monitoring for women with pre-existing diabetes

Continuous glucose monitoring compared to intermittent glucose monitoring for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 1 study in a hospital centre for pregnant women with diabetes in Denmark, 1 study in two secondary care multi-disciplinary obstetric diabetic clinics in the UK, 1 multi-centre study in 31 hospital and diabetic clinics in Canada, England, Scotland, Spain, Italy, Ireland and the USA, and 1 multi-centre study in 22 hospital outpatient obstetric and endocrinology clinics (university, teaching and non-teaching in the Netherlands and 1 university hospital in Belgium).

Intervention: continuous glucose monitoring
Comparison: intermittent glucose monitoring

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with intermittent self-glucose monitoring	Risk with continuous glucose monitoring				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population		RR 0.58 (0.39 to 0.85)	384 (2 RCTs)	⊕⊕⊖⊖ LOW [1 2]	
	292 per 1000	170 per 1000 (114 to 248)				
Caesarean section	Study population		RR 0.94 (0.75 to 1.18)	427 (3 RCTs)	⊕⊕⊕⊖ MODERATE[3]	
	600 per 1000	564 per 1000 (450 to 708)				
Large-for-gestational age	Study population		RR 0.84 (0.57 to 1.26)	421 (3 RCTs)	⊕⊕⊖⊖ LOW [4 5]	
	546 per 1000	459 per 1000 (311 to 688)				
Perinatal mortality (stillbirth and neonatal mortality)	Study population		RR 0.82 (0.05 to 12.61)	71 (1 RCT)	⊕⊕⊖⊖ LOW[6]	
	31 per 1000	26 per 1000 (2 to 394)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] We downgraded (1) level for serious limitations in study design due to unclear risk of allocation concealment and high risk for selective outcome reporting
[2] We downgraded (1) level for serious indirectness due to the two studies reporting this composite outcome in different ways: Voormolen 2018 reported a composite of pregnancy-induced hypertension and pre-eclampsia for women with type 1 diabetes and type 2 diabetes for; and Feig 2017 reporting a composite of worsening chronic, gestational and pre-eclampsia for women with type 1 diabetes
[3] We downgraded (1) level for serious inconsistency due to evidence of statistical heterogeneity $I^2 = 41\%$
[4] We downgraded (1) level for serious imprecision due to wide CI crossing the line of no effect
[5] We downgraded (1) level for serious inconsistency due to evidence of statistical heterogeneity $I^2 = 70\%$
[6] We downgrade (2) levels for very serious imprecision due to evidence derived from a single study, with a small number of events, wide CI crossing the line of no effect

Summary of findings 2. Self-monitoring compared to a different type of self-monitoring for women with pre-existing diabetes

Self-monitoring compared to standard care for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 1 study in a high-risk obstetric clinic at University hospital in the USA
Intervention: self-monitoring
Comparison: standard care

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with standard care	Risk with self-monitoring				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population			(0 studies)		The included study did not report this outcome.
Caesarean section	Study population		RR 0.78 (0.40 to 1.49)	28 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1,2]	
	643 per 1000	501 per 1000 (257 to 958)				

Large-for-gestational age	Study population			(0 studies)		The included study did not report this outcome.
Perinatal mortality (stillbirth and neonatal mortality)	Study population		RR 3.00 (0.13 to 67.91)	28 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1] [2]	There were no events in the standard care group and so anticipated absolute effects could not be calculated.
	0 per 1000	0 per 1000 (0 to 0)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] We downgraded (1) level for serious limitations in design limitations due unclear allocation concealment and high risk for attrition
[2] We downgraded (2) levels for very serious imprecision due to wide CI crossing the line of no effect, few events and small sample size

Summary of findings 3. Self-monitoring at home compared to hospitalisation for women with pre-existing diabetes

Self-monitoring compared to hospitalisation for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 1 study in Sweden with monitoring at home or in hospital
Intervention: self-monitoring
Comparison: hospitalisation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with hospitalisation	Risk with self-monitoring				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population		RR 1.19 (0.41 to 3.51)	100 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1] [2]	
	109 per 1000	129 per 1000				

		(45 to 381)				
Caesarean section	Study population		RR 0.96 (0.65 to 1.44)	100 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1] [2]	
	500 per 1000	480 per 1000 (325 to 720)				
Large-for-gestational age	Study population			(0 studies)		The included study did not report this outcome.
Perinatal mortality (stillbirth and neonatal mortality)	Study population		RR 0.85 (0.05 to 13.24)	100 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1] [2]	
	22 per 1000	18 per 1000 (1 to 288)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] We downgraded (1) level for serious limitations in study design due to unclear randomisation, allocation concealment and high risk for attrition
[2] We downgraded (2) levels for very serious imprecision due to wide CI crossing the line of no effect, few events and small sample size

Summary of findings 4. Pre-prandial compared to post-prandial glucose monitoring for women with pre-existing diabetes

Pre-prandial compared to post-prandial glucose monitoring for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 1 study in a joint metabolic and antenatal clinic in Belfast

Intervention: pre-prandial
Comparison: post-prandial glucose monitoring

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with post-prandial glucose monitoring	Risk with pre-prandial				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population			(0 studies)		The included study did not report this composite outcome.
Caesarean section	Study population		RR 1.45 (0.92 to 2.28)	61 (1 RCT)	⊕⊝⊝⊝ VERY LOW [1,2]	
	467 per 1000	677 per 1000 (429 to 1000)				
Large-for-gestational age	Study population		RR 1.16 (0.73 to 1.85)	61 (1 RCT)	⊕⊝⊝⊝ VERY LOW [1,2]	
	500 per 1000	580 per 1000 (365 to 925)				
Perinatal mortality (stillbirth and neonatal mortality)	Study population		RR 2.91 (0.12 to 68.66)	61 (1 RCT)	⊕⊝⊝⊝ VERY LOW [1,2]	There were no events in the standard care group and so anticipated absolute effects could not be calculated.
	0 per 1000	0 per 1000 (0 to 0)				

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] We downgraded (1) level for serious limitations in study design due to unclear methods of randomisation and high risk of attrition
[2] We downgrade (2) levels for very serious limitations in imprecision due to wide CI crossing the line of no effect, few events and small sample size

Summary of findings 5. Automated telemedicine monitoring compared to conventional for women with pre-existing diabetes

Automated telemedicine monitoring compared to conventional for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 2 studies in antenatal diabetic clinics in Italy, 1 study in gastroenterology and metabolic diseases clinic in Poland
Intervention: automated telemedicine monitoring
Comparison: conventional monitoring

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with conventional monitoring	Risk with automated telemedicine monitoring				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population			(0 studies)		The included studies did not report this composite outcome.
Caesarean section	Study population		RR 0.96 (0.62 to 1.48)	32 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1,2]	
	733 per 1000	704 per 1000 (455 to 1000)				
Large-for-gestational age	Study population			(0 studies)		The included studies did not report this outcome.
Perinatal mortality (stillbirth and neonatal mortality)	Study population			(0 studies)		The included studies did not report this outcome.

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[1] We downgraded (2) levels for very serious design limitations due to high risk for randomisation, allocation concealment, attrition and other bias
[2] We downgraded (2) levels for very serious imprecision due to wide CI crossing the line of no effect, few events and small sample size

Summary of findings 6. Constant CGM compared to Intermittent CGM for women with pre-existing diabetes

Constant CGM compared to Intermittent CGM for women with pre-existing diabetes

Patient or population: women with pre-existing diabetes
Setting: 1 study in University clinic of endocrinology, diabetes and metabolic disorders in Macedonia
Intervention: constant CGM
Comparison: intermittent CGM

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Risk with Intermittent CGM	Risk with constant CGM				
Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)	Study population			(0 studies)		The included study did not report this outcome.
Caesarean section	Study population		RR 0.77 (0.33 to 1.79)	25 (1 RCT)	⊕⊖⊖⊖ VERY LOW [1] [2]	
	538 per 1000	415 per 1000 (178 to 964)				
Large-for-gestational age	Study population			(0 studies)		The included study did not report this outcome.
Perinatal mortality (stillbirth and neonatal mortality)	Study population			(0 studies)		The included study did not report this outcome.

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomised controlled trial; **RR:** Risk ratio

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate quality: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low quality: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low quality: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

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[1] We downgraded (1) level for serious limitations in design due to unclear randomisation and allocation concealment
[2] We downgraded (2) levels for very serious limitations in imprecision due to wide CI crossing the line of no effect, few events and small sample size

BACKGROUND

Description of the condition

Types of diabetes

There are three main types of diabetes mellitus: type 1, type 2 and gestational diabetes mellitus (GDM). Type 1 or insulin-dependent diabetes results from the body's failure to produce sufficient insulin and accounts for a minority of the total burden of diabetes in a population. Type 2 diabetes results from a failure of the body to utilise insulin, causing high blood sugar levels. Type 2 diabetes alone constitutes about 85% to 95% of all diabetes globally (IDF 2010). Type 2 diabetes is a serious and growing global health problem that has evolved in association with rapid cultural and social changes, ageing populations, increasing urbanisation, dietary changes, reduced physical activity and other unhealthy lifestyle and behavioural patterns (WHO 1994). In GDM, women who were not previously diabetic develop carbohydrate intolerance resulting in hyperglycaemia (high blood sugar levels) with first onset or detection occurring during pregnancy (HAPO 2002). GDM develops in one in 25 pregnancies worldwide and it is associated with the increasing incidence of type 2 diabetes post-pregnancy. There are also women who are diagnosed with type 1 or type 2 diabetes before they get pregnant and so have pre-existing diabetes. This review focuses on women with pre-existing diabetes.

Prevalence of diabetes

Diabetes mellitus is found in every population in the world and it is estimated that 6.6% of the global population in the age group of 20 to 79 years old had diabetes in 2010. By 2030, it is estimated that 7.8% of the adult population will have diabetes (IDF 2010).

Diabetes mellitus complicates about 2% to 3% of all pregnancies. Approximately 90% of diabetes in pregnancy is accounted for by GDM. Pre-existing type 1 and type 2 diabetes account for the remaining 10% of diabetes during pregnancy (Moore 2010). This review considers only the care of pregnant women with pre-existing diabetes. A separate Cochrane Review on GDM has been published (Raman 2017).

Complications of diabetes in pregnancy: for mother and baby

Women with diabetes of any kind are at increased risk of morbidity and mortality during pregnancy. Pregnancy outcomes for women with pre-existing diabetes and their infants are poor compared to those for women who do not have diabetes (NICE 2008; NICE 2015). The risks to both women and infants include fetal macrosomia (large baby), preterm birth, birth trauma (to mother and infant), induction of labour or caesarean section, miscarriage, congenital malformation, stillbirth, transient neonatal morbidity, neonatal death, obesity or diabetes, or both developing later in the baby's life (Gonzalez-Gonzalez 2008; Kitzmiller 2008; NICE 2008; NICE 2015).

Women with diabetes have an increased risk of an early miscarriage and are at increased risk of having a baby with malformations. Both of these risks are associated with less than optimal glycaemic control around the time of conception and in the first trimester. The risks appear to be approximately equivalent for women with type 1 and type 2 diabetes. The increased rate of spontaneous miscarriages and fetal malformation appears to be low when glycaemic control is moderately raised, and higher with increasingly poor glycaemic control (IDF 2010; Jensen 2009). Women with diabetes should be encouraged to obtain the best possible glycaemic control before conception (Kitzmiller 2010). Women with uncontrolled glycaemic levels should be discouraged from becoming pregnant until their blood glucose control can be improved.

Macrosomia, defined as infant birthweight greater than 4.5 kg, remains the commonest complication of pregnancy in women with diabetes (IDF 2010; Kitzmiller 2008; NICE 2008; NICE 2015). Macrosomia occurs in 27% to 62% of infants of diabetic mothers compared with 10% of non-diabetic mothers (Gabbe 2003). Nationwide studies from the Netherlands, the UK, and Denmark estimate that the risk of a mother with type 1 diabetes giving birth to a baby who is large-for-gestational age, or has macrosomia ranges from 48.8% to 62.5% (Kitzmiller 2008). Recent data confirm that women with type 2 diabetes have an equally high risk of giving birth to an infant with macrosomia (ACOG 2005; ADA 2004; Roland 2005). For mothers with diabetes, macrosomia leads to an increased risk of perineal lacerations, complications in labour, and delivery by caesarean section (Slocum 2004). There are increased risks for the infants of intracranial haemorrhage, shoulder dystocia, neonatal hypoglycaemia, jaundice, and respiratory distress (Thomas 2006), as well as the longer-term health risks of insulin resistance, obesity and type 2 diabetes (McElduff 2005). Overt diabetes is an undisputed factor for preterm birth (Sibai 2000).

Fetal hyperglycaemia causes fetal hypoxia and acidosis, which may explain the excess stillbirth rates observed in women with poorly controlled diabetes (Kitzmiller 2008). Infants with macrosomia due to poor maternal glycaemic control and fetal hyperinsulinaemia are more likely to develop obesity and glucose intolerance later in life (Fetita 2006; Kitzmiller 2008). Long-term (five to 15 years) follow-up studies of infants of mothers with diabetes suggest that poor glycaemic control during pregnancy has a negative influence on intellectual and psychomotor development (Kitzmiller 2008). Both findings highlight the prolonged effects on offspring of intrauterine exposure to diabetes (Fetita 2006; Kitzmiller 2008).

Glycaemic control prior to conception and in early pregnancy

The increased risks in women with diabetes of an early miscarriage and of having a baby with malformations are associated with suboptimal glycaemic control before or around the time of conception, and in the first trimester. Guidelines recommend that women should achieve the best possible glycaemic control before conception: women who improve their glycaemic control before conception have a reduced rate of fetal malformation (Fuhrmann 1983; IDF 2010; NICE 2008; NICE 2015).

Maternal hyperglycaemia during the first few weeks of pregnancy is strongly associated with increased spontaneous abortions and major congenital malformations (Kitzmiller 1996; Ray 2001). After 12 weeks' gestation, hyperglycaemia induces fetal hyperinsulinaemia, accelerated growth, and excess adiposity in animal models and in women with diabetes (Gabbe 2003). These risks appear to be approximately equivalent for women with type 1 and type 2 diabetes. The increased rate of spontaneous miscarriages appears to be low when the HbA1c is modestly raised, and higher with increasingly poor glycaemic control (Mills 1988; Rosenn 1991). The same pattern is also found with respect to the rate of fetal malformations (Greene 1989; Suhonen 2000).

Description of the intervention

Techniques of blood glucose monitoring

Glucose readings supply trend information that helps to identify and prevent unwanted periods of hypo- and hyperglycaemia that are associated with adverse outcomes for both mother and baby. Women with type 1 and type 2 diabetes are advised to self-monitor their blood glucose throughout pregnancy (IDF 2010).

Techniques of blood glucose monitoring to be considered in this review include self-monitoring of blood glucose (SMBG), continuous glucose monitoring (CGM) and clinic monitoring (for which timing and frequency of monitoring are also considered).

1. Self-monitoring of blood glucose (SMBG): a glucose meter (glucometer), with or without memory, can be used to measure capillary glucose. Conventional intensified glucose monitoring is defined as three to four blood glucose measurements per day (ADA 2011). Post-prandial glucose during pregnancy has been identified as the best predictor of neonatal macrosomia (de Veciana 1995; Moses 1999). Therefore, SMBG protocols for women with type 1 or type 2 diabetes during pregnancy stress the importance of measuring blood glucose after meals (Jovanovič 2009), while for non-pregnant women with diabetes, pre-prandial values are recommended (ADA 2011; NICE 2008; NICE 2015).
2. Continuous glucose monitoring (CGM): the continuous glucose monitors currently available measure blood glucose either with minimal invasiveness through continuous measurement of interstitial fluid (ISF) or with the non-invasive method of applying electromagnetic radiation through the skin to blood vessels in the body. The technologies for bringing a sensor into contact with ISF include inserting an indwelling sensor subcutaneously (into the abdominal wall or arm) to measure ISF in situ or harvesting this fluid by various mechanisms that compromise the skin barrier and delivering the fluid to an external sensor (Choleau 2002). After a warm-up period of up to two hours and a device-specific calibration process, each device's sensor provides a blood glucose reading every one to 10 minutes for up to 72 hours with the minimally invasive technology and up to three months with the non-invasive technology. CGM can provide up to 288 measurements a day (Murphy 2007).
3. Clinic monitoring refers to routine glucose monitoring during antenatal visits either using capillary or whole blood.

Timing and frequency of glucose monitoring

Post-prandial glucose monitoring has been shown to be able to improve glycaemic control and thus reduce the risk of neonatal hypoglycaemia, macrosomia and caesarean delivery (de Veciana 1995), as well as to reduce the incidence of pre-eclampsia and neonatal triceps skinfold thickness (Manderson 2003). Post-prandial glucose values were most strongly associated with increased birthweight in the studies in which both pre- and post-meal glucose were measured (Mello 2000).

Pregnant women with diabetes mellitus are advised to test fasting and one-hour post-prandial blood glucose levels after every meal during pregnancy and those taking insulin are encouraged to test their blood glucose before going to bed at night (NICE 2008; NICE 2015). The American Diabetes Association also recommends SMBG before and after meals and occasionally at night time, to provide optimal results in pregnancy (Kitzmiller 2008).

The optimal frequency and timing of home glucose testing during pregnancy is unknown. In reality the frequency of glucose monitoring will depend on women's compliance, with few managing to carry out high numbers of tests daily (Kerssen 2006).

Educational approaches incorporating additional glucose testing after meals to improve glycaemic control in late gestation have shown potential to reduce birthweight (Howorka 2001).

Glycaemic control during pregnancy among women with pre-existing diabetes

Pregnancy profoundly affects the management of diabetes (Gabbe 2003; Jovanovic 2006). Pregnancy is associated with changes in insulin sensitivity, which may lead to changes in plasma glucose levels. Hormonal changes during pregnancy cause a progressive increase in insulin resistance, necessitating intensive medical nutrition therapy and frequently adjusted insulin administration throughout the pregnancy. The control of hyperglycaemia in pregnant women with pre-existing diabetes is essential in order to avoid the above mentioned adverse maternal and infant outcomes (Kitzmiller 2008). Macrosomia and other neonatal complications are minimised with intensified glycaemic control (Kerssen 2007; Kitzmiller 2008; Suhonen 2000).

If it is safely achievable, women with diabetes should aim to keep fasting blood glucose between 3.5 mmol/L and 5.9 mmol/L and one-hour post-prandial blood glucose below 7.8 mmol/L during pregnancy (NICE 2008; NICE 2015); HbA1c should be kept below 6.0% (ADA 2011). Excellent glycaemic control throughout the pregnancy is associated with the lowest risk for both maternal, fetal and neonatal complications (Kitzmiller 2008). On the other hand, the targets of glycaemic control for non-pregnant women with type 1 or type 2 diabetes are less stringent, i.e. fasting blood glucose to be 3.9 mmol/L to 7.2 mmol/L and HbA1c less than 7.0% (ADA 2011).

How the intervention might work

Maternal glucose levels in women with pre-existing diabetes directly influence those of the fetus. Fetal metabolic complications may give rise to macrosomia, congenital malformation, stillbirth and increased perinatal mortality (IDF 2010; Kapoor 2007; Kitzmiller 2008; NICE 2008; NICE 2015). Blood glucose monitoring allows adjustment of insulin dosage in relation to meal size and type, physical activity, stress and time of the day for women with pre-existing diabetes during pregnancy (Davidson 2005). This will limit the maternal risk of hypoglycaemic episodes while avoiding prolonged periods of hyperglycaemia. However, the frequency and timing of glucose monitoring will also influence maternal and fetal outcomes.

Why it is important to do this review

Self-monitoring of blood glucose is recommended as a key component of diabetes therapy during pregnancy and is included in the management plan (IDF 2010; Kitzmiller 2008; NICE 2008;). No existing systematic reviews consider the benefits of various techniques of blood glucose monitoring on maternal and infant outcomes among pregnant women with pre-existing diabetes. The effectiveness of the various monitoring techniques is unclear. This systematic review aims to generate information to guide pregnant

women with pre-existing diabetes and their clinicians in their choice of monitoring techniques in order to optimise maternal and infant outcomes. All trials that evaluate any techniques of blood glucose monitoring among pregnant women with pre-existing diabetes will be considered. This Cochrane Review is an update of a review that was first published in 2014 (Moy 2014) and subsequently updated in 2017 (Moy 2017).

OBJECTIVES

To compare techniques of blood glucose monitoring and their impact on maternal and infant outcomes among pregnant women with pre-existing diabetes.

METHODS

Criteria for considering studies for this review

Types of studies

We included randomised controlled trials and quasi-randomised trials. Cluster-randomised trials were eligible for inclusion but none were identified. Trials using a cross-over design were not eligible for inclusion. Abstracts were eligible for inclusion if sufficient information was provided to judge the quality and potential for bias of these trials.

Types of participants

Pregnant women with pre-existing diabetes mellitus (type 1 or type 2). Women with gestational diabetes mellitus (GDM) were excluded.

Types of interventions

Techniques of blood glucose monitoring including continuous glucose monitoring (CGM), self-monitoring of blood glucose (SMBG) or clinic monitoring. We also considered the timing and frequency of monitoring.

The following comparisons were considered in this update.

1. Continuous glucose monitoring (CGM) versus intermittent glucose monitoring (i.e. CGM versus standard care)
2. Self-monitoring of blood glucose (SMBG) versus different type of SMBG
3. SMBG at home versus hospitalisation
4. Pre-prandial versus post-prandial glucose monitoring
5. Automated telemedicine monitoring versus conventional system
6. Constant CGM versus intermittent CGM (e.g. use of a glucose monitor 24 hours per day versus use of a monitor 14 days per month)

Types of outcome measures

For this update, we used the Cochrane Pregnancy and Childbirth core outcome set for reviews of diabetes in pregnancy, developed by the Cochrane Pregnancy and Childbirth Australasian satellite.

Primary outcomes

Mother

1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)
2. Caesarean section

Neonatal/infant

1. Large-for-gestational age
2. Perinatal mortality (stillbirth and neonatal mortality)
3. Mortality or morbidity composite (e.g. pregnancy loss (miscarriage, stillbirth, and neonatal death); birth injury; neonatal glycaemia; hyperbilirubinaemia; respiratory distress; and high level neonatal care of more than 24 hours)
4. Neurosensory disability

Secondary outcomes

Mother

1. Pre-eclampsia
2. Pregnancy-induced hypertension
3. Eclampsia
4. Induction of labour
5. Perineal trauma
6. Placental abruption
7. Postpartum haemorrhage
8. Postpartum infection
9. Weight gain during pregnancy
10. Adherence to the intervention
11. Behaviour changes associated with the intervention
12. Relevant biomarker changes associated with the intervention (e.g. adiponectin, free fatty acids, triglycerides, high-density lipoproteins, low-density lipoproteins, insulin)
13. Sense of well-being and quality of life
14. Views of the intervention
15. Breastfeeding (e.g. at discharge, six weeks postpartum)
16. Use of additional pharmacotherapy
17. Glycaemic control during/end of treatment (as defined by trialists) (e.g. HbA1c, fructosamine, fasting blood glucose, post-prandial blood glucose)
18. Maternal hypoglycaemia
19. Maternal mortality
20. Miscarriage
21. Instrumental vaginal birth*

Long-term maternal outcomes

1. Postnatal depression
2. Postnatal weight retention or return to pre-pregnancy weight
3. Body mass index (BMI)
4. GDM in a subsequent pregnancy
5. Type 1 diabetes
6. Impaired glucose tolerance
7. Cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)

Neonatal/infant

1. Stillbirth
2. Neonatal mortality
3. Gestational age at birth
4. Preterm birth (less than 37 weeks' gestation and less than 34 weeks' gestation)

5. Apgar score (less than seven at five minutes)
6. Macrosomia
7. Small-for-gestational age
8. Birthweight and z-score
9. Head circumference and z-score
10. Length and z-score
11. Ponderal index
12. Adiposity (e.g. BMI, skinfold thickness)
13. Shoulder dystocia
14. Bone fracture
15. Nerve palsy
16. Respiratory distress syndrome
17. Hypoglycaemia (variously defined)
18. Hyperbilirubinaemia
19. Neonatal hypocalcaemia
20. Polycythaemia
21. Relevant biomarker changes associated with the intervention (e.g. cord c peptide, cord insulin)
22. Major and minor anomalies

Later infant and childhood secondary outcomes

1. Weight and z-scores
2. Height and z-scores
3. Head circumference and z-scores
4. Adiposity (e.g. as measured by BMI, skinfold thickness)
5. Blood pressure
6. Type 1 diabetes
7. Type 2 diabetes
8. Impaired glucose tolerance
9. Dyslipidaemia or metabolic syndrome
10. Educational achievement

Child in adulthood

1. Weight
2. Height
3. Adiposity (e.g. as measured by BMI, skinfold thickness)
4. Cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)
5. Type 1 diabetes
6. Type 2 diabetes
7. Impaired glucose tolerance
8. Dyslipidaemia or metabolic syndrome
9. Employment, education and social status/achievement

Health service use

1. Number of hospital or health professional visits (e.g. midwife, obstetrician, physician, dietician, diabetic nurse)
2. Number of antenatal visits or admissions
3. Length of antenatal stay
4. Neonatal intensive care unit admission
5. Neonatal intensive care unit length of stay greater than 24 hours*
6. Length of postnatal stay (mother)
7. Length of postnatal stay (baby)
8. Costs to families associated with the management provided
9. Costs associated with the intervention
10. Cost of maternal care
11. Cost of offspring care

Not pre-specified

1. Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite)
2. Neonatal glucose at age one hour
3. Transient tachypnoea
4. Diabetic ketoacidosis
5. Feeding difficulties

*Outcomes not pre-specified in our protocol - see Differences between protocol and review.

Search methods for identification of studies

The following methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Electronic searches

For this update, we searched Cochrane Pregnancy and Childbirth's Trials Register by contacting their Information Specialist (1 November 2018).

The Register is a database containing over 25,000 reports of controlled trials in the field of pregnancy and childbirth. It represents over 30 years of searching. For full current search methods used to populate Pregnancy and Childbirth's Trials Register including the detailed search strategies for CENTRAL, MEDLINE, Embase and CINAHL; the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service, please follow this link.

Briefly, Cochrane Pregnancy and Childbirth's Trials Register is maintained by their Information Specialist and contains trials identified from:

1. monthly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE (Ovid);
3. weekly searches of Embase (Ovid);
4. monthly searches of CINAHL (EBSCO);
5. handsearches of 30 journals and the proceedings of major conferences;
6. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Search results are screened by two people and the full text of all relevant trial reports identified through the searching activities described above is reviewed. Based on the intervention described, each trial report is assigned a number that corresponds to a specific Pregnancy and Childbirth review topic (or topics), and is then added to the Register. The Information Specialist searches the Register for each review using this topic number rather than keywords. This results in a more specific search set that has been fully accounted for in the relevant review sections (Included studies; Excluded studies; Ongoing studies).

In addition, we searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports (1 November 2018 using the search methods detailed in Appendix 1.

Searching other resources

We contacted the author of Feig 2017 for additional information (19 March 2019), no reply received to date (26 April 2019).

We searched the reference lists of retrieved studies.

We did not apply any language or date restrictions.

Data collection and analysis

For methods used in the previous version of this review, *see* Moy 2017.

For this update, the following methods were used for assessing the seven reports that were identified as a result of the updated search.

The following methods section of this review is based on a standard template used by Cochrane Pregnancy and Childbirth.

Selection of studies

Two review authors independently assessed for inclusion all the potential studies identified as a result of the search strategy. We resolved any disagreement through discussion or, if required, we consulted a third review author.

Data extraction and management

We designed a form to extract data. For eligible studies, two review authors extracted the data using the agreed form. We resolved discrepancies through discussion or, if required, we consulted a third review author. Data were entered into Review Manager software (RevMan 2014) and checked for accuracy.

When information regarding any of the above was unclear, we planned to contact authors of the original reports to provide further details.

Assessment of risk of bias in included studies

Two review authors independently assessed risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Any disagreement was resolved by discussion or by involving a third assessor.

(1) Random sequence generation (checking for possible selection bias)

We described for each included study the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.

We assessed the method as:

- low risk of bias (any truly random process, e.g. random number table; computer random number generator);
- high risk of bias (any non-random process, e.g. odd or even date of birth; hospital or clinic record number);
- unclear risk of bias.

(2) Allocation concealment (checking for possible selection bias)

We described for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment.

We assessed the methods as:

- low risk of bias (e.g. telephone or central randomisation; consecutively numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or non-opaque envelopes, alternation; date of birth);
- unclear risk of bias.

(3.1) Blinding of participants and personnel (checking for possible performance bias)

We described for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding was unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed the methods as:

- low, high or unclear risk of bias for participants;
- low, high or unclear risk of bias for personnel.

(3.2) Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcomes.

We assessed methods used to blind outcome assessment as:

- low, high or unclear risk of bias.

(4) Incomplete outcome data (checking for possible attrition bias due to the amount, nature and handling of incomplete outcome data)

We described for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the trial authors, we planned to re-include missing data in the analyses which we undertook.

We assessed methods as:

- low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups);
- high risk of bias (e.g. numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation);

- unclear risk of bias.

(5) Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias and what we found.

We assessed the methods as:

- low risk of bias (where it is clear that all of the study's pre-specified outcomes and all expected outcomes of interest to the review have been reported);
- high risk of bias (where not all the study's pre-specified outcomes have been reported; one or more reported primary outcomes were not pre-specified; outcomes of interest are reported incompletely and so cannot be used; study fails to include results of a key outcome that would have been expected to have been reported);
- unclear risk of bias.

(6) Other bias (checking for bias due to problems not covered by (1) to (5) above)

We described for each included study any important concerns we had about other possible sources of bias.

(7) Overall risk of bias

We made explicit judgements about whether studies were at high risk of bias, according to the criteria given in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). With reference to (1) to (6) above, we planned to assess the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings. In future updates, we will explore the impact of the level of bias through undertaking sensitivity analyses - *see* Sensitivity analysis.

Assessment of the quality of the evidence using the GRADE approach

For this update we assessed the quality of the evidence using the GRADE approach as outlined in the GRADE handbook in order to assess the quality of the body of evidence relating to the following outcomes for all comparisons.

1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia)
2. Caesarean section
3. Large-for-gestational age
4. Perinatal mortality (stillbirth and neonatal mortality)

We used the GRADEpro Guideline Development Tool to import data from Review Manager 5.3 (RevMan 2014) in order to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes was produced using the GRADE approach. The GRADE approach uses five considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the quality of the body of evidence for each outcome. The evidence can be downgraded from 'high quality' by one level for serious (or by two levels for very serious) limitations, depending on assessments for risk of bias, indirectness of evidence, serious inconsistency, imprecision of effect estimates or potential publication bias.

Measures of treatment effect

Dichotomous data

For dichotomous data, we presented results as summary risk ratio with 95% confidence intervals.

Continuous data

We used the mean difference if outcomes were measured in the same way between trials. In future updates, if appropriate, we will use the standardised mean difference to combine trials that measure the same outcome, but use different methods.

Unit of analysis issues

Trials with more than two intervention groups

Had we included trials with more than two techniques of glucose monitoring, we planned to analyse them according to the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011); the relevant pair of interventions would have been selected and the others excluded.

Cluster-randomised trials

We did not identify any cluster-randomised trials for inclusion. However, in future updates, if we identify any cluster-randomised trials we will include them in the analyses along with individually-randomised trials. We will adjust their sample sizes using the methods described in the *Cochrane Handbook for Systematic Reviews of Interventions* using an estimate of the intracluster correlation co-efficient (ICC) derived from the trial (if possible), from a similar trial or from a study of a similar population. If we use ICCs from other sources, we will report this and conduct sensitivity analyses to investigate the effect of variation in the ICC. If we identify both cluster-randomised trials and individually-randomised trials, we plan to synthesise the relevant information. We will consider it reasonable to combine the results from both if there is little heterogeneity between the study designs and the interaction between the effect of intervention and the choice of randomisation unit is considered to be unlikely. We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

Dealing with missing data

For included studies, levels of attrition were noted. In future updates, if more eligible studies are included, the impact of including studies with high levels of missing data in the overall assessment of treatment effect will be explored by using sensitivity analysis.

For all outcomes, analyses were carried out, as far as possible, on an intention-to-treat basis, i.e. we attempted to include all participants randomised to each group in the analyses. The denominator for each outcome in each trial was the number randomised minus any participants whose outcomes were known to be missing.

Assessment of heterogeneity

We assessed statistical heterogeneity in each meta-analysis using the Tau^2, I^2 and Chi^2 statistics. We regarded heterogeneity as substantial if an I^2 was greater than 30% and either a Tau^2 was greater than zero, or there was a low P value (less than 0.10)

in the Chi² test for heterogeneity. Had we identified substantial heterogeneity (above 30%), we planned to explore it by pre-specified subgroup analysis.

Assessment of reporting biases

In future updates, if there are 10 or more studies in the meta-analysis we will investigate reporting biases (such as publication bias) using funnel plots. We will assess funnel plot asymmetry visually. If asymmetry is suggested by a visual assessment, we will perform exploratory analyses to investigate it.

Data synthesis

We carried out statistical analysis using the Review Manager software (RevMan 2014). We used fixed-effect meta-analysis for combining data where it was reasonable to assume that studies were estimating the same underlying treatment effect: i.e. where trials were examining the same intervention, and the trials' populations and methods were judged sufficiently similar.

If there was clinical heterogeneity sufficient to expect that the underlying treatment effects differed between trials, or if substantial statistical heterogeneity was detected, we used random-effects meta-analysis to produce an overall summary, if an average treatment effect across trials was considered clinically meaningful. The random-effects summary was treated as the average of the range of possible treatment effects and we discuss the clinical implications of treatment effects differing between trials. If the average treatment effect was not clinically meaningful, we did not combine trials. Where we used random-effects analyses, the results are presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau² and I².

Subgroup analysis and investigation of heterogeneity

Had we identified substantial heterogeneity, we planned to investigate it using subgroup analyses and to consider whether an overall summary was meaningful, and if it was, to use a random-effects analysis to produce it.

We planned to restrict subgroup analyses to primary outcomes for the following subgroups:

1. types of diabetes mellitus (type 1 versus type 2 diabetes);
2. glycaemic control prior to pregnancy (pre-pregnancy HbA1c within target range versus pre-pregnancy HbA1c out of target range).

However, we did not carry out any subgroup analysis as there were too few trials included in any one comparison. Data for outcomes in included trials were also not reported separately by type of diabetes. Pre-pregnancy glycaemic control for all women was comparable at baseline. These analyses will be conducted in future updates of the review, if more data become available.

Sensitivity analysis

We planned to undertake sensitivity analysis to explore differences between fixed-effect or random-effects analyses for outcomes with statistical heterogeneity.

We also planned to undertake sensitivity analysis to assess the effect on pooled results of studies considered to have a high risk of bias.

However, due to the scarcity of data in any one comparison, no sensitivity analyses were conducted. If more data become available, the planned sensitivity analyses will be carried out in future updates.

RESULTS

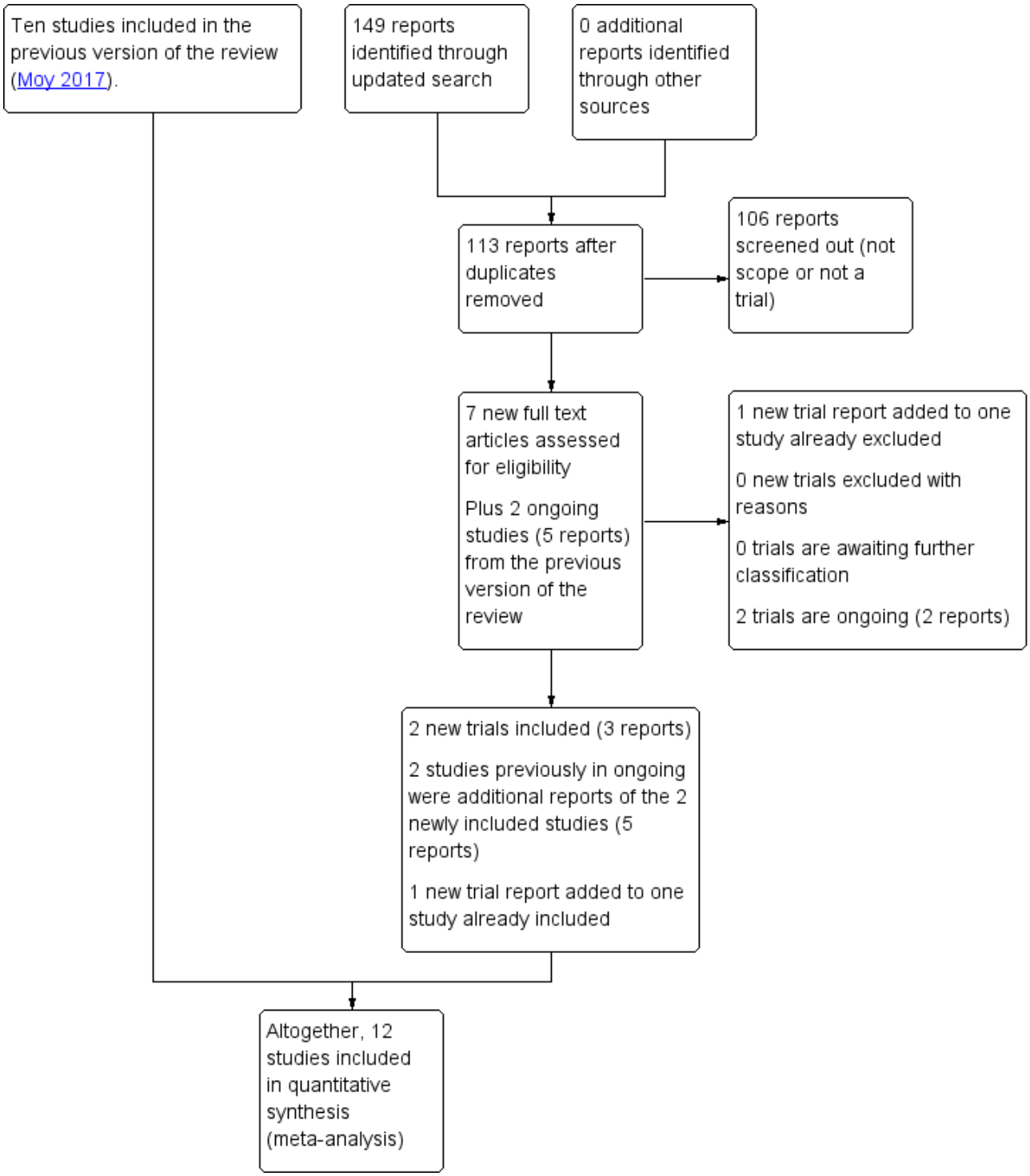
Description of studies

See Characteristics of included studies; Characteristics of excluded studies.

Results of the search

See: Figure 1.

Figure 1. Study flow diagram 2018



For this 2018 update, we identified 149 trial reports to assess and 113 in total after duplicates had been removed. One-hundred and six reports were screened out because they did not meet the scope for this review or were not randomised controlled trials. We then assessed seven trial reports for inclusion. We also reassessed the two ongoing studies listed in the previous version of the review (five reports).

We included two new trials (Feig 2017; Voormolen 2018) (three reports), added one trial report to an already included study (di Biase 1997), and added one trial report to an already excluded study (Bartholomew 2011). No new studies were excluded in this update. Two trials (two reports) are ongoing (Link 2018; Logan 2011), see Ongoing studies. The two studies previously listed in ongoing were additional reports of the newly included studies (five reports).

Included studies

Altogether, this review now comprises 12 included studies (944 women), all of which contributed data. Three of the 12 included trials were from the UK (Manderson 2003; Murphy 2008; Stubbs 1980), two were from Italy (Dalfrà 2009; di Biase 1997), and one each was from Sweden (Hanson 1984), Denmark (Secher 2013), Macedonia (Petrovski 2011), Poland (Wojcicki 2001), the US (Varner 1983), Canada (Feig 2017) and the Netherlands (Voormolen 2018).

For full details, see Characteristics of included studies.

Methods

All included studies were parallel group randomised controlled trials and involved two arms. The randomisation method was not always well described and in one study the allocation process was not truly random, and so was assessed as being 'quasi-randomised' (Dalfrà 2009). All of the studies were described as being 'open-label' and therefore not blinded. Two studies were multi-centre trials: one was based in Canada and involved 31 hospitals in Canada, England, Scotland, Spain, Italy, Ireland and the USA (Feig 2017); and one involved 22 hospitals, university, teaching and non-teaching hospitals in the Netherlands and one university hospital in Belgium (Voormolen 2018). The remaining trials were single centre (Dalfrà 2009; di Biase 1997; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013; Stubbs 1980; Varner 1983; Wojcicki 2001).

Trial dates

Trial dates were not reported in the study reports for six trials (Dalfrà 2009; di Biase 1997; Manderson 2003; Petrovski 2011; Stubbs 1980; Wojcicki 2001).

For the remaining studies, trials dates were reported as follows: 25 March 2013 to 22 March 2016 (Feig 2017); 1 October 1979 to 1 October 1982 (Hanson 1984); September 2003 to 2006 (Murphy 2008); 15 February 2009 to 15 February 2011 (Secher 2013); 1 February 1980 to 16 September 1981 (Varner 1983); and July 2011 to September 2015 (Voormolen 2018).

Participants

The trials included in this review involved a total of 944 women; 660 with type 1 diabetes, 113 with type 2 diabetes, and 171 women with either type 1 or type 2 diabetes (data not reported separately).

Hanson 1984, Murphy 2008 and Secher 2013 included women with pre-existing type 1 and type 2 diabetes (however, only Secher 2013 presented the results separately for type 1 and type 2 diabetes). Only women with pre-existing type 1 diabetes were eligible to participate in di Biase 1997 Feig 2017, Manderson 2003, Petrovski 2011, Stubbs 1980, Varner 1983, and Wojcicki 2001. In one trial (Feig 2017), they ran two trials in parallel for pregnant women and for women planning a pregnancy with type 1 diabetes. However the results for most outcomes were reported separately and so we have included the data for the pregnant women in this review. Women with pre-existing type 1 diabetes and gestational diabetes participated in Dalfrà 2009, however the results are presented separately so only data for women with type 1 diabetes are included in this review. Women with pre-existing type 1 and type 2 diabetes and gestational diabetes participated in Voormolen 2018, however the results are presented separately for some of the outcomes, so only data for women with type 1 and type 2 diabetes are included in this review. The ethnicity of the women was not mentioned in all trials. As these trials originated from the European countries and the USA, it is assumed that majority of the women were white or Caucasians.

Interventions and comparisons

Continuous glucose monitoring (CGM) was compared with intermittent glucose monitoring in trials by Feig 2017, Murphy 2008, Secher 2013 and Voormolen 2018. Stubbs 1980 and Varner 1983 compared self-monitoring of blood glucose (SMBG) at home with standard care. In Stubbs 1980 the SMBG group measured blood glucose with a glucometer seven times a day, twice weekly and the standard care group (non-meter group) checked urine glucose four times daily, with random blood glucose measured at fortnightly clinic visits. In Varner 1983, the SMBG group carried out daily home glucose monitoring four times daily and the standard care group carried out weekly venipuncture three times daily, measured on one day weekly. Hanson 1984 compared self-monitoring blood glucose at home from the 32nd week until the 36th week of gestation, with weekly hospital visits, and hospitalisation during the 37th week to delivery with a group who were hospitalised from 32nd week until delivery. Manderson 2003 compared timing of glucose monitoring, i.e. pre-prandial versus post-prandial. Pre-prandial refers to measurement of blood glucose before meals while post-prandial refers to blood glucose measured two hours after a meal. Automated telemedicine monitoring versus conventional system were compared in studies by Dalfrà 2009, di Biase 1997 and Wojcicki 2001. Automated telemedicine monitoring refers to automated transmission of blood glucose values via telephone or Internet to the physicians, which allows immediate attention from the physicians. Petrovski 2011 compared constant CGM with intermittent CGM. CGM refers to glucose measured in subcutaneous tissues every 10 seconds and an average value is stored every five minutes, providing up to 288 measurements per day.

Outcomes

The primary outcome composite outcome, hypertensive disorders of pregnancy was reported by Feig 2017 (including pre-eclampsia, pregnancy-induced hypertension and worsening chronic hypertension), and by Voormolen 2018 (pre-eclampsia and pregnancy-induced hypertension); caesarean section was reported by Dalfrà 2009; Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013; Varner 1983; large-for-gestational age was reported by Feig 2017; Manderson 2003; Murphy 2008; Secher 2013, (defined as birthweight 90th centile or above); perinatal mortality was reported by Hanson 1984; Manderson 2003; Murphy 2008; Varner 1983); neonatal mortality or morbidity composite was reported by Dalfrà 2009; Feig 2017; Varner 1983; and neurosensory disability was not reported by any trials.

Secondary maternal outcomes reported by the included studies were pre-eclampsia (Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Secher 2013; Voormolen 2018), pregnancy-induced hypertension (Feig 2017; Hanson 1984; Voormolen 2018), placental abruption (Hanson 1984), weight gain during pregnancy (Feig 2017; Dalfrà 2009; Manderson 2003; Petrovski 2011), behaviour changes associated with the intervention (Feig 2017 (using hypoglycaemia fear survey (HFS II) behaviour subscale which measures two distinct aspects of behavioural avoidance to prevent hypoglycaemia), sense of well-being and quality of life (Feig 2017 (using three

different questionnaires (blood glucose monitoring system rating questionnaire (BGMSRQ), problem areas in diabetes (PAID), short-form-12)), use of additional pharmacotherapy (use of additional insulin therapy: Dalfrà 2009; insulin dose: di Biase 1997; Manderson 2003; Petrovski 2011), glycaemic control during/end of treatment (HbA1c) (Dalfrà 2009; di Biase 1997; Feig 2017; Manderson 2003; Murphy 2008; Petrovski 2011; Varner 1983; Wojcicki 2001), maternal hypoglycaemia (Feig 2017; Petrovski 2011) and miscarriage (Feig 2017; Murphy 2008; Secher 2013; Varner 1983).

Secondary perinatal/neonatal outcomes reported by the included studies were stillbirth (reported by Feig 2017; Manderson 2003), neonatal mortality (Murphy 2008; Varner 1983; Voormolen 2018), gestational age at birth (Dalfrà 2009; di Biase 1997; Manderson 2003; Murphy 2008; Varner 1983; Wojcicki 2001), preterm birth less than 37 weeks' gestation (Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013), preterm birth less than 34 weeks' gestation (Feig 2017;) macrosomia (Feig 2017; Dalfrà 2009; Feig 2017; Manderson 2003; Petrovski 2011; Voormolen 2018: defined as birthweight greater than 4 kg in four studies and birthweight above 90th centile in two studies), small-for-gestational age (Feig 2017; Murphy 2008: defined as birthweight 10th centile or below), birthweight (Feig 2017; Dalfrà 2009; Manderson 2003; Murphy 2008; Stubbs 1980; Varner 1983), head circumference (Feig 2017), length (Feig 2017), adiposity (sum of four skin folds (triceps, subscapular, biceps, flank: Feig 2017) and (triceps skinfold thickness and subscapular skinfold thickness: Manderson 2003), shoulder dystocia (Feig 2017), respiratory distress syndrome (Feig 2017, Hanson 1984; Manderson 2003; Varner 1983), hypoglycaemia (Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013; Varner 1983), hyperbilirubinaemia (Feig 2017; Hanson 1984; Manderson 2003; Varner 1983), neonatal hypocalcaemia (Varner 1983), polycythaemia (Varner 1983), relevant biomarker changes associated with the intervention (neonatal cord vein c-peptide: Feig 2017; Varner 1983, (cord IGF-1: Manderson 2003), and major anomalies (Feig 2017; Hanson 1984; Murphy 2008).

The only secondary health service use outcomes reported were antenatal hospital admission (Feig 2017; Hanson 1984), neonatal intensive care (NICU) admissions (Manderson 2003; Murphy 2008) and NICU length of admission > 24 hours (Feig 2017).

Outcomes that were not pre-specified, but are reported in this review are maternal diabetic ketoacidosis (Feig 2017; Petrovski 2011), birth trauma (shoulder dystocia, bone fracture and nerve palsy, pre-specified as individual outcomes but reported as a composite: Feig 2017; Manderson 2003), neonatal glucose at age one hour (Manderson 2003), transient tachypnoea (Manderson 2003), and feeding difficulties (Hanson 1984). Instrumental vaginal birth was reported in one trial (Voormolen 2018), but the data were not presented separately for women with pre-existing diabetes and women with GDM. No other trial reported on instrumental vaginal birth.

Secondary maternal outcomes not reported by any of the included studies were: induction of labour, perineal trauma, postpartum haemorrhage, postpartum infection, adherence to the intervention, relevant biomarker changes associated with the intervention (e.g. adiponectin, free fatty acids, triglycerides, high-density lipoproteins, low-density lipoproteins, insulin), views of the intervention, maternal mortality.

Secondary perinatal/neonatal outcomes not reported by any of the included studies were: Apgar score (less than seven at five minutes), head circumference and z-score, length and z-score, ponderal index, adiposity measured by body mass index (BMI), and minor anomalies.

Health service use outcomes not reported by any of the included studies were: health service use, number of hospital or health professional visits (e.g. midwife, obstetrician, physician, dietician, diabetic nurse), number of antenatal visits, length of antenatal stay, length of postnatal stay (mother), length of postnatal stay (baby), costs to families associated with the management provided, costs associated with the intervention, cost of maternal care, and cost of offspring care.

No studies reported long-term maternal outcomes (postnatal depression, postnatal weight retention or return to pre-pregnancy weight, BMI, impaired glucose tolerance, cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome)), later infant or childhood outcomes (weight and z-scores, height and z-scores, head circumference and z-scores, adiposity (e.g. as measured by BMI, skinfold thickness), blood pressure, type 1 diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidaemia or metabolic syndrome, educational achievement), or child in adulthood outcomes (weight, height, adiposity (e.g. as measured by BMI, skinfold thickness), cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome), type 1 diabetes, type 2 diabetes, impaired glucose tolerance, dyslipidaemia or metabolic syndrome, employment, education and social status/achievement).

Some outcomes were reported in a form that could not be used in this review. Hanson 1984 reported the median antenatal hospital stay and neonatal hospital stay, but did not report the standard deviation of blood glucose values, and only reported HbA1c graphically. Manderson 2003 reported the median and interquartile range for cord insulin and length of stay in neonatal unit, and Secher 2013 reported weight gain in pregnancy, HbA1c, plasma glucose, gestational age at birth, and birthweight as median and range. Where results were reported as medians, we felt it was unlikely that the results were normally distributed, and excluded them from meta-analyses. Percentage of maternal hypoglycaemic episodes was reported by Wojcicki 2001, however the total of all blood glucose data was not available, therefore the frequency was not estimable. Feig 2017 reported the median and interquartile range for the following outcomes, weight gain during pregnancy, postnatal weight retention or return to pre-pregnancy weight, gestational age at birth and length of antenatal stay. Voormolen 2018 reported on many of the outcomes of this review (see Characteristics of included studies), but did not report these separately for pre-gestational and gestational diabetes (we have written to authors requesting separate data for the pre-gestational diabetes group of women).

Sources of trial funding

Sources of trial funding were not reported in two trials (Dalfrà 2009; di Biase 1997).

In Feig 2017, the trial was funded by the Juvenile Diabetes Research Foundation (JDRF) and grants under the JDRF Canadian Clinical Trial Network, a public-private partnership. Metronic supplied

the CGM sensors and CGM systems at reduced cost. In Hanson 1984, the source of funding was reported as being Expressens Perinatal forskningsfond, AIImanna Barnbordshusets Minnesfond, Svenska Diabetesstiftelsen, Nordisk Insulinfond, Swedish Medical Research Council (Project No. 3787), and Tielman's Fund for Pediatric Research. The Department of Health and Social Sevices, Northern lreland, the Northern Ireland Mother and Baby Appeal, the Metabolic Unit Research Fund, Royal Victoria Hospital Belfast, the Royal Maternity Hospital, and the Irish Perinatal Society funded the trial by Manderson 2003. Murphy 2008 was an investigator-initiated study funded by the Ipswich Diabetes Centre Charity Research Fund. The study equipment (six CGMS Gold monitors and 300 sensors) was donated free of charge by Medtronic UK. The research was sponsored by Ipswich Hospital NHS Trust and was independent of all the study funders (Murphy 2008). The Macedonion Ministry of Health and the Health Care Fund of Macedonia funded Petrovski 2011. In Secher 2013, one of the authors received financial support from the European Foundation of the Study of Diabetes and LifeScan, Rigshopitalet's Research Foundation, the Capital Region of Denmark, the Medical Facuty Foundation of Copenhagen University, Aase and Ejnar Danielsen Foundation, and Master Joiner Sophus Jacobsen and his wife Astrid Jacobsens' Foundation. Stubbs 1980 was funded by the Medical Research Council Project Grant and the British Diabetic Association. Varner 1983 was funded by a Research Fellowship from the Iowa Affiliate of the American Diabetes Association. Voormolen 2018 was funded by ZonMw, The Dutch Organization for Health Research and Development .Continuous glucose monitors were purchased at a discounted price from Medtronic® and were reported as having no role in the study design, data collection, data analysis, data interpretation, or writing of the report. Wojcicki 2001 was supported by grants from the Polish State Committee for Scientific Research, the Bayer Diagnostic Division Warsaw, and the Polish Cellular Telephony Centertel.

Trial authors' declarations of interest

Trial authors' declarations of interest were not reported in Dalfrà 2009; di Biase 1997; Manderson 2003; Stubbs 1980; Varner 1983; Wojcicki 2001.

In Murphy 2008, two trial authors received honorariums for speaking at research symposiums sponsored by Medtronic in 2004 and 2005. In Feig 2017, eight authors report grants from the Juvenile Diabetes Research Foundation during the conduct of the study. Two authors report personal fees from Novo Nordisk, Roche and Medtronic, outside the submitted work. One author reports personal fees from Abbott Diabetes Care and Medtronic (MiniMed Academia), outside the submitted work. One author sits on the Medtronic European Scientific Advisory Board. All remaining authors declare no competing interests. The authors declared that they had no competing financial interests in Petrovski 2011 and in Secher 2013, other than those reported under 'funding' interests. In Voormolen 2018, one of the trial authors received a research grant from ZonMW (the Netherlands Organization for Health Research and Development) and a second author received research grants from Abbott, Dexcom, Medtronic and Sensonics, and also received personal fees from Roche Diabetes Care and Sensonics. A third author is supported by an NHMRC Practitioner Fellowshop (GNT1082548) and reports consultancy for ObsEVa, Merck and Guerbet. All other authors declare no support from any organization or conflict of interest.

See the Characteristics of included studies table for more details.

Excluded studies

No new trials were excluded in this update (2019), but one trial report was identified relating to an already excluded study (Bartholomew 2011).

Bartholomew 2011 was excluded as it is a cross-over trial. Two trial registrations (NCT01630759; Walker 1999) were excluded; the former was a trial on women with gestational diabetes mellitus (GDM) while the latter was a clinical trial registration containing insufficient evidence to assess. We contacted the author, but there were no available data or published reports. Temple 2006 was excluded as it was an abstract on an observational study of eight pregnant women with type 1 diabetes using continuous glucose monitoring system (CGMS).

See the Characteristics of excluded studies table for more details.

Risk of bias in included studies

Three of the 12 included studies were at low risk of bias (Feig 2017; Murphy 2008; Secher 2013), eight studies were at moderate risk of bias (di Biase 1997; Hanson 1984; Manderson 2003; Petrovski 2011; Stubbs 1980; Varner 1983; Voormolen 2018; Wojcicki 2001), and one study was at high risk of bias (Dalfrà 2009). See Figure 2 and Figure 3.

Figure 2. 'Risk of bias' summary: review authors' judgements about each risk of bias item for each included study.

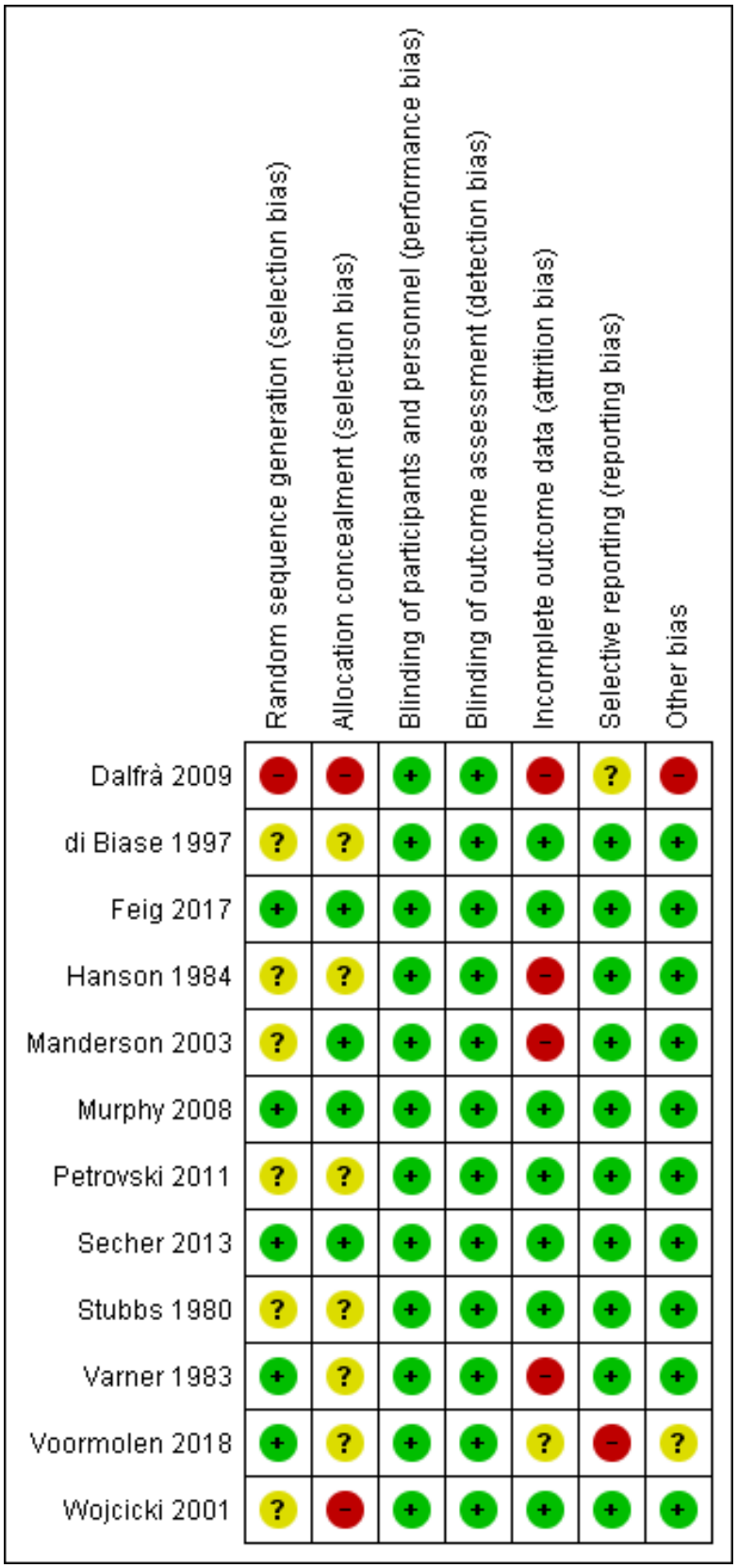
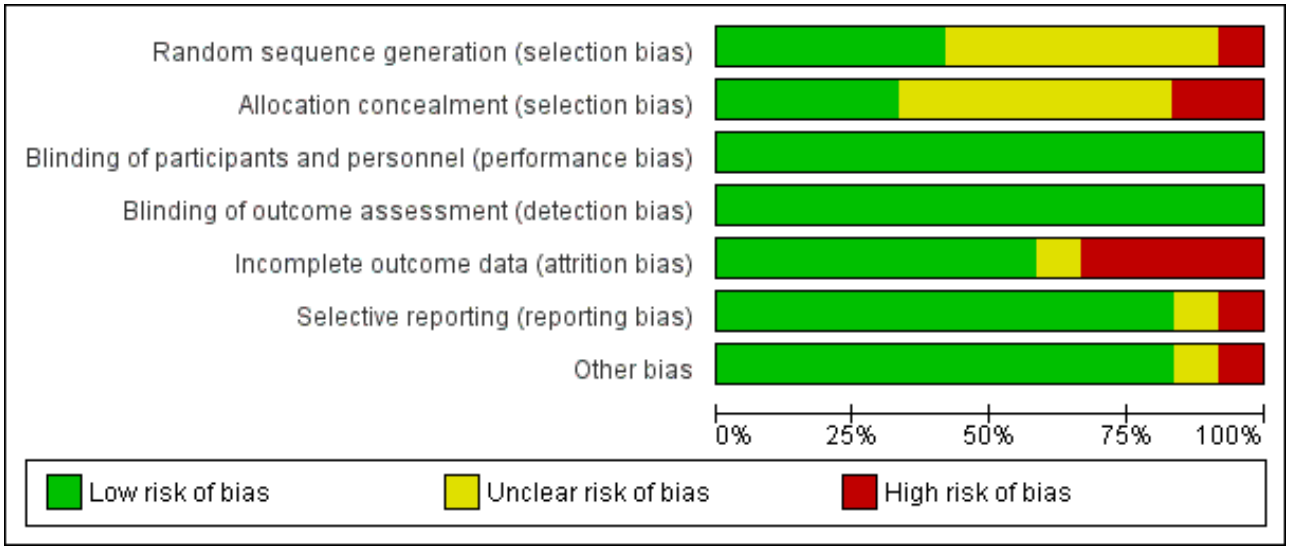


Figure 3. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Allocation

Random sequence generation

Five studies (Feig 2017; Murphy 2008; Secher 2013; Varner 1983; Voormolen 2018) described the random sequence generation using computer-generated random numbers or a random number sequence (low risk of bias). Six trials (di Biase 1997; Hanson 1984; Manderson 2003; Petrovski 2011; Stubbs 1980; Wojcicki 2001) did not report how the sequence was generated (unclear risk of bias). One study was quasi-randomised, allocating women to alternating groups (Dalfrà 2009) (high risk of bias).

Allocation concealment

Adequate and secure concealment of allocation was described in four trials (low risk of bias) (Feig 2017; Manderson 2003; Murphy 2008; Secher 2013); in one trial the randomisation schedule was created remotely by a programme manager, encrypted, and maintained in a secure database, with no access from the research team (Feig 2017), sealed envelopes were used in two of the trials (Manderson 2003; Murphy 2008), while the fourth (Secher 2013) used an automated telephone allocation service (Paravox) provided by an independent organisation. There was no concealment of allocation in Wojcicki 2001 and Dalfrà 2009 (high risk of bias). The other trials only mentioned the participants were randomly allocated into intervention or control groups without describing if there was any concealment of allocation (unclear risk of bias).

Blinding

Blinding of participants and personnel

As different techniques or timing of glucose monitoring were compared, blinding of neither participants nor assessors was feasible. However, since outcome measures were objective it is unlikely that lack of blinding introduced a risk of bias and so all studies were assessed as being at low risk.

Blinding of outcome assessors

As different techniques or timing of glucose monitoring were compared, blinding of neither participants nor assessors was feasible. However, since outcome measures were objective it is unlikely that lack of blinding introduced a risk of bias so all studies were assessed as being at low risk.

Incomplete outcome data

Four trials had high risk of bias for incomplete outcome data. Reasons given for attrition were women not completing the questionnaire (Dalfrà 2009), severe drug addiction, spontaneous abortions and death of mother (Hanson 1984), no results for analysis participants (Manderson 2003) and spontaneous miscarriage (Varner 1983). In other included studies, all women were accounted for in the analysis, or rates of attrition were described (low risk of bias). di Biase 1997and Wojcicki 2001 reported all outcome data. Four trials reported using intention-to-treat analysis (Murphy 2008; Petrovski 2011; Secher 2013; Stubbs 1980). One trial was assessed as being at unclear risk of bias (Voormolen 2018), because there were a high number of women refused to continue using CGM after the first or second time.

Selective reporting

It was unclear if there was any selective reporting in one trial (Dalfrà 2009),10 trials reported all expected outcome data (di Biase 1997; Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013; Stubbs 1980; Varner 1983; Wojcicki 2001) (low risk of bias). One trial (Voormolen 2018) was assessed as being at high risk of bias because there were a number of maternal outcomes that were described in the methods of the full report and the protocol, but were not reported in the results section.

Other potential sources of bias

There were no other obvious potential sources of bias with the exception of Dalfrà 2009 and Voormolen 2018. Dalfrà 2009 did not use an intention-to-treat analysis, and there was no sample size calculation, or information on whether groups were comparable

at baseline (high risk of bias). In Voormolen 2018, we had some concerns over missing outcomes and were unsure of the impact of this, (unclear risk of bias).

Effects of interventions

See: **Summary of findings for the main comparison** Continuous glucose monitoring compared to intermittent glucose monitoring for women with pre-existing diabetes; **Summary of findings 2** Self-monitoring compared to a different type of self-monitoring for women with pre-existing diabetes; **Summary of findings 3** Self-monitoring at home compared to hospitalisation for women with pre-existing diabetes; **Summary of findings 4** Pre-prandial compared to post-prandial glucose monitoring for women with pre-existing diabetes; **Summary of findings 5** Automated telemedicine monitoring compared to conventional for women with pre-existing diabetes; **Summary of findings 6** Constant CGM compared to Intermittent CGM for women with pre-existing diabetes

As there were various methods of glucose monitoring being implemented in the included trials, we structured the review using the following comparisons.

1. Continuous glucose monitoring (CGM) versus intermittent glucose monitoring
2. Self-monitoring versus different types of self-monitoring
3. Self-monitoring at home versus hospitalisation
4. Pre-prandial versus post-prandial glucose monitoring
5. Automated telemedicine monitoring versus conventional system
6. Constant CGM versus intermittent CGM

Comparison 1 - Continuous glucose monitoring (CGM) versus intermittent glucose monitoring

See Summary of findings for the main comparison.

Four studies compared CGM versus intermittent blood glucose monitoring (Feig 2017; Murphy 2008; Secher 2013; Voormolen 2018). The total number of women was 609, 384 type 1 diabetes (T1DM) and 191 with type 2 diabetes (T2DM). Feig 2017 contributed the largest number of women in this comparison (n = 215), all T1DM.

Feig 2017 used a CGM system to measure blood glucose. Women were trained to use the study devices and instructed to use them daily by local diabetes or antenatal clinic teams. CGM users were advised to verify the accuracy of their CGM measurements using their capillary glucose meter before insulin dose adjustment (n = 108). Women in the control group continued their usual method of capillary glucose monitoring (n = 107). Women in both groups were advised to test capillary blood glucose levels at least seven times daily and given written instructions for how to use capillary or CGM measures for insulin dose adjustment. Feig 2017 randomised both pregnant (n = 215) and women planning pregnancy (n = 110), but reported the results separately for the two cohorts. We have only included the data for the pregnant women in this review.

Voormolen 2018 randomised 300 pregnant women with T1DM (n = 109) and T2DM (n = 82), or with gestational diabetes (n = 109). We have only included the data for the women with T1DM and T2DM. However, many of our review outcomes were not reported separately, but mixed with the gestational diabetes cohort and so we have been unable to include all of the data. The CGM group had continuous glucose monitoring in addition to standard care. Women allocated to CGM were instructed to use the device for five to seven days every six weeks and glucose profiles were obtained retrospectively, directly after each use and evaluated by the local endocrinologist. Self-monitoring of blood glucose (SMBG) was required for calibration of CGM. Readings from the CGM were uploaded to a web-based program (n = 147 all women, 90 with T1DM and T2DM). Standard treatment consisted of self-monitoring of blood glucose only (n = 153 all women, 97 with T1DM and T2DM). Women in both intervention and control groups performed SMBG (four to eight times/day: at least fasting, after every meal, at bedtime and, preferably before every meal).

Murphy 2008 used the CGM, which measured glucose in subcutaneous tissues every 10 seconds and an average value is stored every five minutes, providing up to 288 measurements per day (n = 38). The women were required to wear the CGM for seven days at intervals of four to six weeks. They were also advised to measure blood glucose at least seven times a day. The intermittent monitoring of glucose levels was the standard care in which women were advised to monitor glucose at least seven times a day (n = 33).

In Secher 2013, real time CGM for six days at pregnancy visits during eight, 12, 21, 27 and 33 weeks, in addition to routine pregnancy care was implemented on 79 women and intermittent monitoring with self-monitored plasma glucose measurements of seven times daily was implemented on 75 women.

Primary outcomes

Continuous glucose monitoring may reduce the composite outcome of hypertensive disorders of pregnancy (risk ratio (RR) 0.58, 95% confidence interval (CI) 0.39 to 0.84; 2 studies, 384 women; low-quality evidence, Analysis 1.1), although this did not translate into a clear reduction for pre-eclampsia, see secondary outcomes below.

Due to moderate heterogeneity, we used random-effects analysis for caesarean section and there was no clear reduction in rate of caesarean section (average RR 0.94, 95% CI 0.75 to 1.18; 3 studies, 427 women; I^2 = 41%; moderate-quality evidence, Analysis 1.2), or large-for-gestational age (average RR 0.84, 95% CI 0.57 to 1.26; 3 studies, 421 women; I^2 = 70%; low-quality evidence, Analysis 1.3). There was not enough evidence to assess perinatal mortality (RR 0.82, 95% CI 0.05 to 12.61, 71 infants, 1 study, Analysis 1.4, low-quality evidence) or the composite of neonatal mortality or morbidity (RR 0.80, 95% CI 0.61 to 1.06; 1 study, 200 women) as the evidence was based on single studies of low-quality.

Neurosensory disability
This outcome was not reported.

Secondary outcomes

There was no clear reduction in pre-eclampsia (RR 0.65, 95% CI 0.39 to 1.08; 4 studies, 609 women; moderate-quality evidence, Analysis 1.6) or to pregnancy-induced hypertension (RR 0.67, 95% CI 0.38 to 1.16; 2 studies, 384 women; low-quality evidence, Analysis 1.7) with CGM. There was little difference between groups in behaviour changes associated with the intervention as measured using the Hypoglycaemia Fear Survey (HFS II) (Lamb 2017) behaviour subscale at 34 weeks' gestation (mean difference (MD) 1.00, 95% CI -1.06 to 3.06; 1 study, 214 women, Analysis 1.8). The 15 items in HFS behaviour subscale measures behaviours aimed at

avoiding hypoglycaemia and its possible negative consequences, with higher scores indicating higher fear of hypoglycaemia, with scores ranging from zero to 60.

There was also little difference in sense of well-being and quality of life as measured using the Short-Form-12 (SF-12) and Problem Areas in Diabetes (PAID) (Venkataraman 2015) which were measured at 34 weeks' gestation (total score) (MD -0.70, 95% CI -2.50 to 1.10; 1 study, 214 women, Analysis 1.9) (MD 0.80, 95% CI -3.06 to 4.66; 1 study, 214 women, Analysis 1.10). The Short-Form-12 (SF-12) is a health-related quality-of-life questionnaire. It consists of 12 questions that measure eight domains assessing physical and mental health. Physical health domains include General Health (GH), Physical Functioning (PF), Role Physical (RP), and Body Pain (BP). Mental health domains include Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). The instrument has been validated across a number of chronic diseases and conditions. Physical and Mental Health Composite Scales combine the 12 items, with a high score of 50 equating to good mental and physical health (Huo 2018). The Problem Areas in Diabetes (PAID) instrument was developed to measure emotional distress in people with diabetes. It is a 20-item scale consisting of emotional problems commonly reported in type 1 and type 2 diabetes mellitus, and has been found to be a valid and reliable scale in Western populations (Venkataraman 2015), with scores ranging from zero to 100, with higher scores reflecting greater emotional distress. The CGM group scored slightly higher in their Blood Glucose Monitoring System Rating Questionnaire (BGMSRQ) (Peyrot 2009) total score at 34 weeks' gestation (MD 4.30, 95% CI 0.73 to 7.87; 1 study, 214 women, Analysis 1.11). This questionnaire aims to measure different aspects about the method of blood glucose monitoring: measures relate to convenience, interference, burden, control, overall satisfaction, desire to switch monitoring system, willingness to recommend current monitoring system, and comparison of current and prior blood glucose monitoring system.

CGM may make little or no difference to maternal glycaemic control as indicated by HbA1c levels (glycated haemoglobin): the mean HbA1c level in the continuous monitoring group was 0.37% lower, 0.78% lower to 0.04% higher (MD -0.37 %, 95% CI -0.78 to 0.04; 2 studies, 258 women; I^2 = 81%, Analysis 1.12) and although more women in the continuous monitoring group achieved HbA1c levels less than or equal to 6.5% (48 mmol/mol) at 34 weeks (RR 1.27, 95% CI 1.00 to 1.62; 1 study, 187 women, Analysis 1.13), the results are based on a single study.

There was no clear difference between groups for the following outcomes.

1. Maternal hypoglycaemia (severe) (RR 0.92, 95% CI 0.43 to 1.95; 1 study,154 women, Analysis 1.14)
2. Miscarriage (RR 1.24, 95% CI 0.47 to 3.26; 3 studies, 439 women, Analysis 1.15)
3. Stillbirth (RR 0.34, 95% CI 0.01 to 8.17; 1 study, 211 infants, Analysis 1.16)
4. Neonatal mortality (RR 0.92, 95% CI 0.13 to 6.37; 2 studies, 256 infants, Analysis 1.17)
5. Gestational age at birth (weeks) (MD 0.10 weeks, 95% CI -0.57 to 0.77; 1 study, 68 women, Analysis 1.18)
6. Preterm birth < 37 weeks (RR 0.96, 95% CI 0.72 to 1.29; 3 studies, 430 women, Analysis 1.19)
7. Preterm birth < 34 weeks (RR 0.46, 95% CI 0.17 to 1.28; 1 study, 211 women, Analysis 1.20)
8. Macrosomia (average RR 0.84, 95% CI 0.61 to 1.17; 3 studies, 451 women, I^2 = 34%, Analysis 1.21)
9. Birthweight (kg) (MD -0.13 kg, 95% CI -0.38 to 0.12; 2 studies, 267 infants, I^2 = 49%, Analysis 1.22)
10. Small-for-gestational age (RR 2.40, 95% CI 0.55 to 10.51; 2 studies, 269 infants, Analysis 1.23)
11. Head circumference (cm) (MD -0.20, 95% CI -0.79 to 0.39; 1 study, 160 infants, Analysis 1.24)
12. Length (crown-heel length cm) (MD -0.20, 95% CI -0.79 to 0.39; 1 study, 160 infants, Analysis 1.25)
13. Adipositiy (sum of four skin folds mm) (MD -0.20, 95% CI -1.98 to 1.58; 1 study, 160 infants, Analysis 1.26)
14. Shoulder dystocia (RR 3.00, 95% CI 0.12 to 72.77; 1 study, 200 infants, Analysis 1.27)
15. Respiratory distress syndrome (RR 1.00, 95% CI 0.41 to 2.41; 1 study, 200 infants, Analysis 1.28)
16. Neonatal hypoglycaemia (RR 0.66, 95% CI 0.48 to 0.93; 3 studies, 428 infants, Analysis 1.29)
17. Neonatal hyperbilirubinaemia (RR 0.81, 95% CI 0.52 to 1.26; 1 study, 200 infants, Analysis 1.30)
18. Relevant biomarkers associated with the intervention (cord blood c-peptide levels > 566 pmol/L) (RR 0.95, 95% CI 0.68 to 1.33; 1 study, 200 infants, Analysis 1.31)
19. Relevant biomarkers associated with the intervention (cord blood c-peptide levels > 2725 pmol/L) (RR 1.00, 95% CI 0.33 to 3.00; 1 study, 200 infants, Analysis 1.32)
20. Major and minor anomalies (RR 0.71, 95% CI 0.16 to 3.13; 2 studies, 285 infants, Analysis 1.33)
21. Number of hospital admissions (mother) (RR 1.25, 95% CI 0.84 to 1.85; 1 study, 207 women, Analysis 1.34)
22. Neonatal intensive care unit admissions (average RR 0.76, 95% CI 0.42 to 1.35; 2 studies, 274 infants, Analysis 1.35)
23. Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (RR 5.00, 95% CI 0.24 to 102.85; 1 study, 200 infants, Analysis 1.37)
24. Diabetic ketoacidosis (RR 1.01, 95% CI 0.14 to 7.03; 1 study, 207 women, Analysis 1.38)

It may reduce neonatal hypoglycaemia (RR 0.66, 95% CI 0.48 to 0.93; 3 studies, 428 infants, Analysis 1.29) and NICU admission of more than 24 hours (RR 0.63, 95% CI 0.42 to 0.93; 1 study, 200 infants, Analysis 1.36).

None of the studies reported on our remaining secondary outcomes.

Comparison 2 - Self-monitoring versus a different type of self-monitoring

See Summary of findings 2.

Two trials (Stubbs 1980; Varner 1983) compared self-monitoring with a different type of self-monitoring (standard care). In one trial (Stubbs 1980), a total of 13 pregnant women with T1DM were randomly allocated into self-monitoring of blood glucose (SMBG) at home, seven times a day, twice per week. Another six women were allocated to standard care (urine check four times daily) and random blood glucose testing measured fortnightly during clinic visits.

In the other trial (Varner 1983), 30 T1DM women were assigned to self-monitoring (n = 15) and standard care (n = 15). The self-monitoring group carried out daily home glucose monitoring four times daily and the standard care group carried out weekly venipuncture three times daily, measured on one day weekly. One woman in each group had a first trimester spontaneous miscarriage, so results are presented for the remaining 28 women and infants. The self-monitoring group was required to monitor fasting plus two-hour post-prandial morning, afternoon and evening glucose daily, while the standard care group were measured one day per week.

Primary outcomes

It is uncertain whether self-monitoring reduces the risk of caesarean section (risk ratio (RR) 0.78, 95% confidence interval (CI) 0.40 to 1.49, 1 study, 28 women, Analysis 2.1, very low-quality evidence) (Varner 1983). Varner 1983 also reported perinatal mortality and it was too small to show any differences between groups (perinatal mortality: RR 3.00, 95% CI 0.13 to 67.91, 1 study, 28 infants, very low-quality evidence, Analysis 2.2).

Hypertensive disorders of pregnancy, large-for-gestational age, neonatal mortality and morbidity composite and neurosensory disability were not reported in either study.

Secondary outcomes

It is uncertain whether self-monitoring makes any difference in maternal glycaemic control for post-prandial blood glucose (MD -0.70 mmol/L, 95% CI -2.15 to 0.75; 1 study, 13 women, Analysis 2.3), or HbA1c (MD -0.10 %, 95% CI -1.93 to 1.73, 1 study, 28 women, Analysis 2.4). There were too few women to show any differences in miscarriage (RR 1.00, 95% CI 0.07 to 14.55, 1 study, 30 women, Analysis 2.5), neonatal mortality (RR 3.00, 95% CI 0.13 to 67.91, 1 study, 28 women, Analysis 2.6), or respiratory distress syndrome (RR 3.00, 95% CI 0.13 to 67.91, 1 study, 28 infants, Analysis 2.9). It is uncertain whether there are any differences in gestational age between self-monitoring groups (MD 0.40 weeks, 95% CI -1.65 to 2.45, 1 study, 28 infants, Analysis 2.7), and or in infant birthweight (MD -0.18 kg, 95% CI -0.49 to 0.13, 2 studies, 41 infants, Analysis 2.8) due to limitations in small sample sizes.

Again it is uncertain whether there are any differences for neonatal hypoglycaemia (RR 0.57, 95% CI 0.21 to 1.52, 1 study, 28 infants, Analysis 2.10), neonatal jaundice (hyperbilirubinaemia) (RR 0.56, 95% CI 0.25 to 1.24, 1 study, 28 infants, Analysis 2.11), hypocalcaemia (RR 1.00, 95% CI 0.07 to 14.45, 1 study, 28 infants, Analysis 2.12), polycythaemia (RR 0.33, 95% CI 0.01 to 7.55, 1 study, 28 infants, Analysis 2.13) and neonatal cord vein C-peptide (MD 0.13 ng/nl, 95% CI -0.50 to 0.76, 1 study, 28 infants, Analysis 2.14).

None of the studies reported on our remaining secondary outcomes.

Comparison 3 - Self-monitoring at home versus hospitalisation

See Summary of findings 3.

Only one study compared home self-monitoring with hospitalisation (Hanson 1984). In this study, a total of 100 pregnant women with T1DM and T2DM were randomised. The home self-monitoring group had 54 women while the hospital group had 46 women. The women from the home group self-monitored their blood glucose from the 32nd until 36th week of gestation and then were hospitalised during the 37th week until delivery; the hospital group women were hospitalised from 32nd week until delivery. Blood glucose was monitored four times daily (7 AM, 9.30 AM, 3 PM and 7 PM) in both groups.

Primary outcomes

This study of 100 women did not report on the composite outcome, hypertensive disorders of pregnancy. It reported pre-eclampsia and hypertension in pregnancy, but as separate outcomes**.**

The results were uncertain for caesarean section (RR 0.96, 95% CI 0.65 to 1.44, Analysis 3.2, very low-quality evidence*),* and the sample size was too small to assess perinatal mortality (RR 0.85, 95% CI 0.05 to 13.24, Analysis 3.3, very low-quality evidence*).*

Large-for-gestational age, mortality or morbidity composite, and neurosensory disability were not reported.

Secondary outcomes

It is uncertain whether there is any difference between self-monitoring and hospitalisation were shown in the reported secondary outcomes: placental abruption (RR 1.70, 95% CI 0.16 to 18.19, Analysis 3.6); preterm birth < 37 weeks (RR 0.85, 95% CI 0.45 to 1.60, Analysis 3.7); respiratory distress syndrome (RR 2.56, 95% CI 0.28 to 23.74, Analysis 3.8); neonatal hypoglycaemia (RR 1.01, 95% CI 0.50 to 2.03, Analysis 3.9); neonatal jaundice (hyperbilirubinaemia) (RR 2.27, 95% CI 0.64 to 8.07, Analysis 3.10); major anomalies (RR 0.27, 95% CI 0.03 to 2.54, Analysis 3.11).

As would be expected from the nature of the intervention, a lower proportion of women in the self-monitoring group had antenatal hospital admission (RR 0.19, 95% CI 0.11 to 0.33, Analysis 3.12).

Maternal glycaemic control was reported, however only mean blood glucose was given without standard deviations, and HbA1c was only presented graphically, so we were not able to include these data in the analyses. The mean blood glucose values during the study period were 6.0 mmol/L for the hospital group and 5.9 mmol/L for the home group.

Outcomes that were not pre-specified

There were no differences between self-monitoring and hospitalisation in terms of feeding difficulties (RR 0.85, 95% CI 0.41 to 1.78, Analysis 3.13).

None of the studies reported on our remaining secondary outcomes.

Comparison 4 - Pre-prandial versus post-prandial glucose monitoring

See Summary of findings 4.

Only one trial compared pre-prandial and post-prandial glucose monitoring (Manderson 2003). Sixty-one T1DM women were randomly assigned to pre-prandial (n = 31) or post-prandial (n = 30) blood glucose monitoring. The pre-prandial group monitored their blood glucose before breakfast and pre-prandially for each meal. The post-prandial group monitored blood glucose after breakfast and one hour after the commencement of each meal.

Primary outcomes

In one study of 61 women (61 infants), it is uncertain whether there is any difference between pre-prandial and post-prandial glucose monitoring for caesarean section (RR 1.45, 95% CI 0.92 to 2.28, Analysis 4.1, very low-quality evidence), large-for-gestational age (RR 1.16, 95% CI 0.73 to 1.85; Analysis 4.2, very low-quality evidence) and perinatal mortality (RR 2.91, 95% CI 0.12 to 68.66, Analysis 4.3, very low-quality evidence).

The study did not report the composite outcomes, hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia), mortality or morbidity composite, or neurosensory disability.

Secondary outcomes

It is uncertain whether there are any differences between pre-prandial and post-prandial glucose monitoring for the following outcomes: pre-eclampsia (RR 6.43, 95% CI 0.82 to 50.11, Analysis 4.4); weight gain in pregnancy (MD -0.90 kg, 95% CI -3.86 to 2.06, Analysis 4.5); use of additional pharmacotherapy shown by insulin dose in units/day and units/kg (MD -17.40 units/day, 95% CI -43.41 to 8.61, Analysis 4.6; MD -0.20 units/kg, 95% CI -0.45 to 0.05, Analysis 4.7); glycaemic control shown by mean HbA1c (MD 0.30 %, 95% CI -0.08 to 0.68, Analysis 4.8); stillbirth (RR 2.91, 95% CI 0.12 to 68.66, Analysis 4.9); gestational age at birth (MD 0.20 weeks, 95% CI -0.84 to 1.24, Analysis 4.10); preterm birth < 37 weeks (RR 1.33, 95% CI 0.62 to 2.84, Analysis 4.11); macrosomia (RR 2.18, 95% CI 0.75 to 6.32, Analysis 4.12), birthweight (MD 0.24 kg, 95% CI -0.10 to 0.58, Analysis 4.13); subscapular skinfold thickness (adiposity) (MD 0.60 mm, 95% CI -0.18 to 1.38, Analysis 4.14); birth trauma (shoulder dystocia, bone fracture, nerve palsy) (RR 0.48, 95% CI 0.05 to 5.06, Analysis 4.16); respiratory distress syndrome (RR 0.97, 95% CI 0.06 to 14.78, Analysis 4.17); neonatal hypoglycaemia (RR 1.09, 95% CI 0.48 to 2.45, Analysis 4.18); neonatal jaundice (hyperbilirubinaemia) (RR 1.16, 95% CI 0.40 to 3.40, Analysis 4.19); cord IGF-1 (MD 1.30 µg/L, 95% CI -0.70 to 3.30, Analysis 4.20); neonatal glucose at age one hour (not pre-specified) (MD -0.20, 95% CI -0.88 to 0.48, Analysis 4.21); transient tachypnoea (not pre-specified) (RR 2.58, 95% CI 0.76 to 8.81, Analysis 4.22); and neonatal intensive care admissions (RR 1.04, 95% CI 0.62 to 1.74, Analysis 4.23).

Infants in the pre-prandial monitoring group had higher triceps skinfold thickness (adiposity) (MD 0.60 mm, 95% CI 0.04 to 1.16, Analysis 4.15), although the difference is small and should be considered in the context of no clear difference in large-for-gestational age, birthweight, macrosomia, and subscapular skinfold thickness.

None of the studies reported on our remaining secondary outcomes.

Comparison 5 - Automated telemedicine monitoring versus conventional system

See Summary of findings 5.

Three studies (Dalfrà 2009; di Biase 1997; Wojcicki 2001) compared automated telemedicine monitoring versus conventional system. Dalfrà 2009 included both pregnant women with T1DM (n = 32, data included in this review) and women with gestational diabetes (n = 203, data excluded from this review). Women in the telemedicine group were asked to submit their blood glucose data every week, and had a medical examination at the diabetes clinic once a month, while women in the control group had a medical examination every two weeks. di Biase 1997 (n = 20) and Wojcicki 2001 (n = 32) recruited T1DM women. di Biase 1997 used a DIANET system, which was an automated monitoring system using a telemedicine system with patient unit, diabetes workstation and the communication link to send all data to the diabetologist. The intermittent monitoring was conventional monitoring where the women were instructed to perform three or more tests of blood glucose per day using BM20-800 strips with the results checked during routine clinic visits. Wojcicki 2001 used a telematic management system with the a glucometer connected to a modem interface where the blood glucose measurements could be transmitted to the central clinical control unit. The conventional group would only have their measurements examined during the routine clinical examinations every three weeks. All women (in both groups) were encouraged to measure their blood glucose at least six times per day.

Primary outcomes

Again, it is uncertain from one study (Dalfrà 2009) whether there is any difference between automated telemedicine monitoring and conventional monitoring for caesarean section (RR 0.96, 95% CI 0.62 to 1.48, 1 study, 32 women, Analysis 5.1, very low-quality evidence) and the composite of neonatal mortality or morbidity (RR 1.18, 95% CI 0.53 to 2.62, 1 study, 32 infants, Analysis 5.2).

di Biase 1997 and Wojcicki 2001 did not report these primary outcomes, and none of the studies contributing data to this comparison reported hypertensive disorders of pregnancy, large-for-gestational age, perinatal mortality (stillbirth and neonatal mortality), and neurosensory disability.

Secondary outcomes

In one study of 20 women (di Biase 1997), women in the automated telemedicine group had a higher mean insulin requirement at the end of the study (MD 18.40 units/day, 95% CI 12.88 to 23.92, Analysis 5.5). The women in the automated telemedicine group also had lower mean maternal fasting blood glucose before breakfast and before lunch at the end of the study (before breakfast: MD -1.00 mmol/L, 95% CI -1.22 to -0.78, Analysis 5.6; before lunch: MD -1.10 mmol/L, 95% CI -1.32 to -0.88, Analysis 5.7). There was high heterogeneity between studies for maternal HbA1c (random-effects MD -0.17 %, 95% CI -0.82 to 0.48, 3 studies, 82 women, Tau^2 = 0.27, I^2 = 82%, Analysis 5.8) and maternal post-prandial blood glucose (random-effects MD -0.80 mmol/L, 95% CI -1.67 to 0.08, 3 studies, 50 women,Tau^2 = 0.35, I^2 = 86%, Analysis 5.9). Post hoc sensitivity analyses show that this was due to measurements from di Biase 1997. This study showed differences between groups in HbA1c and post-prandial blood glucose, however the other two studies did not. It seems likely that the higher insulin doses given to women in the automated telemedicine group resulted in lower blood glucose measures.

It was uncertain whether there was any difference between groups for: weight gain in pregnancy (MD -0.70, 95% CI -4.95 to 3.55, 1 study, 32 women, Analysis 5.10); use of additional insulin therapy (RR 1.00, 95% CI 0.89 to 1.12, 1 study, 32 women, Analysis 5.4); gestational age (MD 0.24 weeks, 95% CI -0.39 to 0.88, 3 studies, 84 women, Analysis 5.3); macrosomia (RR 1.18, 95% CI 0.31 to 4.43, 1 study, 32 infants, Analysis 5.11); or birthweight (MD -0.16 kg, 95% CI -0.64 to 0.32, 1 study, 32 infants, Analysis 5.12).

The percentage of maternal hypoglycaemic episodes was reported by Wojcicki 2001, however, the total of all blood glucose data were not available, therefore the frequency was not estimable.

None of the studies reported on our remaining secondary outcomes.

Comparison 6 - Constant CGM versus intermittent CGM

See Summary of findings 6.

Only one study compared constant CGM and intermittent CGM (Petrovski 2011). Twenty-five T1DM women were randomised into constant CGM (n = 12) and intermittent CGM (n = 13) groups. The women in the constant CGM group wore the glucose sensor 24 hours per day while the intermittent CGM group wore the glucose sensor 14 days per month. The women in the intermittent CGM group measured blood glucose at least six times daily when not using the glucose sensor.

Primary outcomes

It is uncertain whether constant CGM makes any difference to rates of caesarean section (RR 0.77, 95% CI 0.33 to 1.79, 1 study, 25 women, very low-quality evidence, Analysis 6.1). Other primary outcomes were not reported (hypertensive disorders of pregnancy, large-for-gestational age, perinatal mortality (stillbirth and neonatal mortality), mortality or morbidity composite, and neurosensory disability).

Secondary outcomes

Constant CGM makes little or no difference to weight gain in pregnancy (MD 0.50 kg, 95% CI -1.82 to 2.82, 1 study, 25 women, Analysis 6.2), insulin dosage (third trimester: MD -0.03, 95% CI -1.30 to 1.24, 1 study, 25 women, Analysis 6.3); maternal blood glucose (first trimester: MD -0.50 mmol/L, 95% CI -2.70 to 1.70, 1 study, 25 women, Analysis 6.4; third trimester: MD -0.14 mmol/L, 95% CI -2.00 to 1.72, 1 study, 25 women, Analysis 6.5); maternal HbA1c (first trimester: MD -0.30 %, 95% CI -1.13 to 0.53, 1 study, 25 women, Analysis 6.6; third trimester: MD -0.09 %, 95% CI -0.69 to 0.51, 1 study, 25 women, Analysis 6.7), maternal hypoglycaemia (RR 0.54, 95% CI 0.06 to 5.24, 1 study, 25 women, Analysis 6.8), diabetic ketoacidosis (not pre-specified) (RR 0.36, 95% CI 0.02 to 8.05, 1 study, 25 women, Analysis 6.9), preterm birth < 37 weeks (RR 1.08, 95% CI 0.08 to 15.46, 1 study, 25 infants, Analysis 6.10), and macrosomia (RR 1.08, 95% CI 0.08 to 15.46, 1 study, 25 infants, Analysis 6.11). There were no events for neonatal hypoglycaemia (1 study, 25 infants Analysis 6.12).

None of the studies reported on our remaining secondary outcomes.

DISCUSSION

Summary of main results

The objective of this review was to assess the various techniques of glucose monitoring among pregnant women with pre-existing type 1 and type 2 diabetes and their impact on maternal and infant outcomes. We included 12 trials comparing six different pairs of glucose monitoring techniques: continuous glucose monitoring (CGM) versus intermittent glucose monitoring (Feig 2017; Murphy 2008; Secher 2013; Voormolen 2018), self-monitoring versus a different type of self-monitoring (Stubbs 1980; Varner 1983), self-monitoring versus hospitalisation (Hanson 1984), pre-prandial versus post-prandial glucose monitoring (Manderson 2003), automated telemedicine monitoring versus conventional (Dalfrà 2009; di Biase 1997; Wojcicki 2001), and constant CGM versus intermittent CGM (Petrovski 2011). This review update includes a total of 12 trials (944) women (type 1 diabetes: 660 women; type 2 diabetes: 113 women; type 1 or type 2 (unspecified): 171 women. All trials originated from European countries, the USA and Canada.

With the addition of two new studies (406 women) to one of the comparisons (comparison 1 - continuous glucose monitoring (CGM) versus intermittent glucose monitoring), the evidence suggests that CGM may reduce hypertensive disorders of pregnancy, though it should be noted that only two of the four relevant studies reported data for this composite outcome. Conversely, this did not translate into a clear reduction for pre-eclampsia. There was no clear reduction in caesarean section or large-for-gestational age with CGM. There was not enough evidence to assess perinatal mortality or mortality or morbidity composite as the evidence was based on single studies of low quality. CGM appears to reduce neonatal hypoglycaemia. Neurosensory disability was not reported.

For the remaining five comparisons: self-monitoring versus a different type of self-monitoring (two studies, 43 women); self-monitoring at home versus hospitalisation (one study, 100 women); pre-prandial versus post-prandial glucose monitoring (one study, 61 women); automated telemedicine monitoring versus conventional system (three studies, 84 women); and constant CGM versus intermittent CGM (one study, 25 women), it is uncertain whether any of the interventions has any impact on any of our GRADE outcomes (hypertensive disorders of pregnancy, caesarean section, large-for-gestational age) because the quality of the evidence was found to be very low. There was not enough evidence to assess perinatal mortality and neonatal mortality and morbidity composite. Other important outcomes, such as neurosensory disability, were not reported in any of these comparisons.

Outcomes relating to cost were not reported by any of the studies. Resource use (antenatal hospital admissions, neonatal intensive care admissions and neonatal intensive care unit length of admission > 24 hours) was reported only by single trials in three out of the six comparisons and so pooling of data was not possible.

Overall completeness and applicability of evidence

With the addition of two new studies (406 women) to one of the comparisons examining CGM versus intermittent monitoring, there was evidence to suggest that CGM may have an impact on hypertensive disorders of pregnancy, although there was no clear reduction for other outcomes associated with hypertension, such as pre-eclampsia. The pooling of the data for hypertension disorders needs to be viewed with caution. Only two of the four relevant studies reported on this composite outcome of 'hypertensive disorders of pregnancy' including pre-eclampsia, pregnancy-induced hypertension, eclampsia, and they report it slightly differently (Feig 2017; Voormolen 2018). Voormolen 2018 reports a composite of pre-eclampsia and pregnancy-induced hypertension for women with both type 1 and type 2 diabetes and Feig 2017 reports a composite of worsening chronic, gestational hypertension and pre-eclampsia for women with only type 1 diabetes. The ‘worsening chronic’ could be omitted from the analysis to make the two randomised controlled trials (RCTs) more comparable for pooling, although this makes only a small

difference to the overall results (17/100 CGM and 27/102 versus 18/100 and 28/102). The real issue is that Murphy 2008 and Secher 2013 cannot be included in the analysis for this composite outcome because they both only report on pre-eclampsia and not on pregnancy-induced hypertension. The results for pre-eclampsia therefore must be considered the most robust result in terms of complete reporting as all four RCTs report on it. The evidence base for the effectiveness of other monitoring techniques analysed in the other five comparisons is weak and based on mainly single studies with very low-quality evidence and cannot be said to justify overall completeness of evidence.

All the included trials were conducted in Western countries - Europe, the USA and Canada - and it can be assumed that a majority of the women were Caucasian. Most of the pregnant women in the included studies had type 1 diabetes (n = 792) with much fewer having type 2 diabetes (n = 152). There were six pairs of intervention techniques in the included trials. There was difficulty in pooling the results due to this variation. The review's primary outcome, neurosensory disability, was not reported in any of the trials. The only secondary health service use outcomes reported were antenatal hospital admission, neonatal intensive care admissions and neonatal intensive care unit length of admission > 24 hours. Many of the reviews secondary maternal and perinatal/neonatal outcomes were not reported: induction of labour, perineal trauma, postpartum haemorrhage, postpartum infection, adherence to the intervention, maternal mortality, Apgar score (less than seven at five minutes). No studies reported long-term maternal or infant outcomes and patient-reported outcomes such as behaviour changes associated with the intervention and sense of well-being and quality of life.

Quality of the evidence

Three of the 12 included studies were at low risk of bias (Feig 2017; Murphy 2008; Secher 2013), eight studies were at moderate risk of bias (di Biase 1997; Hanson 1984; Manderson 2003; Petrovski 2011; Stubbs 1980; Varner 1983; Voormolen 2018; Wojcicki 2001), and one study was at high risk of bias (Dalfrà 2009). Five trials (Feig 2017; Murphy 2008; Secher 2013; Varner 1983; Voormolen 2018) described the random sequence generation while adequate and secure concealment of allocation was described in four trials (Feig 2017; Manderson 2003; Murphy 2008; Secher 2013). It was unclear if there was any selective reporting in one trial (Dalfrà 2009), while 10 studies reported all expected outcome data (di Biase 1997; Feig 2017; Hanson 1984; Manderson 2003; Murphy 2008; Petrovski 2011; Secher 2013; Stubbs 1980; Varner 1983; Wojcicki 2001. In one trial, some outcomes reported in the protocol and methods of the trial report did not appear to have been adequately reported in the full trial report (Voormolen 2018) and was considered to be at high risk for this domain. Most of the trials had small numbers of women; six trials (Dalfrà 2009; Di Biase 1997; Petrovski 2011; Stubbs 1980; Varner 1983; Wojcicki 2001) only had a range of 13 to 32 participants. Any potential bias is likely to have been overshadowed by the small number and size of trials with their different intervention techniques of monitoring and reported outcomes. The trials are too small to show differences in important outcomes such as macrosomia, preterm birth, miscarriage or death of baby.

All the reported GRADE outcomes for comparisons 2, 3, 4, 5 and 6 were assessed as being very low-quality evidence (Summary of findings 2; Summary of findings 3; Summary of findings 4; Summary of findings 5; Summary of findings 6). We downgraded most outcomes in these tables once for serious concerns due to limitations in design and twice for very serious imprecision (wide confidence intervals (CIs) crossing the line of no effect, small sample sizes, and few events).

Comparison 1 included more data than the other comparisons (four studies, 609 women), from studies assessed as being at lower risk of bias (Summary of findings for the main comparison). Consequently, we graded caesarean section as moderate-quality evidence with downgrading one level for serious inconsistency due to evidence of statistical heterogeneity. We graded hypertensive disorders of pregnancy as low-quality evidence with downgrading two levels for serious limitations in study design and serious indirectness due to two studies reporting the composite outcome in different ways. We graded large-for-gestational as low quality with downgrading two levels due to serious imprecision (wide CI crossing line of no effect) and serious inconsistency (statistical heterogeneity). We graded perinatal mortality (stillbirth and neonatal mortality) as low quality with downgrading two levels for very serious imprecision due to evidence derived from a single study, with a small number of events and wide CI crossing the line of no effect.

GRADE outcomes were often not reported. Caesarean section was the only GRADE outcome reported by studies in every comparison. The composite outcome of hypertensive disorders of pregnancy was only reported by studies in comparison 1. Large-for-gestational age was only reported by studies in comparisons 1 and 4. Perinatal mortality (stillbirth and neonatal mortality) was reported by studies in comparisons 1, 2, 3 and 4.

Potential biases in the review process

We attempted to minimise bias during the review process by having two people assess the eligibility of studies, assess risk of bias and extract data. GRADE quality assessments were also checked by a second person. We attempted to be as inclusive as possible in our search. However, we cannot rule out the possibility that we have missed relevant studies that were not published or are still ongoing. In addition, the proposed subgroup and sensitivity analyses could not be performed.

Agreements and disagreements with other studies or reviews

With the addition of two new studies (406 women) to one of the comparisons (comparison 1 - continuous glucose monitoring (CGM) versus intermittent glucose monitoring), the evidence suggests that CGM may reduce hypertensive disorders of pregnancy, though as already stated, only two of the four relevant studies reported data for this composite outcome. Conversely, this did not translate into a clear reduction for pre-eclampsia. CGM probably makes little or no difference to caesarean section, but may reduce neonatal hypoglycaemia. The findings from our review are on the whole very similar to another Cochrane Review (Raman 2017), which examined different methods and settings for glucose monitoring in gestational diabetes, and observed no clear differences between the CGM and self-monitoring groups for any of their maternal or infant outcomes (caesarean section, large-for-gestational age, perinatal deaths). Hypertensive disorders of pregnancy were not reported by either study for their CGM comparison. The results for other comparisons were similar to findings from our review for telemedicine and self-monitoring, in that there was insufficient

evidence to show any clear effect for any of the outcomes examined (Raman 2017). Other reviews also found limited evidence for the effectiveness of real-time CGM use in children, adults and patients with poorly controlled diabetes (Ghandi 2011; Langendam 2012; Pickup 2011). However, these reviews indicated that higher compliance of wearing the CGM device improves glycosylated haemoglobin A1c level (HbA1c) to a larger extent, and this is in line with our finding of a possible improvement in glycaemic control for women using CGM.

There were no available reviews on self-monitoring of blood glucose (SMBG) among pregnant women with pre-existing diabetes and so the findings of this review cannot be compared with any other. This review's findings are not altogether consistent with the findings of others that considered methods for blood glucose monitoring techniques amongst other diabetic populations. SMBG has been found to be effective for patients with type 1 diabetes (DCCT 1993) and patients with type 2 diabetes who are using insulin (Karter 2001). One Cochrane Review (Malanda 2012), concluded that SMBG in newly diagnosed patients with type 2 diabetes who are not using insulin is beneficial in lowering HbA1c. However, when the duration of diabetes is over one year, the overall glycaemic effects of SMBG are small at short term and subside after one year.

Women with type 1 and type 2 diabetes are advised to self-monitor their blood glucose throughout pregnancy (IDF 2010). The control of hyperglycaemia in pregnant women with pre-existing diabetes can reduce adverse maternal and infant outcomes (Kitzmiller 2008). A Cochrane Review has reported that pregnant women with type 1 or type 2 diabetes with tight to moderate glycaemic control had significantly lower risks for pre-eclampsia, caesarean section and macrosomia (Middleton 2016). However, the evidence base for the relative effectiveness of monitoring techniques is inconclusive.

Other than the above mentioned studies or reviews, we are not aware of any other published reviews on techniques of glucose monitoring among pregnant women with pre-existing diabetes.

AUTHORS' CONCLUSIONS

Implications for practice

Two new studies (406 women) have been incorporated to one of the comparisons for this update. Although the evidence suggests that continuous glucose monitoring (CGM) in comparison to intermittent glucose monitoring may reduce hypertensive disorders of pregnancy, this did not translate into a clear reduction for pre-eclampsia, and so this result should be viewed with caution. There was no evidence of a difference for other primary outcomes for this comparison. The evidence base for the effectiveness of other monitoring techniques analysed in the other five comparisons is weak and based on mainly single studies with very low-quality evidence. The body of evidence from randomised trials assessing the effects of different techniques of monitoring blood glucose for women with pre-existing diabetes is therefore incomplete. More trials are needed to confirm the potential benefits of CGM and the effects of other techniques of monitoring in order to inform practice.

Implications for research

More research is needed to identify the most effective techniques of blood glucose monitoring in pregnant women and to confirm the effectiveness of CGM. The current evidence is limited by the small number of randomised controlled trials (RCTs) for most of the comparisons assessed, small sample sizes, and the variable methodological quality of the RCTs. More evidence is needed to assess the effects of different techniques of monitoring blood glucose for women with pre-existing diabetes on outcomes for mothers and their children, including use and costs of health care, long-term outcomes and patient-reported outcomes. Future RCTs may consider collecting and reporting on the standard outcomes suggested in this review.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Dalfrà 2009

Methods	Quasi-randomised trial. Women were sequentially assigned to telemedicine and control groups (not randomised). **Period of study:** not reported.
Participants	88 women with gestational diabetes in the telemedicine group and 115 in the control group; 17 women with type 1 diabetes in the telemedicine group and 15 in the control group. **Inclusion criteria:** pregnant women with type 1 diabetes (enrolled in the study at their first visit after conception. Women with gestational diabetes included after a week from the diagnosis of gestational diabetes. **Exclusion criteria:** not described.
Interventions	**Intervention:** automated telemedicine monitoring. **Control:** conventional system.
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Neonatal morbidity composite (presence of macrosomia (4000 g) and complications). 3. Gestational age at birth. 4. Use of additional insulin therapy. 5. Glycaemic control (maternal). 6. Weight gain.

Dalfrà 2009 *(Continued)*

	7. Macrosomia. 8. Birthweight.
Notes	**Setting:** 12 diabetes clinics. **Country:** Italy. **Funding:** not mentioned. **Declarations of interest:** not reported. **Comments:** data for women with gestational diabetes and type 1 diabetes are presented separately.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Quote: "Women were sequentially assigned to two groups: one patient was followed up using the telemedicine approach and the next using the conventional approach (usual care)."
Allocation concealment (selection bias)	High risk	No attempt was made to conceal allocation.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No attempt was made to blind women or personnel. Women were aware of whether they were being monitored using telemedicine or usual care. However, the outcomes were measured objectively and would not have been influenced by blinding or not blinding.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	High risk	4/36 women with type 1 diabetes and 37/240 women with gestational diabetes were excluded because they did not complete questionnaires at the end of the study. It is unclear whether these were women with type 1 diabetes or gestational diabetes.
Selective reporting (reporting bias)	Unclear risk	This study was assessed from a published report, without the study protocol. The main outcomes were reported separately for type 1 diabetes and GDM, however some outcomes were not reported separately or were only reported in the text.
Other bias	High risk	The study did not use an intention-to-treat analysis. There is no sample size calculation, or information on whether groups were comparable at baseline. Women with type 1 diabetes only make up a small part of the whole study (32 out of 235 women).

di Biase 1997

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** not mentioned.
Participants	**Number randomised:** 20. Eligible were type 1 diabetes mellitus (IDDM) pregnant patients attending the Diabetes Unit specialising in the treatment of diabetes in pregnancy during the period of study.

di Biase 1997 *(Continued)*

	Inclusion criteria: type 1 DM pregnant patients. **Exclusion criteria:** not mentioned in the text.
Interventions	**Intervention:** DIANET system - continuous automated monitoring system using a telemedicine system - patient unit, diabetes workstation and the communication link (n = 10). **Control:** conventional monitoring - performed 3 or more tests of blood glucose per day using BM20-800 strips (n = 10).
Outcomes	**Outcomes used in this review** 1. Gestational age at birth. 2. Insulin requirement at end of study. 3. Glycaemic control (maternal).
Notes	**Setting:** Diabetes Unit specialising in the treatment of diabetes in pregnancy. **Country:** Italy. **Funding:** not mentioned. **Declarations of interest:** not reported. **Comments** 1. No sample size estimation reported. 2. No type 2 DM pregnant patients included. 3. Patients enrolled at 9.5 ± 10 weeks, study ended at 37.6 ± 0.4 weeks. 4. Hypoglycaemic episodes were graded in categories of 1 (mild) to 4 (severe). 5. Trial not registered ?? 6. Therapeutic adjustment by the Diabetes Unit was performed every week by a visit to the control group. 7. The experimental group had their data stored in DIANET system transmitted to the team weekly. This allowed feedback to both patients and clinicians. 8. Clinic visit for experimental group is once every 15-30 days as they stayed at a longer distance from the clinics than the control group.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote from report - "Patients were consecutively chosen by 1 of the investigators. Stratified block randomisation was used to divide patients into 2 groups at baseline." The patients were randomly assigned to a control or DIANET group. Comment: methods of sequence allocation not stated.
Allocation concealment (selection bias)	Unclear risk	Comment: not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.

di Biase 1997 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: reported results of all participants (n = 20).
Selective reporting (reporting bias)	Low risk	As reported in the article all outcomes listed have been mentioned.
Other bias	Low risk	No obvious risk to other bias.

Feig 2017

Methods	Multi-centre, parallel randomised controlled trial – open-label. They ran 2 trials in parallel for pregnant participants and for participants planning a pregnancy. **Period of study:** 25 March 2013 - 22 March 2016. We report the results for pregnant participants.
Participants	**Number randomised:** 325 (215 pregnant, 110 planning pregnancy). **Inclusion criteria:** women aged 18-40 years, with type 1 diabetes for a minimum of 12 months, receiving intensive insulin therapy via multiple daily injections or an insulin pump, who were pregnant or planning pregnancy. **Exclusion criteria:** regular CGM users and women with severe nephropathy or medical conditions such as psychiatric illness requiring hospitalisation. Women using automatic insulin delivery options, such as low glucose suspend pumps, were not excluded.
Interventions	**Intervention:** real-time CGM in addition to capillary glucose monitoring. CGM system was aGuardian REAL-Time or MiniMed Minilink system, both Medtronic, Northridge CA. Participants were trained to use the study devices and instructed to use them daily by local diabetes or antenatal clinic teams. CGM users were advised to verify the accuracy of CGM measurements using their capillary glucose meter before insulin dose adjustment, as per the regulatory labelling instructions (n = 108). **Control:** standard - capillary glucose monitoring alone (home glucose monitoring). Participants in the control group continued their usual method of capillary glucose monitoring. Participants in both groups were advised to test capillary blood glucose levels at least 7 times daily (before and 1-2 hours after meals and before bed) and given written instructions for how to use capillary or CGM measures for insulin dose adjustment, customised for methods of insulin delivery. Both groups had the same target glucose range of 3.5 to 7.8 mmol/L and same target HbA1c levels of no higher than 6.5% (48 mmol/mol) during pregnancy (n = 107).
Outcomes	**Outcomes used in this review** 1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia). 2. Caesarean section. 3. Large-for-gestational age. 4. Mortality or morbidity composite (in the report this is defined as: pregnancy loss (miscarriage, stillbirth, and neonatal death); birth injury; neonatal glycaemia; hyperbilirubinaemia; respiratory distress; and high-level neonatal care for more than 24 hours). 5. Weight gain during pregnancy (reported as median and IQR). 6. Behaviour changes associated with the intervention. 7. Sense of well-being and quality of life (Questionnaires relating to fear of hypoglycaemia, coping with diabetes, quality of life, and satisfaction with monitoring device).

Feig 2017 *(Continued)*

8. Glycaemic control during/end of treatment (as defined by trialists) (e.g. HbA1c, fructosamine, fasting blood glucose, post-prandial blood glucose) - HbA1c, total insulin dose.
9. Maternal hypoglycaemia (severe).
10. Miscarriage.
11. Postnatal weight retention or return to pre-pregnancy weight – maternal weight gain (from entry to 34 weeks).
12. Cardiovascular health (as defined by trialists, including blood pressure, hypertension, cardiovascular disease, metabolic syndrome) - hypertension.
13. Stillbirth.
14. Gestational age at birth – median (IQR).
15. Preterm birth (less than 37 weeks' gestation and less than 34 weeks' gestation).
16. Macrosomia (≥ 4000 g).
17. Small-for-gestational age (< 10th centile).
18. Birthweight and z-score (birthweight g) mean (SD).
19. Head circumference (cm) mean (SD) and z-score.
20. Length and z-score (crown-heel length (cm).
21. Adiposity (e.g. BMI, skinfold thickness) Sum of 4 skin folds (triceps, subscapular, biceps, flank).
22. Shoulder dystocia.
23. Respiratory distress syndrome.
24. Hypoglycaemia (variously defined).
25. Hyperbilirubinaemia.
26. Relevant biomarker changes associated with the intervention (e.g. cord c peptide, cord insulin) – Cord blood C-peptide levels > 566 pmol/L, > 2725 pmol/L.
27. Major and minor anomalies – congenital anomaly.
28. Number of antenatal visits or admissions – number of hospital admissions.
29. Length of antenatal stay – maternal length of stay – days – median (IQR).
30. Neonatal intensive care unit length of stay greater than 24 hours.
31. Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite) – birth injury and shoulder dystocia.
32. Diabetic ketoacidosis – DKA – page 22 in supplementary file – table 19a.

Notes

Setting: 31 hospitals in Canada, England, Scotland, Spain, Italy, Ireland and the USA.

Country: Canada.

Funding: the trial was funded by Juvenile Diabetes Research Foundation (JDRF) grants #17-2011-533, and grants under the JDRF Canadian Clinical Trial Network, a public-private partnership including JDRF and FedDev Ontario and supported by JDRF #80-2010-585. Metronic supplied the CGM sensors and CGM systems at reduced cost. HRM conducts independent research supported by the National Institute for Health Research (Career Development Fellowship, CDF-2013-06-035), and is supported by Tommy's charity. The funders had no role in the trial design, data collection, data analysis, or data interpretation.

Declarations of interest: 8 authors report grants from the Juvenile Diabetes Research Foundation during the conduct of the study. Two authors report personal fees from Novo Nordisk, Roche and Medtronic, outside the submitted work. 1 author reports personal fees from Abbott Diabetes Care and Medtronic (MiniMed Academia), outside the submitted work. 1 author sits on the Medtronic European Scientific Advisory Board. All remaining authors declare no completing interests.

Comments

1. A sample size calculation was reported.
2. They ran 2 trials in parallel for pregnant participants and for participants planning a pregnancy - we report only on the trial of pregnant participants.
3. The study protocol was approved by the Health Research Authority, East of England Research Ethics Committee for all UK sites and at each individual centre for all other sites. Regional Ethical Committee.

Feig 2017 *(Continued)*

4. All participants provided written informed consent.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Treatments allocated by a web-based system using a computer-generated randomisation list with permuted block sizes and stratified by method of insulin delivery (pump or multiple injections) and baseline HbA1c (< 7.5% vs ≥ 7.5% or 58 mmol/mol for the pregnancy trial).
Allocation concealment (selection bias)	Low risk	Randomisaton schedule created by a programming manager, encrypted, and maintained in a secure database – the co-ordinating team and investigators had no access.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Used masked sensors – for control group – so suggests blinding and also HbA1c measures done at a central laboratory and were unavailable to participants and healthcare teams during the trial.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	All HbA1c measures done at a central laboratory. Samples were shipped after delivery and collection of cord blood and were unavailable to participants and healthcare teams during the trial.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Authors report that about 20% data were missing, lost to follow-up. For primary outcome – change in HbA1c – 82% (89/108) and 79% (84/107) included in analysis from CGM and home monitoring groups. Also stated that "For the primary outcome, the patterns of change were similar between analyses of imputed and available HbA_{1c} data". There is a study flow diagram and missing data appear balanced across groups.
Selective reporting (reporting bias)	Low risk	Cross-checked the protocol with main published report and methods section – also checked Appendices in supplementary file – most of the outcomes appear to have been reported.
Other bias	Low risk	Groups balanced at baseline – differences noted in smoking, automated insulin delivery option, hypertension, severe hypoglycaemia in past year or during early pregnancy pre-randomisation – but report states "any minor imbalances in baseline characteristics between CGM and control group participants were within the expected bounds for random allocation".

Hanson 1984

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** 1 October 1979 - 1 October 1982.
Participants	**Number randomised:** 100. Eligible were type 1 diabetes mellitus (IDDM) and type 2 diabetes mellitus (NIDDM) pregnant patients attending the from 5 hospitals in Stockholm during the period of study. **Inclusion criteria:** patients with a diagnosis of diabetes, either insulin-dependent or non-insulin-dependent prior to pregnancy.

Hanson 1984 *(Continued)*

	Exclusion criteria: not mentioned in text.
Interventions	**Intervention:** patients self-monitored their blood glucose at home from the 32nd week until the 36th week of gestation. Weekly hospital visit from 32-36 weeks and then hospitalised during the 37th week until delivery (n = 54). **Control:** patients were hospitalised from 32nd week until delivery (n = 46).
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Perinataly mortality (stillbirth and neonatal mortality). 3. Pre-eclampsia. 4. Pregnancy-induced hypertension. 5. Placental abruption. 6. Preterm birth < 37 weeks. 7. Respiratory distress syndrome. 8. Neonatal hypoglycaemia. 9. Neonatal jaundice. 10.HbA1c. 11.Major anomalies. 12.Antenatal hospital admission. 13.Neonatal hospital stay. 14.Feeding difficulties.
Notes	**Setting:** 5 hospitals in Stockholm. **Country:** Sweden. **Funding:** Expressens Perinatal forskningsfond, AIImanna Barnbordshusets Minnesfond, Svenska Diabetesstiftelsen, Nordisk Insulinfond, Swedish Medical Research Council (Project No. 3787), and Tielman's Fund for Pediatric Research. **Declarations of interest:** not reported. **Comments** 1. No sample size estimation reported. 2. Twins were included (2 pairs). 3. If complications occurred, home monitoring situation was interrupted. 4. The study was approved by the Regional Ethical Committee. 5. Informed consent was obtained from all participants.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: not mentioned.
Allocation concealment (selection bias)	Unclear risk	Comment: not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.

Hanson 1984 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. Objective measurements used.
Incomplete outcome data (attrition bias) All outcomes	High risk	Comment: 1 excluded for severe drug addiction, 8 spontaneous abortions and 1 mother died.
Selective reporting (reporting bias)	Low risk	No obvious risk to selective reporting.
Other bias	Low risk	No obvious risk to other bias.

Manderson 2003

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** not mentioned.
Participants	**Number randomised:** 61 Eligible were type 1 diabetes mellitus (IDDM) pregnant patients attending or referred to the Regional Joint Metabolic/Antenatal Clinic at the Royal Maternity Hospital, Belfast during the period of study. **Inclusion criteria:** type 1 DM pregnant women at 16 weeks' gestation. **Exclusion criteria:** women without results due to reasons such as: stillbirth, abortions, major congenital abnormalities.
Interventions	**Intervention:** pre-prandial glucose monitoring (n = 31). **Control:** post-prandial glucose monitoring (n = 30).
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Large-for-gestational age. 3. Perinatal mortality (stillbirth and neonatal mortality). 4. Pre-eclampsia. 5. Weight gain during pregnancy. 6. Insulin dose. 7. Maternal glycaemic control (HbA1c, fasting blood glucose, post-prandial blood glucose, fructosamine). 8. Stillbirth. 9. Gestational age (at birth). 10. Preterm birth < 37 weeks. 11. Macrosomia. 12. Birthweight (kg). 13. Respiratory distress syndrome. 14. Neonatal hypoglycaemia. 15. Neonatal jaundice. 16. Cord IGF. 17. Neonatal glucose at age 1 hour. 18. Transient tachypnoea.

Manderson 2003 *(Continued)*

	19.Neonatal intensive care admissions.
Notes	**Setting:** Regional Joint Metabolic/Antenatal Clinic at the Royal Maternity Hospital, Belfast. **Country:** UK. **Funding:** Department of Health and Social Sevices, Northern lreland, the Northern Ireland Mother and Baby Appeal, the Metabolic Unit Research Fund, Royal Victoria Hospital, Belfast, the Royal Maternity Hospital, Royal Victoria Hospital, Belfast, and the Irish Perinatal Society. **Declarations of interest:** not reported. **Comments** 1. No sample size estimation reported. 2. No type 2 DM pregnant patients included. 3. Only white women were included. 4. Patients were reviewed fortnightly or more frequently if clinically indicated. 5. Insulin doses were adjusted to achieve fasting glucose values between 60 mg/dL and 90 mg/dL (3.3 mmol/L and 5.0 mmol/L), pre-prandial values between 60 mg/dL and 105 mg/dL (3.3 mmol/L and 5.9 mmol/L), and post-prandial values less than 140 mg/dL (7.8 mmol/L). 6. Post-prandial glucose monitoring may significantly reduce the incidence of pre-eclampsia and neonatal triceps skinfold thickness compared with pre-prandial monitoring.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote - "Women were randomly assigned at 16 weeks' gestation to 1 of 2 blood glucose monitoring protocols". Comment: method not mentioned.
Allocation concealment (selection bias)	Low risk	Quote - "allocations were via a sealed envelope system, which the patient selected from a box at the clinic visit".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote - "74 patients were recruited. 13 were excluded because they did not have results for analysis. This left 61 diabetic women (31 pre-prandial and 30 post-prandial monitoring) with results suitable for analysis".
Selective reporting (reporting bias)	Low risk	No obvious risk to selective reporting.
Other bias	Low risk	No obvious risk to other bias.

Murphy 2008

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial.

Murphy 2008 *(Continued)*

	Period of study: September 2003 to 2006.
Participants	**Number randomised:** 71. Eligible were type 1 (IDDM) and type 2 (NIDDM) diabetes mellitus pregnant patients attending 2 secondary care diabetic antenatal clinics in the UK during the period of study. **Inclusion criteria** 1. Type 1 and type 2 DM pregnant women at 16 weeks' gestation. 2. Provided written informed consent. 3. Willing to wear a continuous glucose monitor. **Exclusion criteria** 1. Women with severe medical or psychological comorbidity.
Interventions	I**ntervention:** continuous glucose monitor which measured glucose in subcutaneous tissues every 10 seconds and an average value is stored every 5 minutes, providing up to 288 measurements per day (n = 38). The participants were required to wear the CGMS for 7 days at intervals of 4-6 weeks. They were also advised to measure blood glucose at least 7 times a day. **Control:** intermittent self-monitoring of glucose levels (n = 33), at least 7 times a day (standard care).
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Large-for-gestation age. 3. Perinatal mortality (stillbirth and neonatal mortality). 4. Pre-eclampsia. 5. Maternal glycaemic control (HbA1c). 6. Miscarriage. 7. Neonatal mortality. 8. Gestational age at birth. 9. Preterm birth at < 37 weeks. 10.Macrosomia. 11.Birthweight. 12.Small-for-gestational age. 13.Neonatal hypoglycaemia. 14.Major and minor anomalies. 15.Neonatal intensive care admissions.
Notes	**Setting:** secondary care diabetic antenatal clinics. **Country:** UK. **Funding:** this was an investigator initiated study funded by the Ipswich Diabetes Centre Charity Research Fund. HRM also received salary support from Diabetes UK. The study equipment (6 x CGMS Gold monitors and 300 sensors) was donated free of charge by Medtronic UK. The research was sponsored by Ipswich Hospital NHS Trust and was independent of all the study funders. **Declarations of interest:** 2 trial authors received honorariums for speaking at research symposiums sponsored by Medtronic in 2004 and 2005. **Comments** 1. Sample size estimation was reported. 2. Both type 1 and type 2 DM pregnant patients were included. 3. The women were predominantly white European.

Murphy 2008 *(Continued)*

4. The continuous glucose monitor (CGM) to be worn up to 7 days at intervals of 4 to 6 weeks between 8 and 32 weeks' gestation.
5. In addition to the CGM, intermittent self-monitoring of glucose levels was implemented in the intervention group.
6. Therapeutic adjustments to diet, exercise, and insulin regimens were discussed with the obstetric diabetes team, based on the combined intermittent capillary glucose and continuous glucose data for women allocated to CGM or the intermittent capillary glucose data alone for women allocated to standard antenatal care.
7. The women were advised to measure blood glucose levels at least 7 times a day and were provided with several targets: 3.5 mmol/L to 5.5 mmol/L before meals, < 7.8 mmol/L 1 hour after meals, and < 6.7 mmol/L 2 hours after meals.
8. The women were seen every 2-4 weeks for up to 28 weeks, fortnightly until 32 weeks, and weekly thereafter, with assessments of fetal growth at 28, 32, and 36 weeks.
9. Short-acting insulin analogues were used before meals with intermediate acting insulin, long-acting analogues, or pump therapy. The women with type 2 diabetes were treated with insulin before pregnancy or as soon as pregnancy was confirmed.
10. Majority (90%) of women were White European, with the rest being Asian and others.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote - "The study statistician used computer generated randomised numbers in blocks of 20".
Allocation concealment (selection bias)	Low risk	Quote - "Concealed in sealed envelopes. Research nurses trained in accordance with good clinical practice guidelines provided the women with their group allocation".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: intention-to-treat analysis was applied.
Selective reporting (reporting bias)	Low risk	All expected outcomes appear to have been reported.
Other bias	Low risk	No obvious risk to other bias.

Petrovski 2011

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** not mentioned.
Participants	**Number randomised:** 25.

Petrovski 2011 *(Continued)*

	Eligible were type 1 diabetes mellitus (IDDM) pregnant patients attending the University Clinic of Endocrinology, Diabetes and Metabolic Disorders in Skopje during the period of study. **Inclusion criteria** 1. On continuous subcutaneous insulin infusion (CSII) for at least 3 months before conception. 2. Singleton pregnancy. **Exclusion criteria** 1. Not mentioned.
Interventions	I**ntervention:** constant CGM - 24 hours/day (n = 12). **Control:** intermittent CGM - 14 days per month (n = 13), measured blood glucose at least 6 times a day every second week (when not using the CGM).
Outcomes	**Outcomes used in this review** 1. Caesarean section rates. 2. Weight gain during pregnancy. 3. Maternal glycaemic control (HbA1c, mean blood glucose). 4. Severe hypoglycaemia (maternal). 5. Diabetic ketoacidosis. 6. Preterm birth < 37 weeks. 7. Macrosomia. 8. Neonatal hypoglycaemia.
Notes	**Setting:** University Clinic of Endocrinology, Diabetes and Metabolic Disorders in Skopje. **Country:** Macedonia. **Funding:** Macedonion Ministry of Health and the Health Care Fund of Macedonia. **Declarations of interest:** the authors declared that they had no competing financial interests. **Comments** 1. No sample size estimation reported. 2. No type 2 DM pregnant patients included. 3. All patients were followed for 1 to 3 weeks by a diabetologist and obstetrician. 4. The device could alert increased or decreased glucose levels, insulin pump was automatically suspend insulin delivery if necessary.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote - "Patients were randomised into 2 groups". Comment: method not mentioned.
Allocation concealment (selection bias)	Unclear risk	Not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.

Petrovski 2011 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Intention-to-treat analysis.
Selective reporting (reporting bias)	Low risk	All expected outcomes reported.
Other bias	Low risk	No obvious risk to other bias.

Secher 2013

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** 15 February 2009 to 15 February 2011.
Participants	**Number randomised:** 154. Eligible were 123 type 1 (IDDM) and 31 type 2 (NIDDM) pregnant patients referred to the Centre for Pregnant Women with Diabetes, Rigshospitalet, before 14 completed gestational weeks. **Inclusion criteria** 1. Type 1 and type 2 DM pregnant women before 14 completed weeks of gestation. 2. Provided written informed consent. 3. Willing to wear a CGM. **Exclusion criteria** 1. Present use of real-time CGM. 2. Severe mental or psychiatric barriers. 3. Diabetic nephropathy. 4. Severe concurrent comorbidity (e.g. severe psoriasis, previous gastric bypass surgery).
Interventions	**Intervention:** real time CGM for 6 days at pregnancy visits during 8, 12, 21, 27 and 33 weeks, in addition to routine pregnancy care. **Control:** routine pregnancy care with self-monitored plasma glucose measurements of 7 times daily.
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Large-for-gestational age. 3. Pre-eclampsia. 4. Pregnancy-induced hypertension. 5. Miscarriage. 6. Preterm birth <37 weeks. 7. Neonatal hypoglycaemia.
Notes	**Setting:** Centre for Pregnant women with Diabetes, Rigshospitalet. **Country:** Denmark.

Secher 2013 *(Continued)*

Funding: 1 of the authors received financial support from the European Foundation of the Study of Diabetes and LifeScan, Rigshopitalet's Research Foundation, the Capital Region of Denmark, the Medical Facuty Foundation of Copenhagen Univeristy, Aase and Ejnar Danielsen Foundation, and Master Joiner Sophus Jacobsen and his wife Astrid Jacobsens' Foundation. 1 author holds stocks in Novo Nordisk. 1 author received financial support from Novo Nordisk Foundation. The real-time CGM monitors and links were supplied, and glucose sensors were offered at a reduced price by Medtronic.

Declarations of interest: the authors declared no other potential conflicts of interest, other than those reported under 'funding'. interests.

Comments

1. Sample size estimation was reported.
2. Women gave written informed consent.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote - "a computer generated randomization program was used".
Allocation concealment (selection bias)	Low risk	Quote - "..treatment allocation was properly concealed using automated telephone allocation service (Paravox) provided by an independent organization".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote - "Intention-to-treat analysis was carried out".
Selective reporting (reporting bias)	Low risk	All expected outcomes reported.
Other bias	Low risk	No obvious risk to other bias.

Stubbs 1980

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** not mentioned.
Participants	**Number randomised:** 13. Eligible were type 1 (IDDM) diabetes mellitus pregnant patients attending King College's Hospital. **Inclusion criteria:** type 1 DM pregnant women at 30-31 weeks' gestation. **Exclusion criteria:** not mentioned.

Stubbs 1980 *(Continued)*

Interventions	**Intervention:** 1) glucometer group (n = 7) measured blood glucose at home - 7 times a day, twice weekly (before and after each main meal and before bedtime). **Control:** non-meter group (n = 6) - checked urine glucose 4 times daily, random blood glucose measured at the fortnightly clinic visits.
Outcomes	**Outcomes used in this review** 1. Maternal glycaemic control (post-prandial blood glucose). 2. Birthweight.
Notes	**Setting:** King's College hospital. **Country:** UK. **Funding:** Medical Research Council Project Grant and the British Diabetic Association. **Declarations of interest:** not reported. **Comments** 1. Sample size estimation was not reported. 2. Type 2 DM pregnant patients were not included. 3. A third group (normal women, n = 8) was included for comparison. 4. The women were at 30-31 weeks' gestation at the beginning of study. 5. Women in the intervention group had their diet and insulin dosage adjusted by telephone or clinic consultation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: not mentioned.
Allocation concealment (selection bias)	Unclear risk	Comment: not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Comment: iIntention-to-treat.
Selective reporting (reporting bias)	Low risk	All expected outcomes reported.
Other bias	Low risk	No obvious risk to other bias.

Varner 1983

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** 1 February 1980 to 16 September 1981.
Participants	**Number randomised:** 30. Eligible were type 1 diabetes mellitus (IDDM) pregnant patients attending the High Risk Obstetric Clinic at the University of Iowa Hospitals and Clinics during the period of study. **Inclusion criteria:** less than 20 weeks' gestation. **Exclusion criteria:** not mentioned.
Interventions	I**ntervention:** daily home glucose monitoring (n = 15) - fasting, 2-hour post-prandial morning, afternoon and evening glucose values were measured daily. **Control:** weekly venipuncture (n = 15) - fasting, 2 hours after breakfast, and 2 hours after lunch glucose levels measured on 1 day each week.
Outcomes	**Outcomes used in this review** 1. Caesarean section. 2. Perinatal mortality. 3. Maternal glycaemic control (HbA1c). 4. Miscarriage. 5. Neonatal mortality. 6. Gestational age at birth. 7. Birthweight. 8. Respiratory distress syndrome. 9. Neonatal hypoglycaemia. 10. Neonatal jaundice. 11. Neonatal hypocalcaemia. 12. Neonatal polycythaemia. 13. Neonatal cord vein C-peptide.
Notes	**Setting:** High Risk Obstetric Clinic at the University of Iowa Hospitals and Clinics, Iowa. **Country:** USA. **Funding:** Research Fellowship from the Iowa Affiliate of the American Diabetes Association. **Declarations of interest:** not reported. **Comments** 1. No sample size estimation reported. 2. No type 2 DM pregnant patients included. 3. Patients telephoned their physicians weekly to report their blood glucose values or possible complications. 4. Insulin was adjusted by the patients with physicians' consultation.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote - "Patients were assigned to control and experimental groups using a random number sequence".

Varner 1983 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Comment: not mentioned.
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of outcome assessment. However, all outcomes were objectively measured.
Incomplete outcome data (attrition bias) All outcomes	High risk	2 patients from each group had a first trimester spontaneous miscarriage and were excluded (2 out of 30 = 7%).
Selective reporting (reporting bias)	Low risk	All expected outcomes reported.
Other bias	Low risk	No obvious risk to other bias.

Voormolen 2018

Methods	Nationwide multicentre, open-label, parallel, pragmatic randomised controlled trial **Period of study:** July 2011 to September 2015
Participants	**Number randomised:** 300 pregnant women type 1 (n = 109), type 2 (n = 82), or with gestational diabetes (n = 109). **Inclusion criteria:** pregnant women with pre-existing DM, at gestational age of before 16 weeks, or had GDM requiring insulin therapy before 30 weeks gestational age. **Exclusion criteria:** women with multiple pregnancies, under 18 years of age, or who had severe medical or psychological comorbidity
Interventions	**Intervention:** CGM:iPro2 (Medtronic, Northridge, California) - CGM in addition to standard care – self-monitoring. Women allocated to CGM were instructed to use the device for 5-7 days every 6 weeks and glucose profiles were obtained retrospectively, directly after each use and evaluated by the local endocrinologist. SMBG is required for calibration of CGM. Readings from the CGM are uploaded to a web-based program; (n = 147 all women, 50 with T1DM, 40 T2DM). **Control:** standard treatment - self-monitoring of blood glucose only (n = 153 all women, 97 with type 2 diabetes). All participants in both intervention and control groups performed SMBG (4-8 times/day: at least fasting, after every meal, at bedtime and, preferably before every meal).
Outcomes	**Outcomes used in this review** 1. Hypertensive disorders of pregnancy (including pre-eclampsia, pregnancy-induced hypertension, eclampsia). 2. Caesarean section*. 3. Large-for-gestational age*. 4. Induction of labour*. 5. Glycaemic control during/end of treatment (as defined by trialists) (e.g. HbA1c, fructosamine, fasting blood glucose, post-prandial blood glucose)*. 6. Instrumental vaginal birth*. 7. Neonatal mortality.

Voormolen 2018 *(Continued)*

8. Gestational age at birth*.
9. Preterm birth*.
10. Macrosomia (≥ 4000 g).
11. Small-for-gestational age (< 10th centile)*.
12. Birthweight and z-score (birthweight g) mean (SD)*.
13. Shoulder dystocia*.
14. Neonatal hypocalcaemia*.
15. Major and minor anomalies – congenital anomaly*.
16. Neonatal intensive care unit admission*.
17. Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite) – birth injury and shoulder dystocia*.

* outcome not reported separately for pre-gestational and gestational diabetes

Notes

Setting: 22 hospitals (university, teaching and non-teaching in the Netherlands and 1 university hospital in Belgium.

Country: the Netherlands**.**

Funding: the trial was funded by ZonMw, The Dutch Organization for Health Research and Development 80-82310-97-11157. The funder had no role in the study design, data collection, data analysis, data interpretation or writing of the report. Continuous glucose monitors were purchased at a discounted price from Medtronic® and they had no role in the study design, data collection, data analysis, data interpretation, or writing of the report.

Declarations of interest: 1 of the trial authors received a research grant from ZonMW (the Netherlands Organization for Health Research and Development) and a second author received research grants from Abbott, Dexcom, Medtronic and Sensonics, and also received personal fees from Roche Diabetes Care and Sensonics. A third author is supported by an NHMRC Practitioner Fellowshop (GNT1082548) and reports consultancy for ObsEVa, Merck and Guerbet. All other authors declare no support from any organization or conflict of interest.

Comments

1. A sample size calculation was reported.
2. They included both women with pre-gestational diabetes (type 1 and type 2) and women with GDM. However, for most of our review outcomes, the data were not separated out by pre-gestational and GDM women.
3. The study was approved by the ethics committee of the Academic Medical Centre Amsterda, (reference number MEC AMC 10/322) and by the boards of management of all participating hospitals.
4. Written consent was obtained from all participating women.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Web-based computerised programme using 1:1 randomisation, stratified according to type of diabetes
Allocation concealment (selection bias)	Unclear risk	Not clearly described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding – but outcome measures mainly objective, so unlikely to be affected by lack of blinding
Blinding of outcome assessment (detection bias)	Low risk	No blinding – but outcome measures mainly objective, so unlikely to be affected by lack of blinding

Voormolen 2018 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	High number of patients refused continued use of the CGM after the first or second time – a total of 66% of participants used CGM according to study protocol. However, there was a clear flow of participants in trial profile figure and reasons for dropouts, withdrawal provided. Conducted analyses on intention-to-treat and per-protocol basis; 4 drop-outs from CGM group and 6 from standard group so primary analyses were carried out according to the intention-to-treat principle – 143/147 included from the (CGM group) and 147/153 (standard group in the intention-to-treat analysis). Quite a high drop out rate – 95 women in the CGM group and 144 from the control group were included in the per-protocol analyses. 48 discontinued intervention and 3 discontinued protocol for standard group leaving: 95/147 (66%) intervention group and 144/153 (98%) standard group
Selective reporting (reporting bias)	High risk	**Maternal outcomes not reported** 1. Severe hypoglycaemia **Neonatal outcomes not reported** 1. Preterm birth < 37 weeks' gestation 2. Birth trauma 3. Culture proven sepsis 4. Respiratory distress syndrome 5. Bronchopulmonary dysplasia 6. Intraventricular haemorrhage 7. Necrotising enterocolitis The above were outcomes in the methods of the full report – but were not presented in the results section. The protocol also reported the following outcomes that were not reported in the results: mode of delivery, perinatal death, glucose variability, costs and resource utilisation
Other bias	Unclear risk	Baseline characteristics – groups were similar. Data not presented separately for pre-gestational diabetes (type 1 and type 2 diabetes) and GDM patients for most of the outcomes.

Wojcicki 2001

Methods	Randomised, parallel-group, open-label, 2-armed, active controlled trial. **Period of study:** not mentioned.
Participants	**Number randomised:** 32. Eligible were type 1 diabetes mellitus (IDDM) pregnant patients attending the Clinic of Gastroenterology and Metabolic Diseases of the Medical Academy in Warsaw during the period of study. **Inclusion criteria** 1. Duration of pregnancy less than 16 weeks. 2. No diseases. 3. Acceptable intelligence level according to the modified Wechsler-Bellevue Scale for Adults. 4. Glycaemic control in the range of HbA1c < 9.5%.

Wojcicki 2001 *(Continued)*

	Exclusion criteria 1. Not mentioned.
Interventions	**Intervention:** Telematic Management System (Central Clinical Unit and Patients' Teletransmission Modules) (n = 15) - daily transfer of glycaemic data to diabetologist, at least 6 blood glucose measurements daily. **Control:** Standard care without Telematic Management System (n = 15), 6 blood glucose measurement daily and routine clinic visit every 3 weeks.
Outcomes	**Outcomes used in this review** 1. Gestational age at birth. 2. Maternal glycaemic control (HbA1c, mean blood glucose). 3. Hypoglycaemia (maternal).
Notes	**Setting:** Clinic of Gastroenterology and Metabolic Diseases of the Medical Academy in Warsaw. **Country:** Poland. **Funding:** supported by grants from the Polish State Committee for Scientific Research, the Bayer Diagnostic Division Warsaw, and the Polish Cellular Telephony Centertel. **Declarations of interest:** not reported. **Comments** 1. No sample size estimation reported. 2. No type 2 DM pregnant patients included. 3. 2 participants in the intervention group were excluded as they had pneumonia and Meniere's disease not diagnosed before randomisation. 4. Intensive insulin treatment was provided with multi-injection technique with 6 blood glucose measurements per day (before and 60 minutes after the 3 main meals). 5. Each patient was followed up every 3 weeks by the same diabetologist. 6. Patients from the intervention group had their blood glucose data transmitted to the diabetologist daily. Thus the diabetologist was able to examine the metabolic state and to intervene if necessary.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomisation stated but method of sequence generation not clear. Quote: "Before randomization written consent was taken.....".
Allocation concealment (selection bias)	High risk	Not possible as the same diabetologist was seeing both groups and knew to which group the participant belonged (control group could access the diabetologist by phone any time).
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, this may not affect the results as all outcomes were objectively measured.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Comment: no blinding of participants and personnel. However, all outcomes were objectively measured.

Wojcicki 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	All participants accounted for and all data reported.
Selective reporting (reporting bias)	Low risk	No obvious risk to selective reporting.
Other bias	Low risk	No obvious risk to other bias.

BMI: body mass index
CGM: continuous glucose monitoring
CGMS: continuous glucose monitoring system
DM: diabetes mellitus
GDM: gestational diabetes mellitus
IDDM: insulin-dependent diabetes mellitus
IGF-1: insulin-like growth factor-1
IQR: interquartile range
NIDDM: non insulin-dependent diabetes mellitus

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Bartholomew 2011	Cross-over trial. Included women with GDM AND pre-existing type 2 diabetes: results are not presented separately.
NCT01630759	Clinical trial registration - for gestational diabetics only - started in January 2012, expected to complete by April 2013.
Temple 2006	Abstract of an observational study of 8 type 1 diabetic pregnant women using CGMS.
Walker 1999	Clinical trial registration - contacted author, no published data or report available.

CGMS: continuous glucose monitoring system
GDM: gestational diabetes mellitus

Characteristics of ongoing studies *[ordered by study ID]*

Link 2018

Trial name or title	Link H, NCT03504592. Utilizing mHealth to improve diabetes in an obstetric population. https://clinicaltrials.gov/ct2/show/NCT03504592 (first received 20 April 2018).
Methods	Randomised, parallel single-centre trial, open-label - USA
Participants	Inclusion criteria: 18 to 60 years, pregnant, English speaking, diagnosed with diabetes during pregnancy or with known pre-existing diabetes, have a smart phone
Interventions	MHealth technology - participants to record blood glucose values with the assistance of a smart phone device compared to traditional care method of clinic
Outcomes	Primary: completeness and accuracy of blood glucose record Secondary: patient satisfaction, glucose values at goal, % change in HbA1C, clinic visits, unscheduled healthcare access episodes

Link 2018 *(Continued)*

Starting date	1 May 2018
Contact information	Heather Link, email: heather_link@urmc.rochester.edu
Notes	Estimated study completion - June 2019

Logan 2011

Trial name or title	Managing diabetes during pregnancy in the wireless age: a RCT of glucose telemonitoring. https://clinicaltrials.gov/ct2/show/NCT01474525 (first received 18 November 2011).
Methods	Randomised, parallel single-centre trial, open-label - Canada
Participants	Inclusion criteria: pregnant, diagnosed with gestational diabetes or type 2 diabetes, comfortable with instructions in English and be able to express themselves using simple phrases in English
Interventions	Home blood glucose telemonitoring system (system designed to send the measured blood glucose values directly to a hospital server, values recorded by glucometer are sent to a Blackberry cell phone, which services as the platform for data-transmission to the central server) compared to usual care
Outcomes	Primary: mean blood glucose, based on the highest post-prandial blood glucose reading each day, by trimester Secondary outcomes: mean fasting and post-prandial blood glucose by trimester, percentage of values within recommended guidelines, adherence, onset of labour and mode of delivery Fetal outcomes: gestational age at delivery, birthweight, percentage of macrosomia, large-for-gestational age, small-for-gestational age, Apgar at 1 and 5 minutes Perinatal complications: premature, NICU admission, jaundice, shoulder dystocia, hypoglycaemia Provider usage: number of log-ins onto the system, average amount of time spent on the system per week
Starting date	January 2010
Contact information	Alexander G Logan, email: logan@lunenfeld.ca
Notes	Estimated study completion - March 2012

HbA1C: haemoglobin A1C (glycated haemoglobin)
NICU: neonatal intensive care unit
RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. Continuous glucose monitoring versus intermittent glucose monitoring

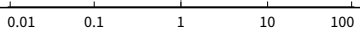
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hypertensive disorders of pregnancy	2	384	Risk Ratio (M-H, Fixed, 95% CI)	0.58 [0.39, 0.85]
2 Caesarean section	3	427	Risk Ratio (M-H, Random, 95% CI)	0.94 [0.75, 1.18]
3 Large-for-gestational age	3	421	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.57, 1.26]
4 Perinatal mortality (stillbirth and neonatal mortality)	1	71	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.05, 12.61]
5 Mortality or morbidity composite (pregnancy loss (miscarriage, stillbirth, and neonatal death); birth injury; neonatal glycaemia; hyperbilirubinaemia; respiratory distress; and high level neonatal care of more than 24 hours)	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.80 [0.61, 1.06]
6 Pre-eclampsia	4	609	Risk Ratio (M-H, Fixed, 95% CI)	0.65 [0.39, 1.08]
7 Pregnancy-induced hypertension	2	384	Risk Ratio (M-H, Fixed, 95% CI)	0.67 [0.38, 1.16]
8 Behaviour changes associated with the intervention (range of score 10-50 - high score= greater fear of hypoglycaemia)	1	214	Mean Difference (IV, Fixed, 95% CI)	1.00 [-1.06, 3.06]
9 Sense of well-being and quality of life (Short form 12 (SF-12), total score at 34 weeks' gestation)	1	214	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.50, 1.10]
10 Sense of well-being and quality of life (Problem areas in diabetes (PAID), total score at 34 weeks' gestation)	1	214	Mean Difference (IV, Fixed, 95% CI)	0.80 [-3.06, 4.66]
11 Sense of well-being and quality of life (BGMSRQ, total score at 34 weeks' gestation)	1	214	Mean Difference (IV, Fixed, 95% CI)	4.30 [0.73, 7.87]
12 Glycaemic control - Maternal HbA1c	2	258	Mean Difference (IV, Random, 95% CI)	-0.37 [-0.78, 0.04]
13 Glycaemic control - Achieved maternal HbA1c <= 6.5% (48 mmol/mol) at 34 weeks	1	187	Risk Ratio (M-H, Fixed, 95% CI)	1.27 [1.00, 1.62]
14 Maternal hypoglycaemia (severe)	1	154	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.43, 1.95]
15 Miscarriage	3	439	Risk Ratio (M-H, Fixed, 95% CI)	1.24 [0.47, 3.26]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16 Stillbirth	1	211	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.01, 8.17]
17 Neonatal mortality	2	256	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.13, 6.37]
18 Gestational age at birth	1	68	Mean Difference (IV, Fixed, 95% CI)	0.10 [-0.57, 0.77]
19 Preterm birth < 37 weeks	3	430	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.72, 1.29]
20 Preterm birth < 34 weeks	1	211	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.17, 1.28]
21 Macrosomia	3	451	Risk Ratio (M-H, Random, 95% CI)	0.84 [0.61, 1.17]
22 Birthweight	2	267	Mean Difference (IV, Random, 95% CI)	-0.13 [-0.38, 0.12]
23 Small-for-gestational age	2	269	Risk Ratio (M-H, Fixed, 95% CI)	2.40 [0.55, 10.51]
24 Head circumference (cm)	1	160	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.79, 0.39]
25 Length (crown-heel length cm)	1	160	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.79, 0.39]
26 Adiposity (sum of 4 skin folds (tricepts, subscapular, biceps, flank) mm)	1	160	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.98, 1.58]
27 Shoulder dystocia	1	200	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.12, 72.77]
28 Respiratory distress syndrome	1	200	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.41, 2.41]
29 Neonatal hypoglycaemia	3	428	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.48, 0.93]
30 Neonatal hyperbilirubinaemia	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.52, 1.26]
31 Relevant biomarker changes associated with the intervention (cord blood c-peptide levels > 566 pmol/L)	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.68, 1.33]
32 Relevant biomarker changes associated with the intervention (cord blood c-peptide levels > 2725 pmol/L)	1	200	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.33, 3.00]
33 Major and minor anomalies	2	285	Risk Ratio (M-H, Fixed, 95% CI)	0.71 [0.16, 3.13]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
34 Number of hospital admissions (mother)	1	207	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.84, 1.85]
35 Neonatal intensive care unit admissions	2	274	Risk Ratio (M-H, Random, 95% CI)	0.76 [0.42, 1.35]
36 Neonatal intensive care unit length of admission > 24 hours	1	200	Risk Ratio (M-H, Fixed, 95% CI)	0.63 [0.42, 0.93]
37 Birth trauma (shoulder dystocia, bone fracture, nerve palsy)	1	200	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [0.24, 102.85]
38 Diabetic ketoacidosis (mother)	1	207	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.14, 7.03]

Analysis 1.1. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 1 Hypertensive disorders of pregnancy.

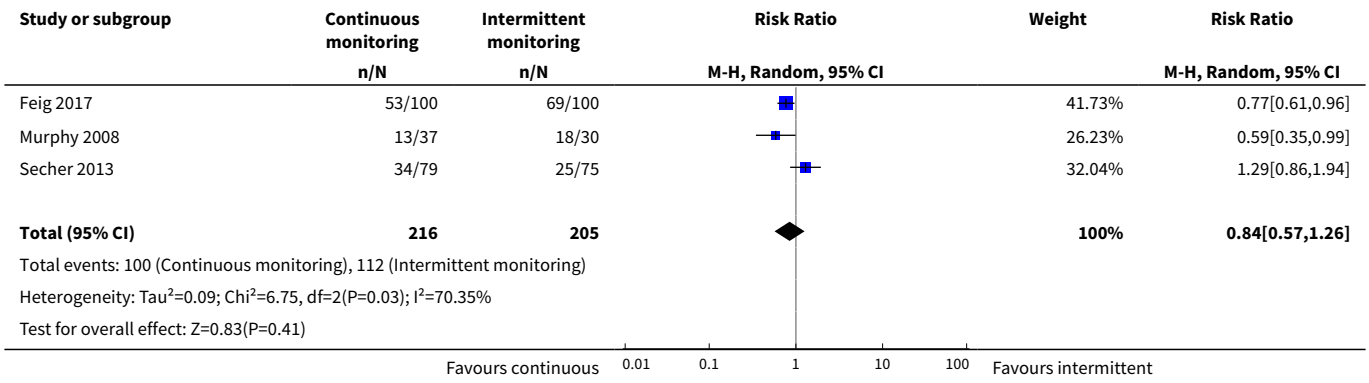
Study or subgroup	Continuous n/N	Intermittent n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Feig 2017	18/100	28/102		49.43%	0.66[0.39,1.11]
Voormolen 2018	14/89	29/93		50.57%	0.5[0.29,0.89]
Total (95% CI)	**189**	**195**		**100%**	**0.58[0.39,0.85]**
Total events: 32 (Continuous), 57 (Intermittent)					
Heterogeneity: Tau^2=0; Chi^2=0.44, df=1(P=0.51); I^2=0%					
Test for overall effect: Z=2.78(P=0.01)					



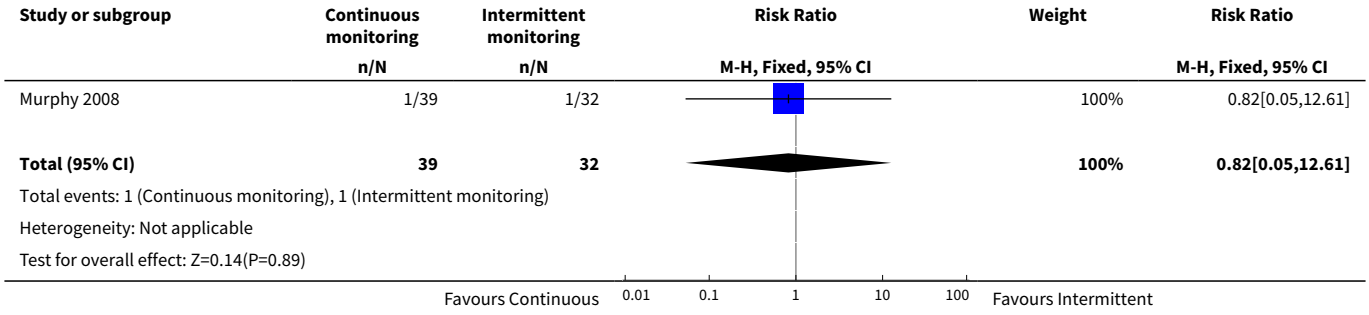
Analysis 1.2. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 2 Caesarean section.

Study or subgroup	Continuous monitoring n/N	Intermittent monitoring n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Feig 2017	63/100	74/102		49.96%	0.87[0.72,1.05]
Murphy 2008	27/38	19/33		26.64%	1.23[0.86,1.76]
Secher 2013	28/79	33/75		23.4%	0.81[0.54,1.19]
Total (95% CI)	**217**	**210**		**100%**	**0.94[0.75,1.18]**
Total events: 118 (Continuous monitoring), 126 (Intermittent monitoring)					
Heterogeneity: Tau^2=0.02; Chi^2=3.41, df=2(P=0.18); I^2=41.32%					
Test for overall effect: Z=0.56(P=0.57)					

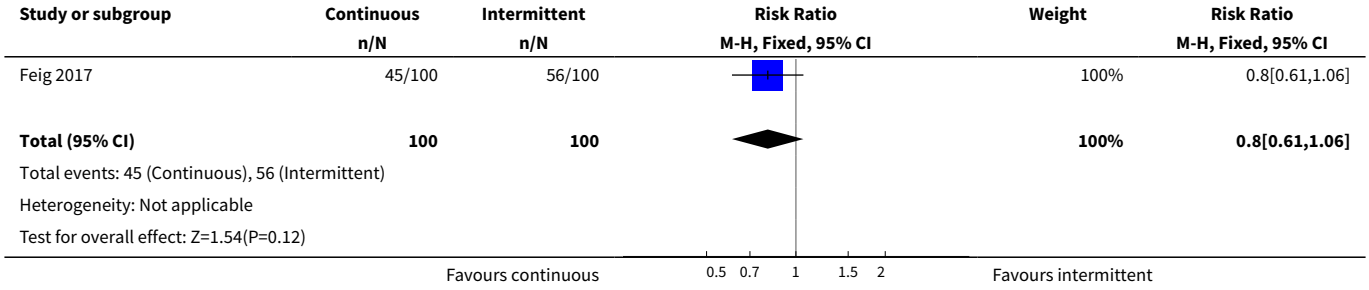
Analysis 1.3. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 3 Large-for-gestational age.



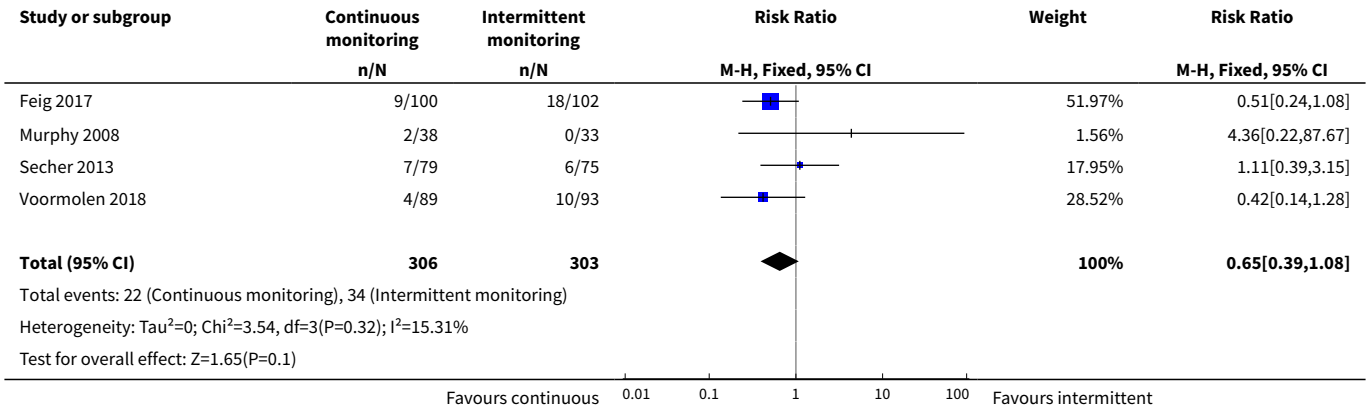
Analysis 1.4. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 4 Perinatal mortality (stillbirth and neonatal mortality).



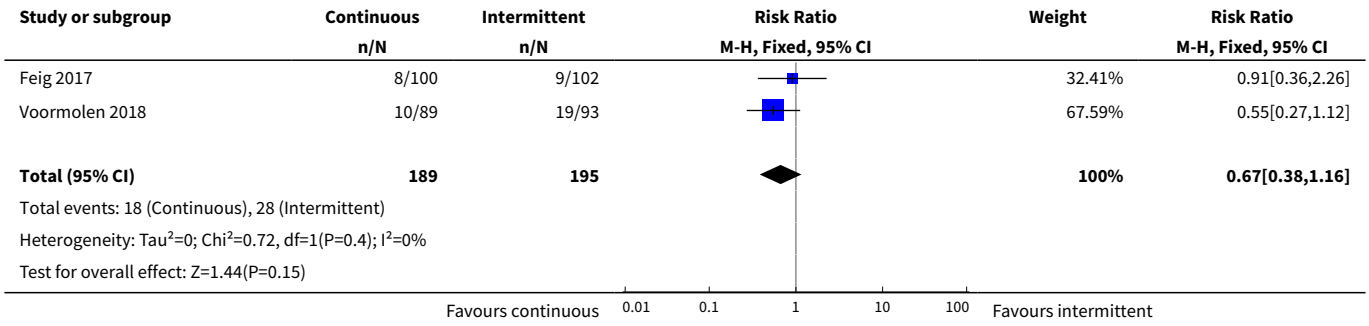
Analysis 1.5. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 5 Mortality or morbidity composite (pregnancy loss (miscarriage, stillbirth, and neonatal death); birth injury; neonatal glycaemia; hyperbilirubinaemia; respiratory distress; and high level neonatal care of more than 24 hours).



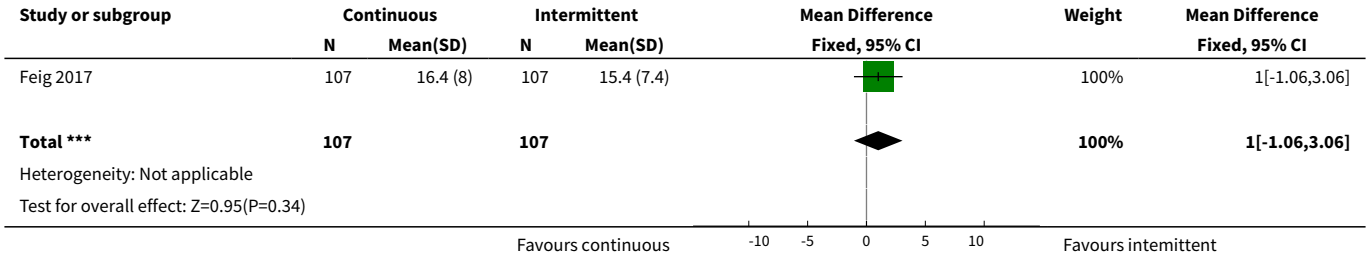
Analysis 1.6. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 6 Pre-eclampsia.



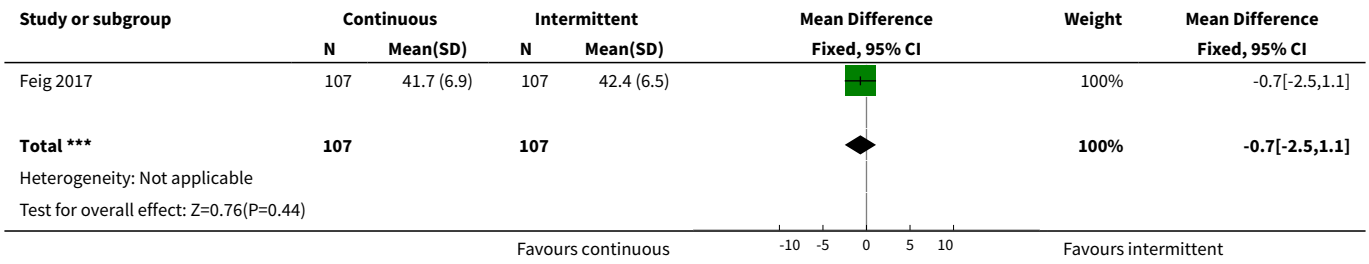
Analysis 1.7. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 7 Pregnancy-induced hypertension.



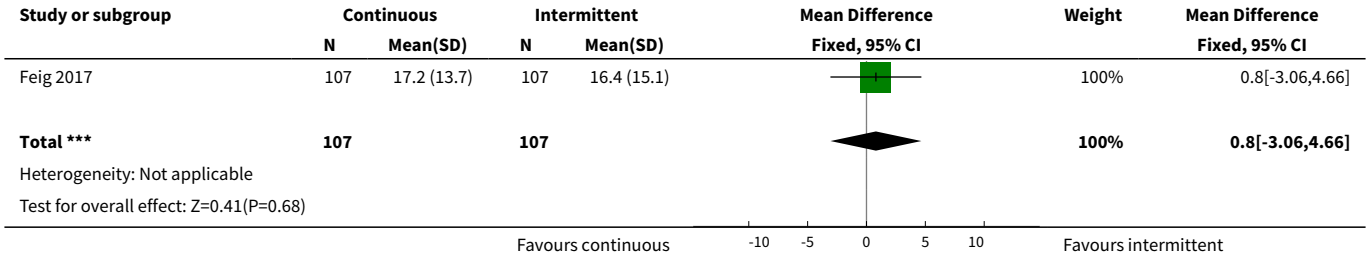
Analysis 1.8. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 8 Behaviour changes associated with the intervention (range of score 10-50 - high score= greater fear of hypoglycaemia).



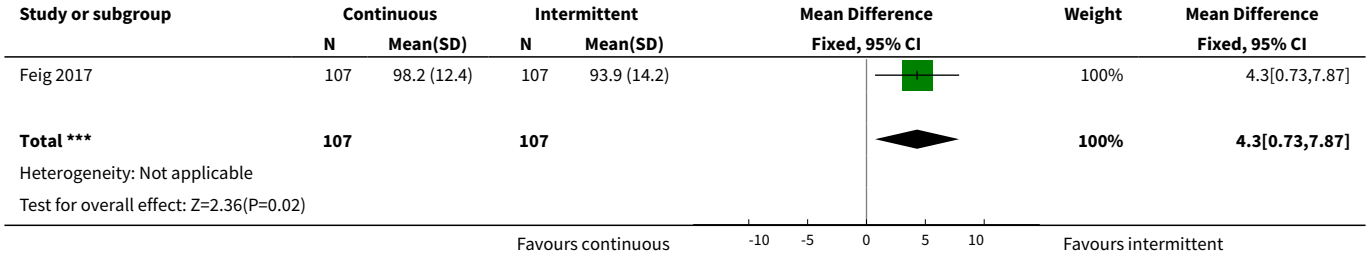
Analysis 1.9. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 9 Sense of well-being and quality of life (Short form 12 (SF-12), total score at 34 weeks' gestation).



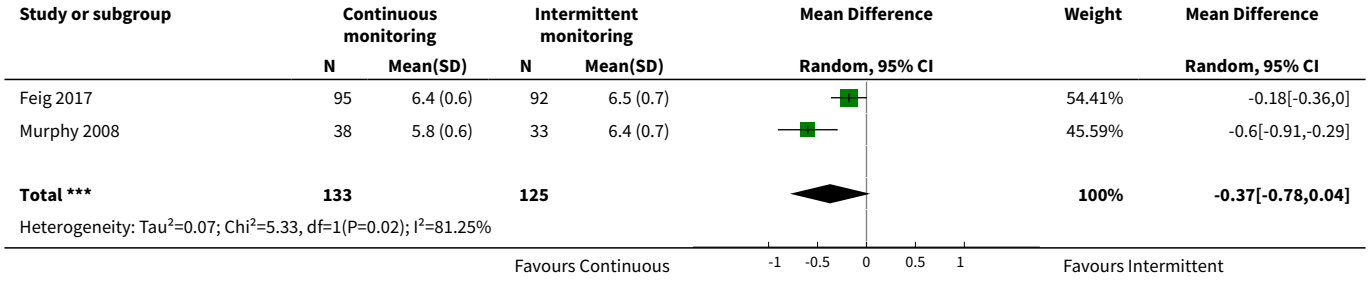
Analysis 1.10. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 10 Sense of well-being and quality of life (Problem areas in diabetes (PAID), total score at 34 weeks' gestation).

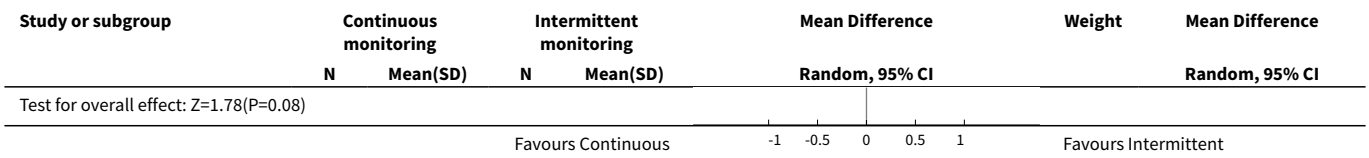


Analysis 1.11. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 11 Sense of well-being and quality of life (BGMSRQ, total score at 34 weeks' gestation).

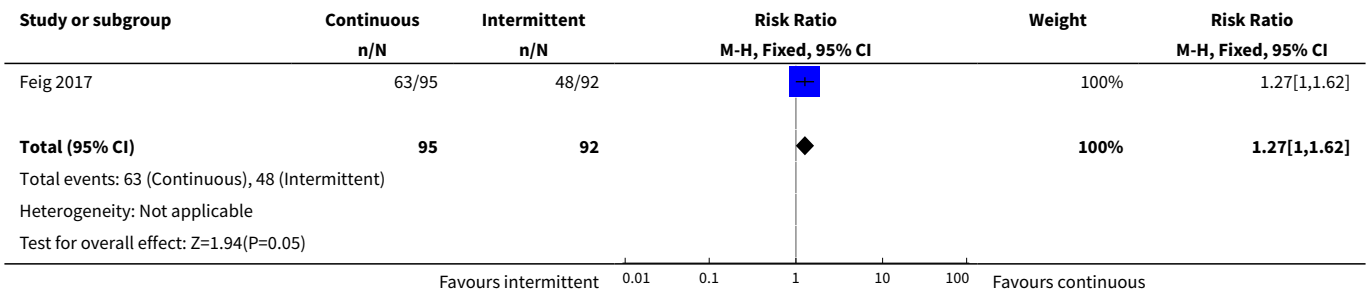


Analysis 1.12. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 12 Glycaemic control - Maternal HbA1c.

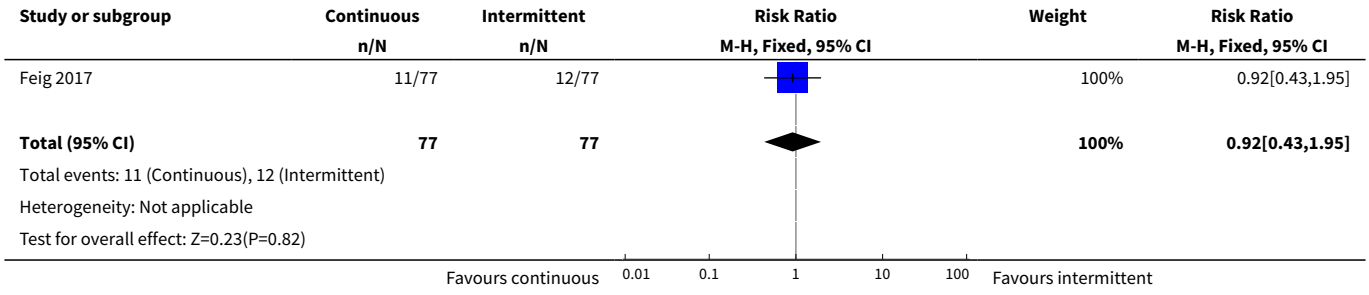




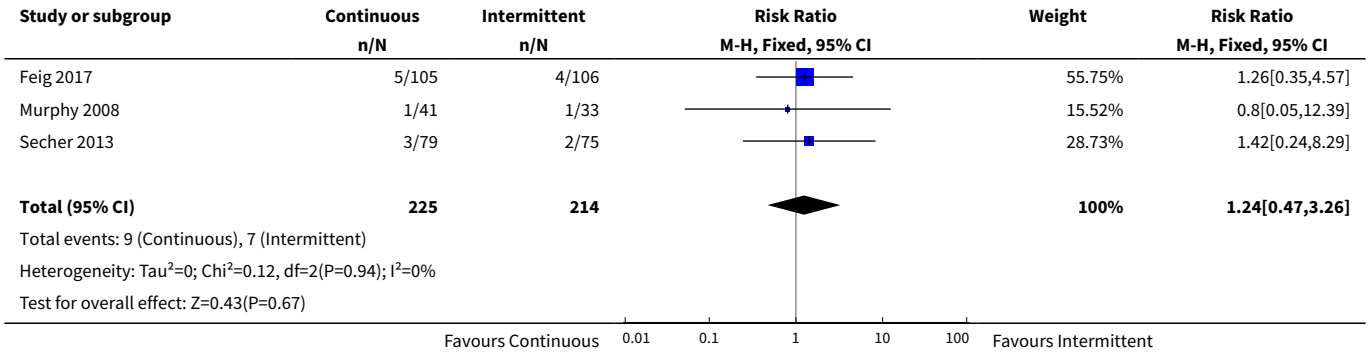
Analysis 1.13. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 13 Glycaemic control - Achieved maternal HbA1c <= 6.5% (48 mmol/mol) at 34 weeks.



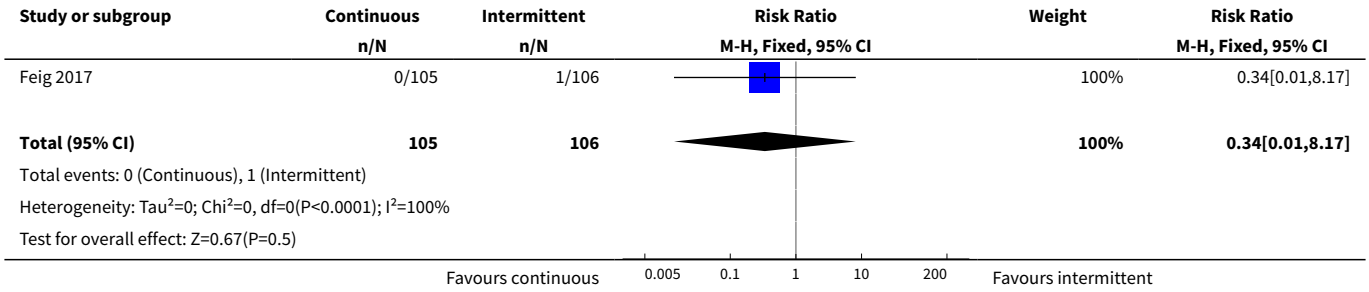
Analysis 1.14. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 14 Maternal hypoglycaemia (severe).



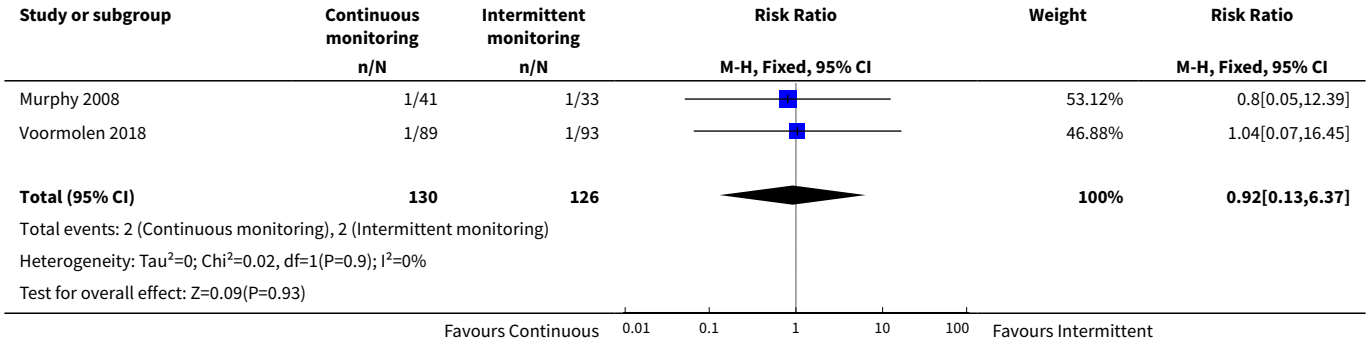
Analysis 1.15. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 15 Miscarriage.



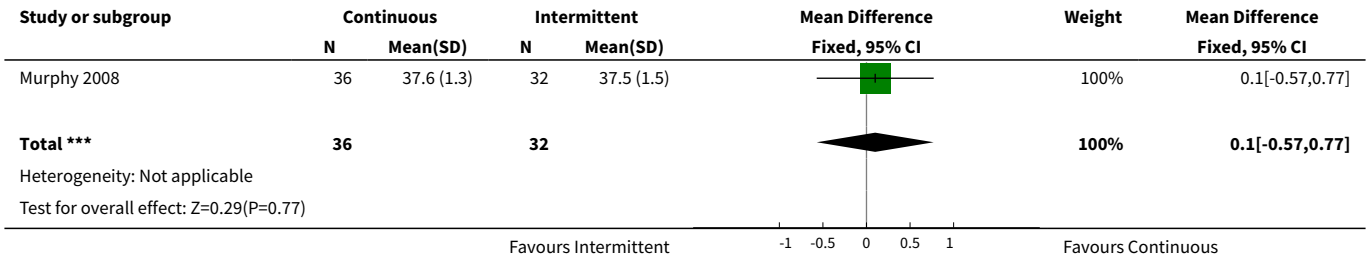
Analysis 1.16. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 16 Stillbirth.



Analysis 1.17. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 17 Neonatal mortality.

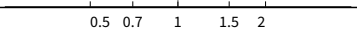


Analysis 1.18. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 18 Gestational age at birth.



Analysis 1.19. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 19 Preterm birth < 37 weeks.

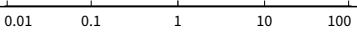
Study or subgroup	Continuous monitoring n/N	Intermittent monitoring n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Feig 2017	38/100	43/102		69.19%	0.9[0.64,1.26]
Murphy 2008	6/41	6/33		10.8%	0.8[0.29,2.26]
Secher 2013	16/79	12/75		20.01%	1.27[0.64,2.49]
Total (95% CI)	**220**	**210**		**100%**	**0.96[0.72,1.29]**
Total events: 60 (Continuous monitoring), 61 (Intermittent monitoring)					
Heterogeneity: Tau^2=0; Chi^2=0.89, df=2(P=0.64); I^2=0%					
Test for overall effect: Z=0.25(P=0.81)					



Favours Continuous — Favours Intermittent

Analysis 1.20. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 20 Preterm birth < 34 weeks.

Study or subgroup	Continuous n/N	Intermittent n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Feig 2017	5/105	11/106		100%	0.46[0.17,1.28]
Total (95% CI)	**105**	**106**		**100%**	**0.46[0.17,1.28]**
Total events: 5 (Continuous), 11 (Intermittent)					
Heterogeneity: Not applicable					
Test for overall effect: Z=1.49(P=0.14)					



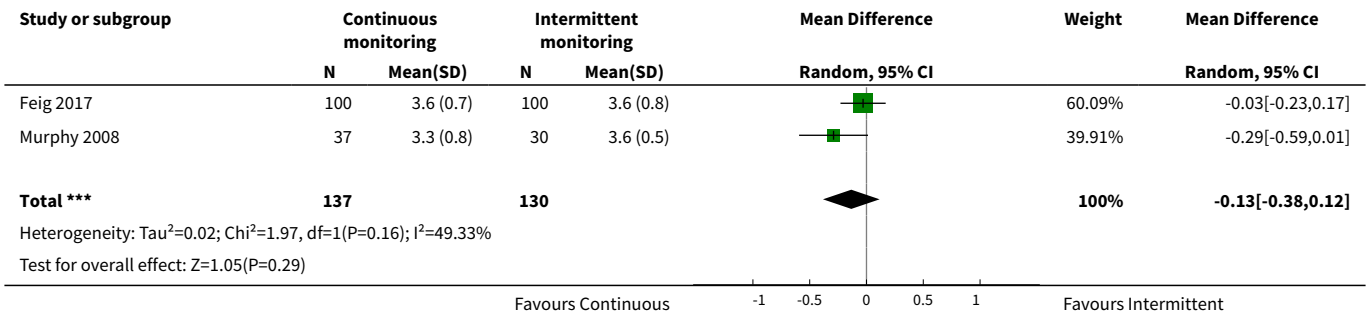
Favours continuous — Favours intermittent

Analysis 1.21. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 21 Macrosomia.

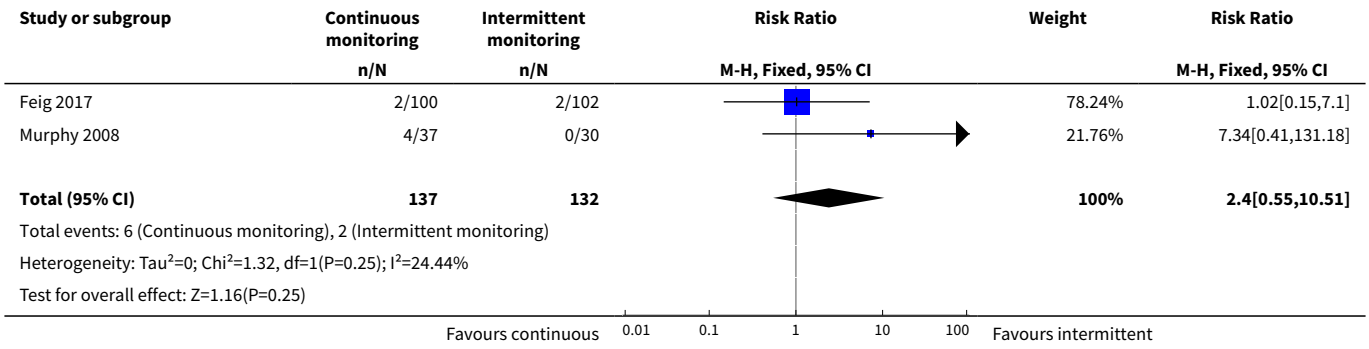
Study or subgroup	Continuous n/N	Intermittent n/N	Risk Ratio M-H, Random, 95% CI	Weight	Risk Ratio M-H, Random, 95% CI
Feig 2017	23/100	27/102		31.11%	0.87[0.54,1.41]
Murphy 2008	13/37	18/30		27.6%	0.59[0.35,0.99]
Voormolen 2018	33/89	33/93		41.29%	1.04[0.71,1.54]
Total (95% CI)	**226**	**225**		**100%**	**0.84[0.61,1.17]**
Total events: 69 (Continuous), 78 (Intermittent)					
Heterogeneity: Tau^2=0.03; Chi^2=3.04, df=2(P=0.22); I^2=34.25%					
Test for overall effect: Z=1.04(P=0.3)					

Favours continuous — Favours intermittent

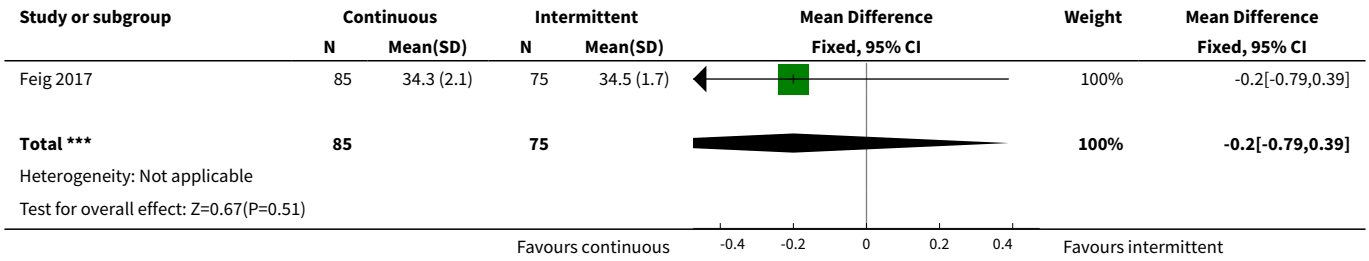
Analysis 1.22. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 22 Birthweight.



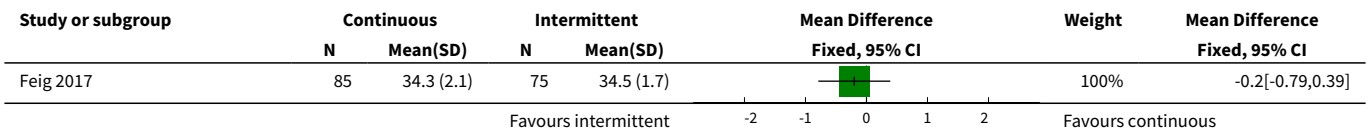
Analysis 1.23. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 23 Small-for-gestational age.

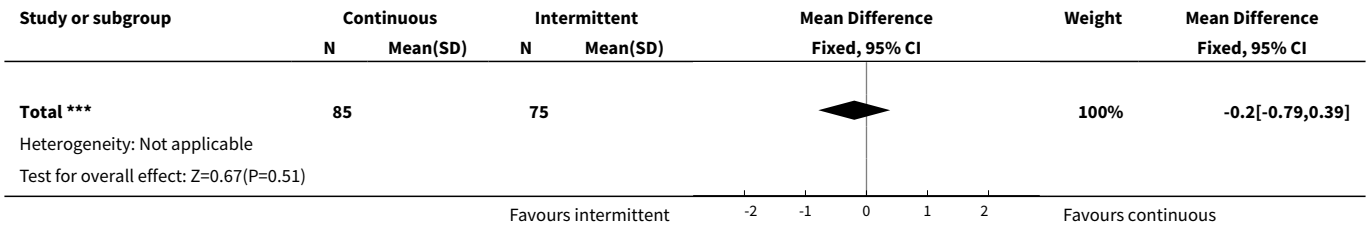


Analysis 1.24. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 24 Head circumference (cm).

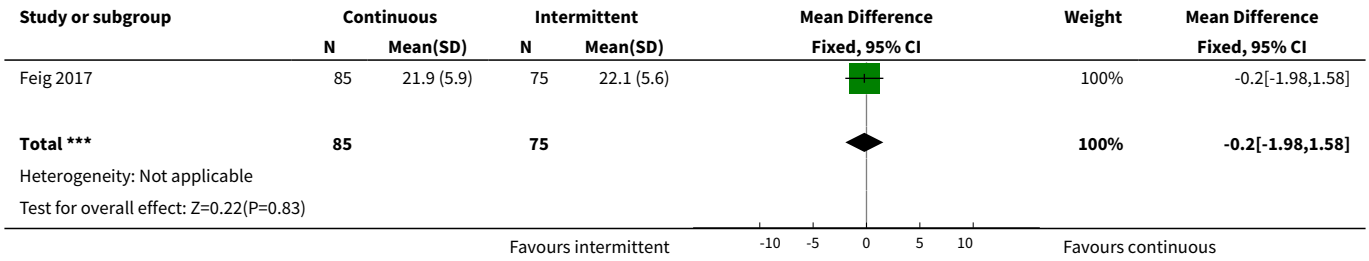


Analysis 1.25. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 25 Length (crown-heel length cm).

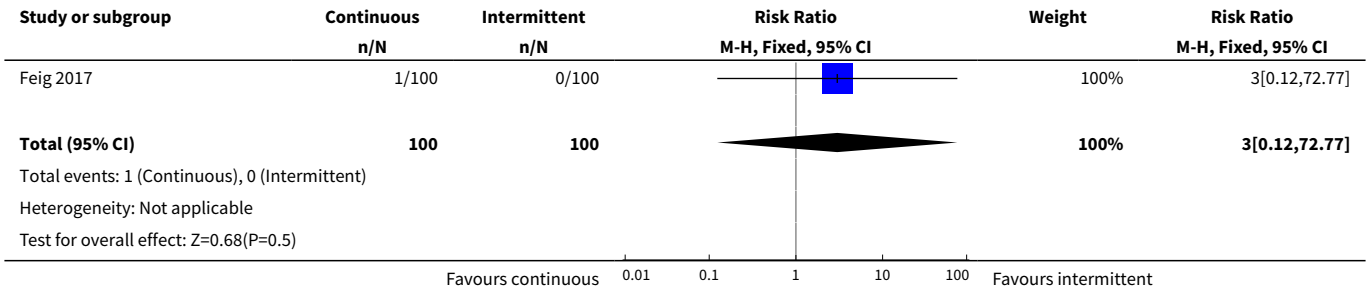




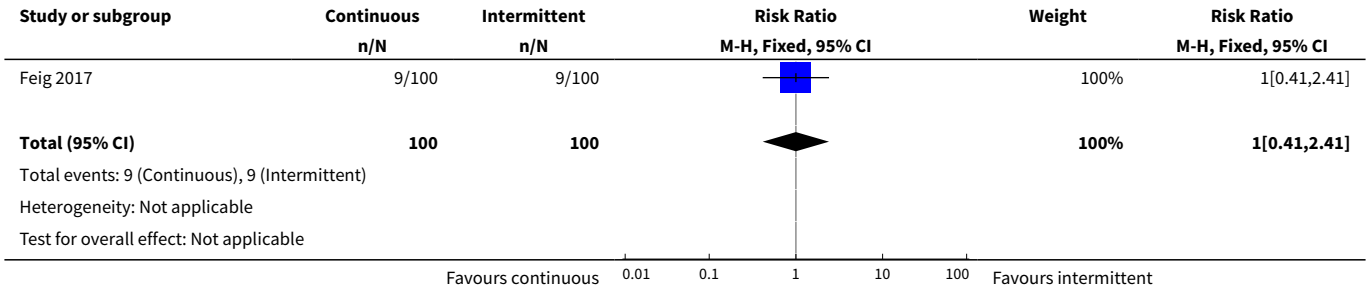
Analysis 1.26. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 26 Adiposity (sum of 4 skin folds (tricepts, subscapular, biceps, flank) mm).



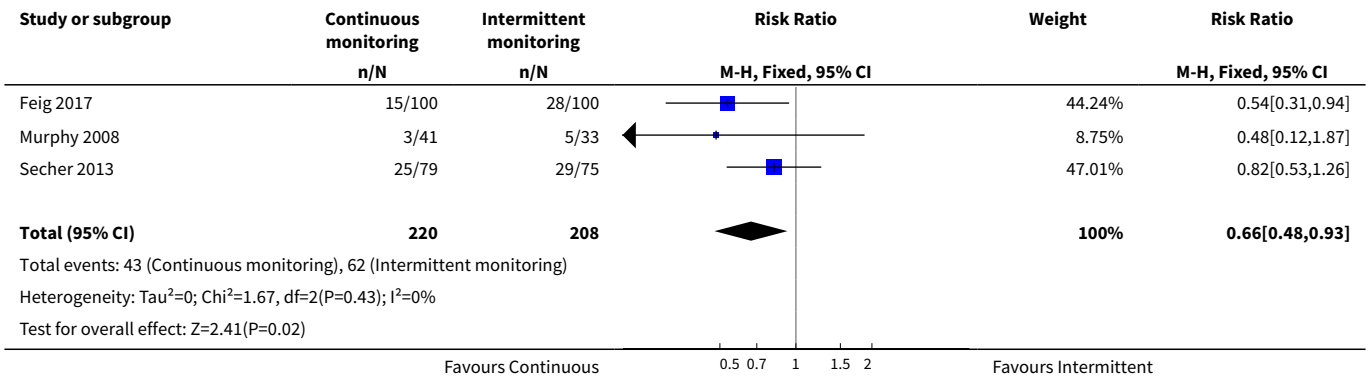
Analysis 1.27. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 27 Shoulder dystocia.



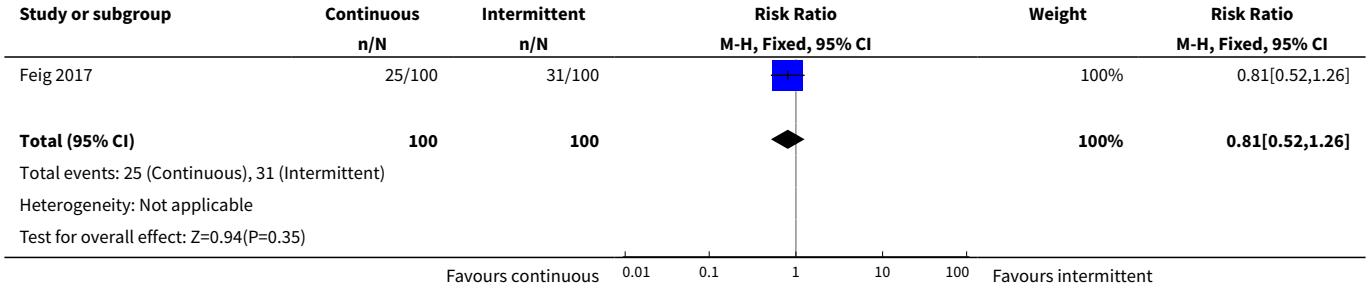
Analysis 1.28. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 28 Respiratory distress syndrome.



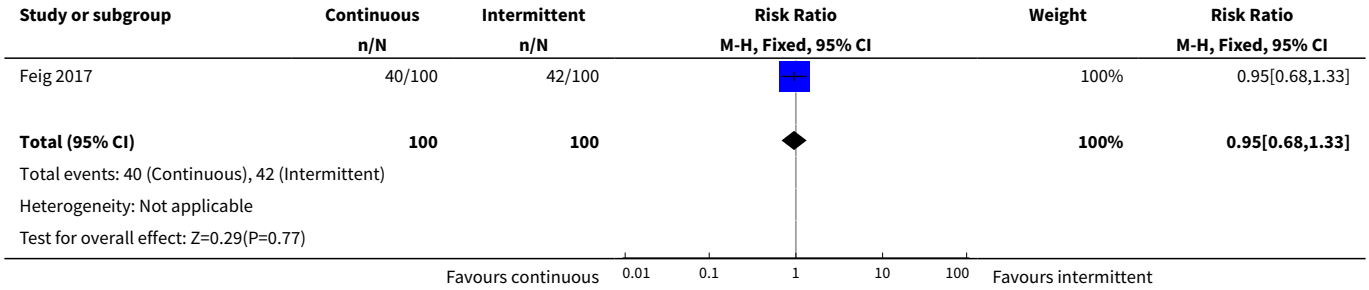
Analysis 1.29. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 29 Neonatal hypoglycaemia.



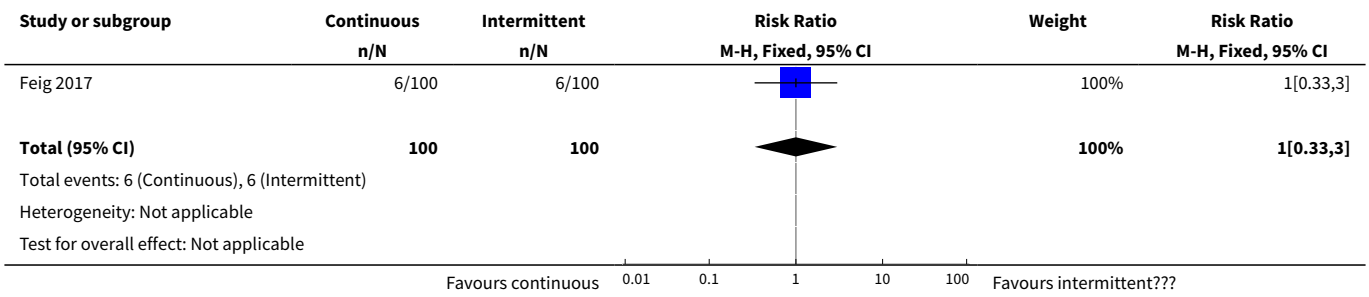
Analysis 1.30. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 30 Neonatal hyperbilirubinaemia.



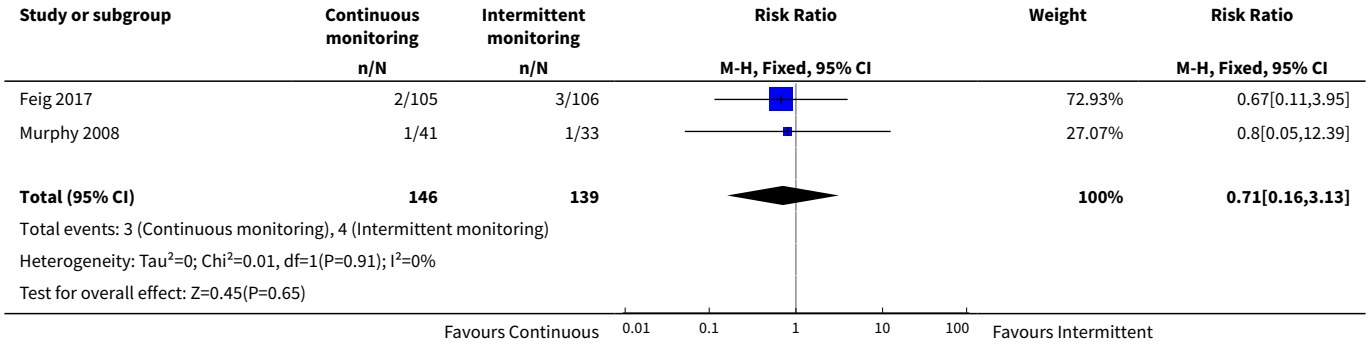
Analysis 1.31. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 31 Relevant biomarker changes associated with the intervention (cord blood c-peptide levels > 566 pmol/L).



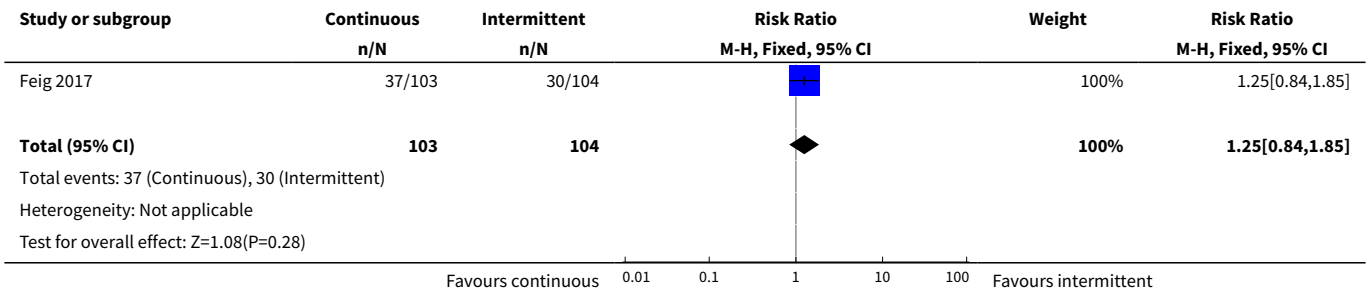
Analysis 1.32. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 32 Relevant biomarker changes associated with the intervention (cord blood c-peptide levels > 2725 pmol/L).



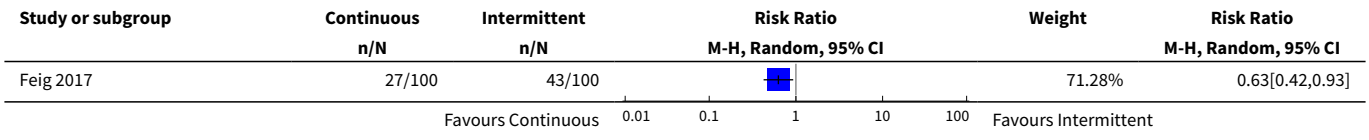
Analysis 1.33. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 33 Major and minor anomalies.

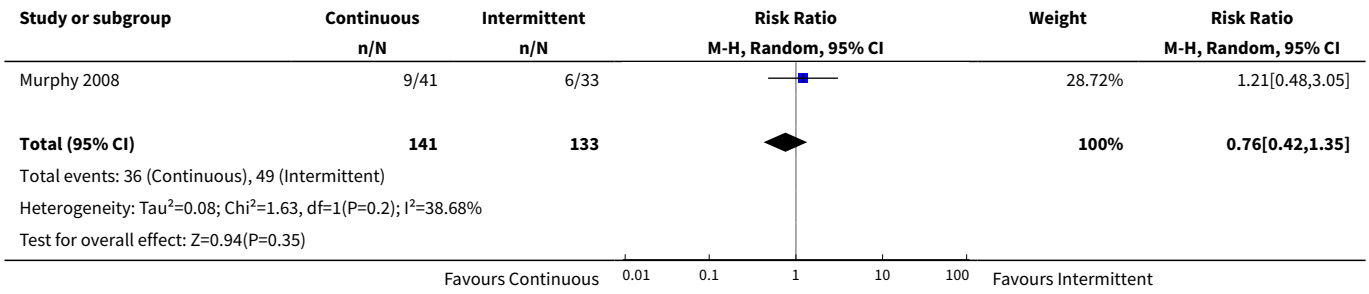


Analysis 1.34. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 34 Number of hospital admissions (mother).

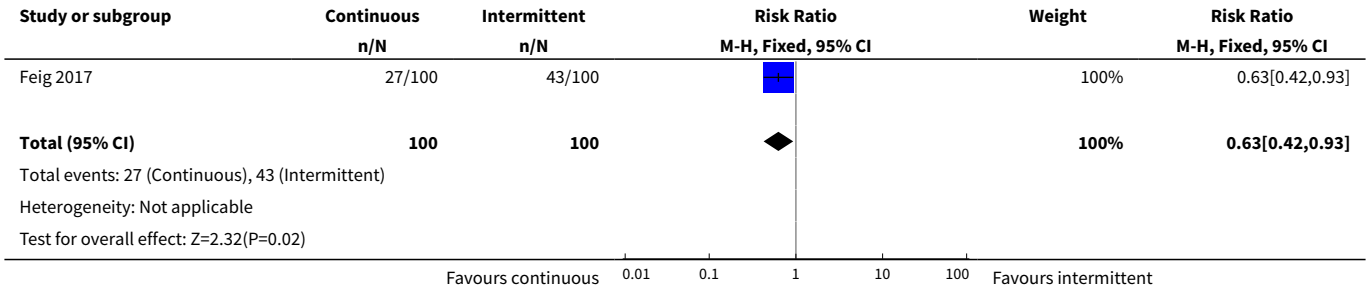


Analysis 1.35. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 35 Neonatal intensive care unit admissions.

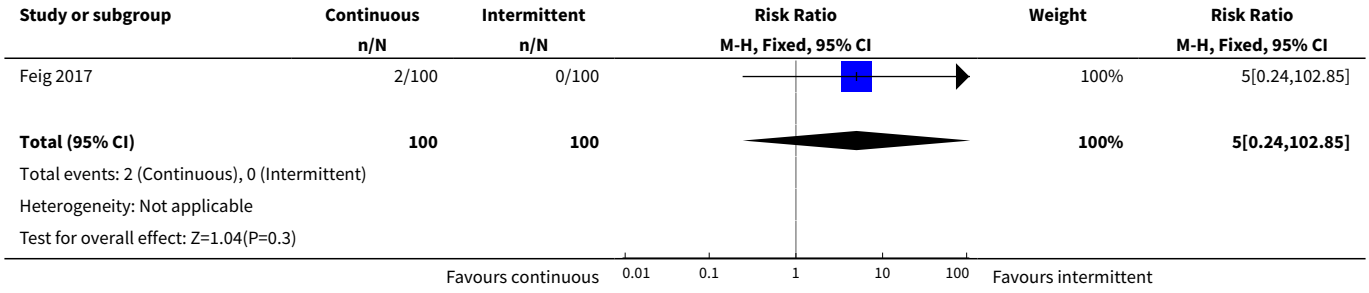




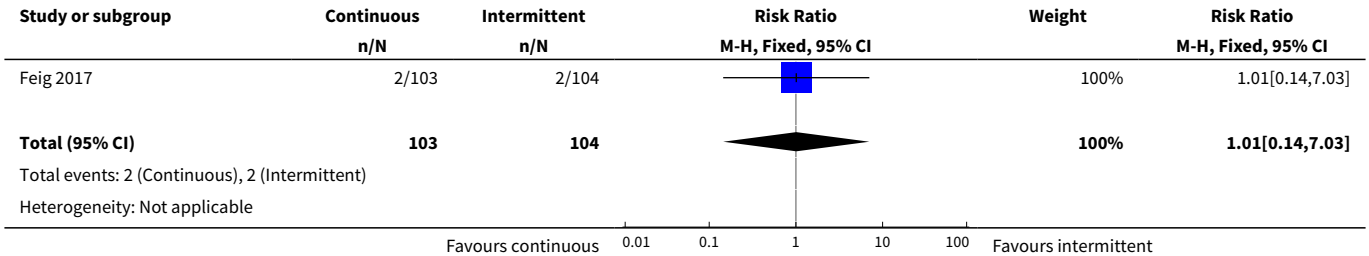
Analysis 1.36. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 36 Neonatal intensive care unit length of admission > 24 hours.

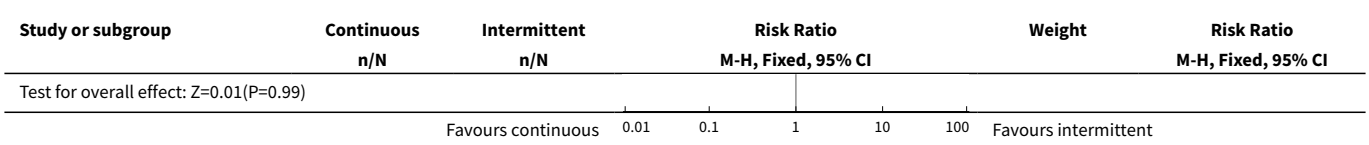


Analysis 1.37. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 37 Birth trauma (shoulder dystocia, bone fracture, nerve palsy).



Analysis 1.38. Comparison 1 Continuous glucose monitoring versus intermittent glucose monitoring, Outcome 38 Diabetic ketoacidosis (mother).



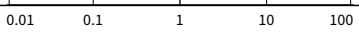


Comparison 2. Self-monitoring versus different type of self monitoring

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	28	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.40, 1.49]
2 Perinatal mortality (stillbirth and neonatal mortality)	1	28	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 67.91]
3 Glycaemic control during/end of treatment (maternal post-prandial blood glucose)	1	13	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.15, 0.75]
4 Glycaemic control during/end of treatment (maternal HbA1c)	1	28	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-1.93, 1.73]
5 Miscarriage	1	30	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 14.55]
6 Neonatal mortality	1	28	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 67.91]
7 Gestational age at birth	1	28	Mean Difference (IV, Fixed, 95% CI)	0.40 [-1.65, 2.45]
8 Birthweight	2	41	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.49, 0.13]
9 Respiratory distress syndrome	1	28	Risk Ratio (M-H, Fixed, 95% CI)	3.0 [0.13, 67.91]
10 Neonatal hypoglycaemia	1	28	Risk Ratio (M-H, Fixed, 95% CI)	0.57 [0.21, 1.52]
11 Neonatal jaundice (hyperbilirubinaemia)	1	28	Risk Ratio (M-H, Fixed, 95% CI)	0.56 [0.25, 1.24]
12 Neonatal hypocalcaemia	1	28	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.07, 14.45]
13 Neonatal polycythaemia	1	28	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.55]
14 Neonatal cord vein C-peptide	1	28	Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.50, 0.76]

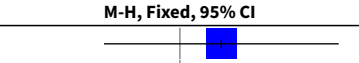
Analysis 2.1. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 1 Caesarean section.

Study or subgroup	Self monitoring n/N	Standard care (urine) n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Varner 1983	7/14	9/14		100%	0.78[0.4,1.49]
Total (95% CI)	**14**	**14**		**100%**	**0.78[0.4,1.49]**
Total events: 7 (Self monitoring), 9 (Standard care (urine))					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.75(P=0.45)					



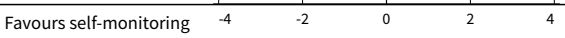
Analysis 2.2. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 2 Perinatal mortality (stillbirth and neonatal mortality).

Study or subgroup	Self monitoring n/N	Standard care (urine) n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Varner 1983	1/14	0/14		100%	3[0.13,67.91]
Total (95% CI)	**14**	**14**		**100%**	**3[0.13,67.91]**
Total events: 1 (Self monitoring), 0 (Standard care (urine))					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.69(P=0.49)					



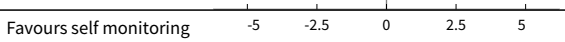
Analysis 2.3. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 3 Glycaemic control during/end of treatment (maternal post-prandial blood glucose).

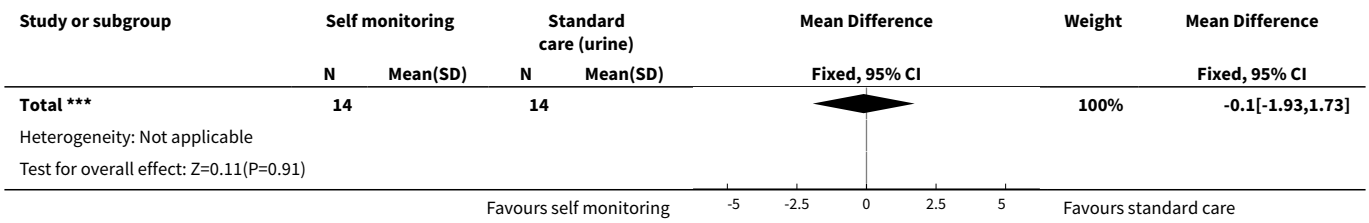
Study or subgroup	Self monitoring N	Mean(SD)	Standard care (urine) N	Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Stubbs 1980	7	4.6 (1.1)	6	5.3 (1.5)		100%	-0.7[-2.15,0.75]
Total ***	**7**		**6**			**100%**	**-0.7[-2.15,0.75]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.95(P=0.34)							



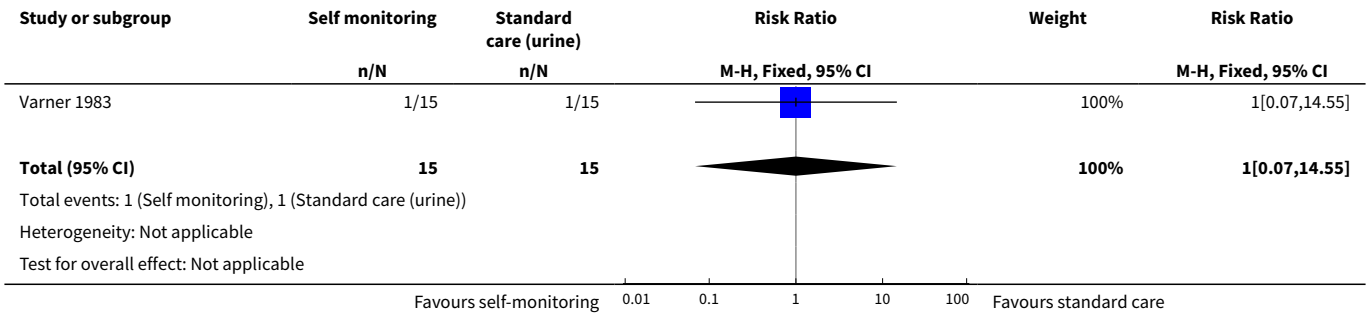
Analysis 2.4. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 4 Glycaemic control during/end of treatment (maternal HbA1c).

Study or subgroup	Self monitoring N	Mean(SD)	Standard care (urine) N	Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Varner 1983	14	7.1 (2.1)	14	7.2 (2.8)		100%	-0.1[-1.93,1.73]

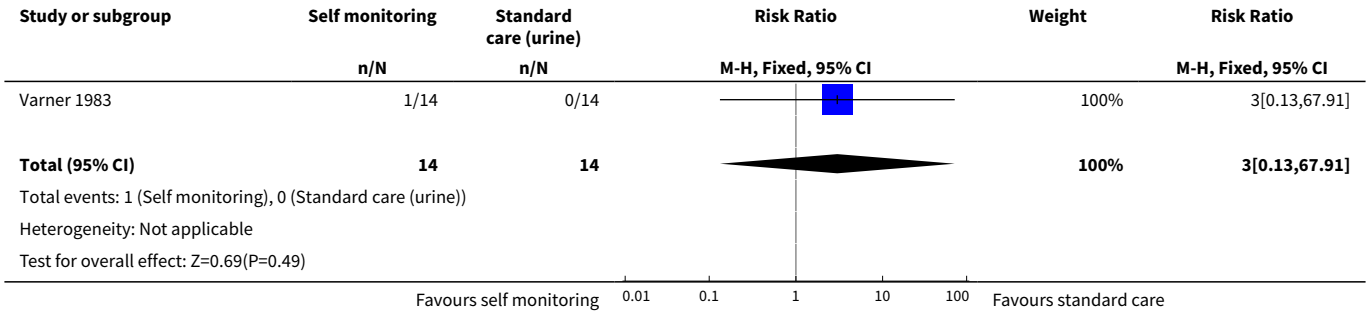




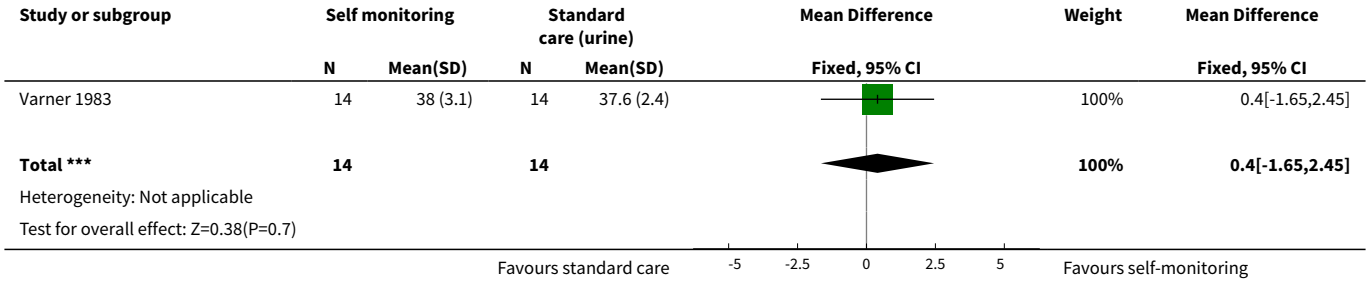
Analysis 2.5. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 5 Miscarriage.



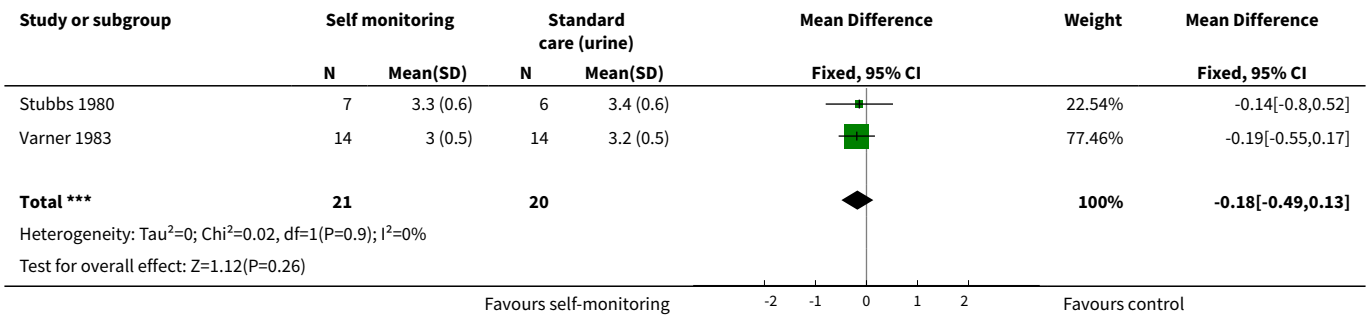
Analysis 2.6. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 6 Neonatal mortality.



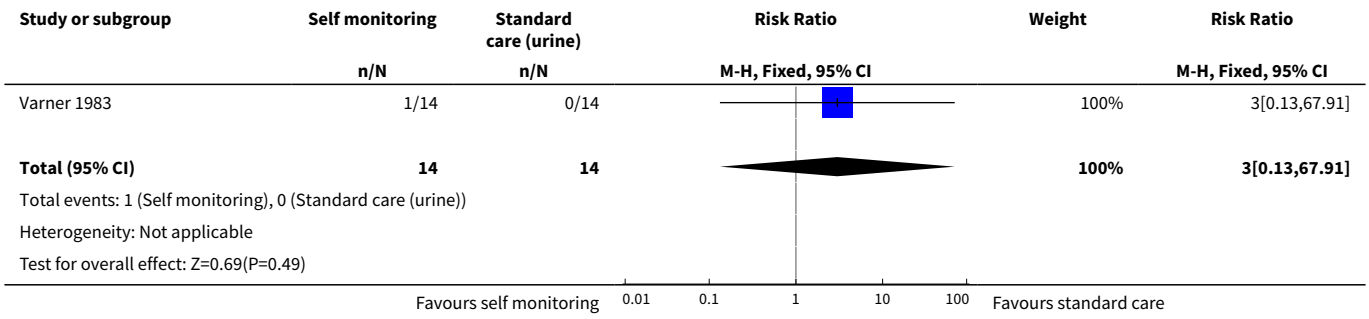
Analysis 2.7. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 7 Gestational age at birth.



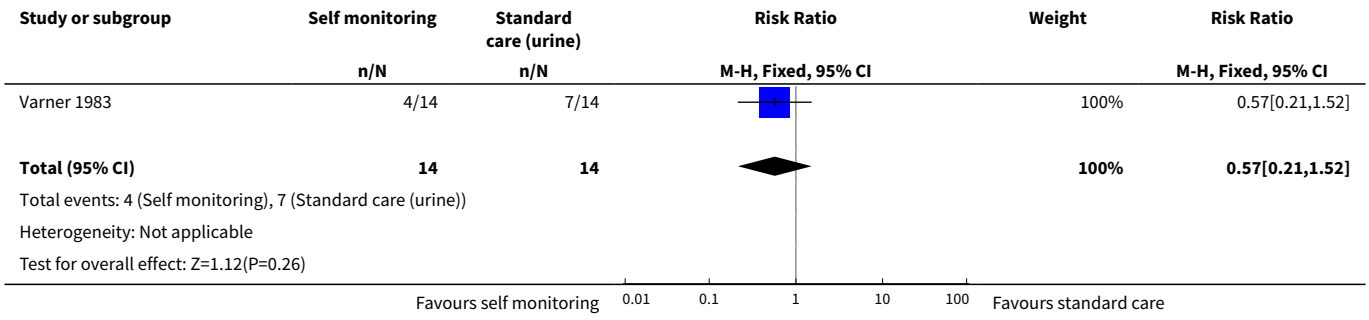
Analysis 2.8. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 8 Birthweight.



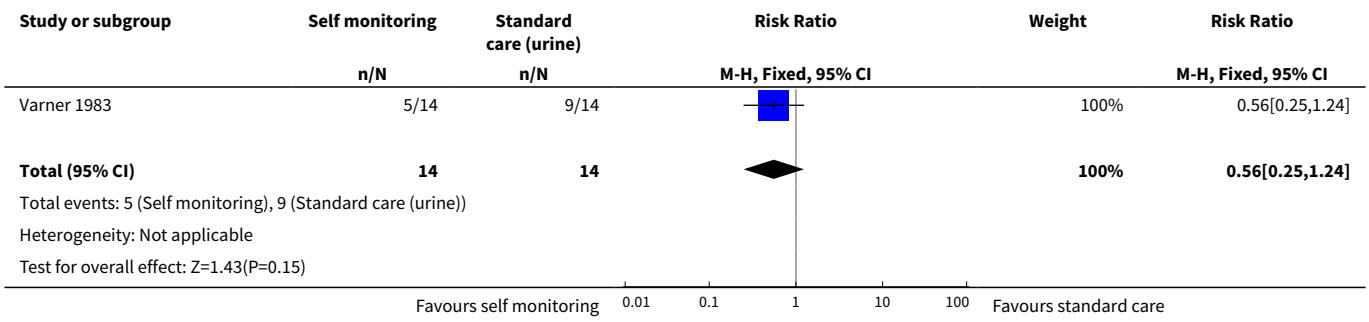
Analysis 2.9. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 9 Respiratory distress syndrome.



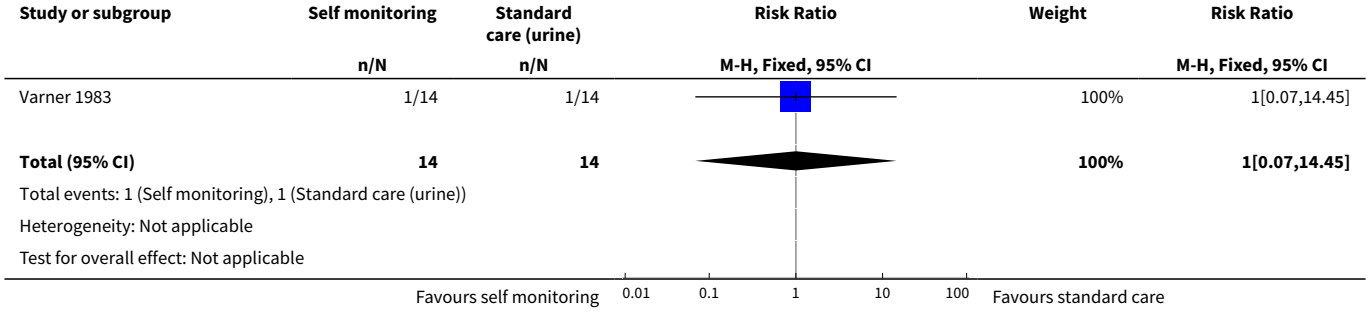
Analysis 2.10. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 10 Neonatal hypoglycaemia.



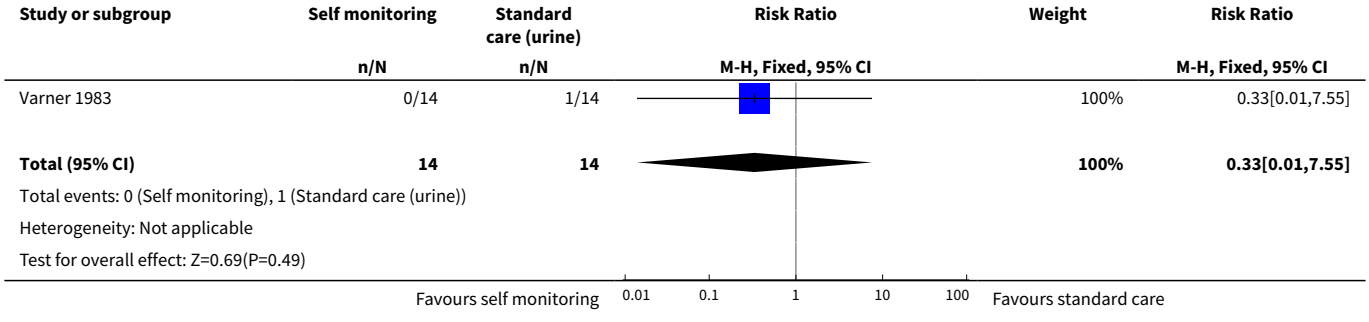
Analysis 2.11. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 11 Neonatal jaundice (hyperbilirubinaemia).



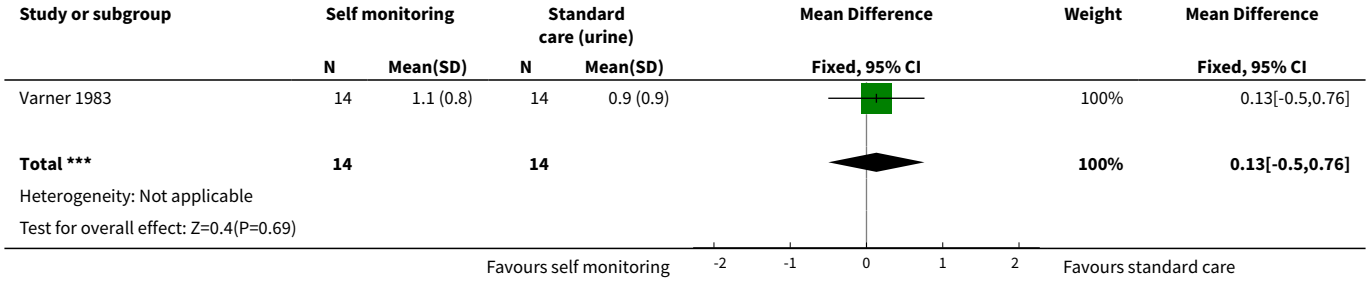
Analysis 2.12. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 12 Neonatal hypocalcaemia.



Analysis 2.13. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 13 Neonatal polycythaemia.



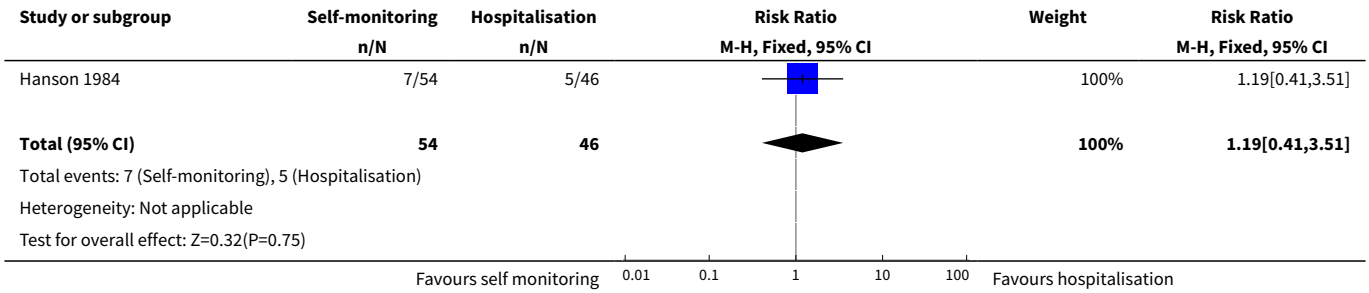
Analysis 2.14. Comparison 2 Self-monitoring versus different type of self monitoring, Outcome 14 Neonatal cord vein C-peptide.



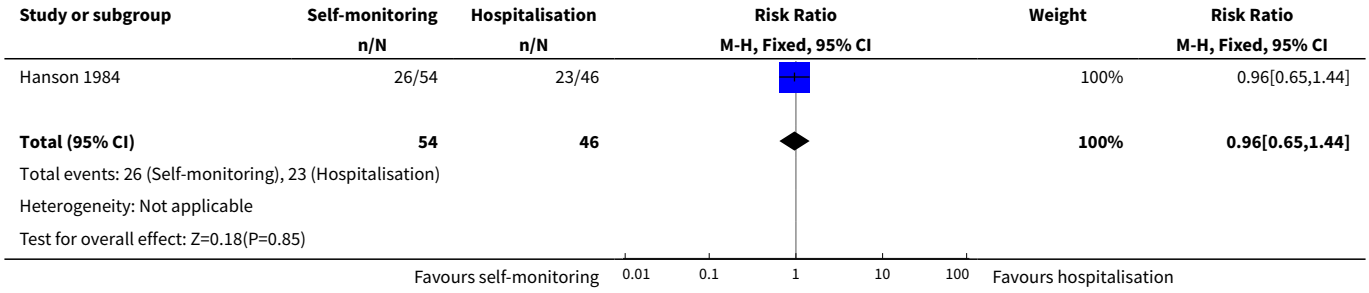
Comparison 3. Self-monitoring at home versus hospitalisation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Hypertensive disorders of pregnancy	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.41, 3.51]
2 Caesarean section	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.65, 1.44]
3 Perinatal mortality (stillbirth and neonatal mortality)	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.05, 13.24]
4 Pre-eclampsia	1	100	Risk Ratio (M-H, Fixed, 95% CI)	4.26 [0.52, 35.16]
5 Pregnancy-induced hypertension	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.08, 2.22]
6 Placental abruption	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.70 [0.16, 18.19]
7 Preterm birth < 37 weeks	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.45, 1.60]
8 Respiratory distress syndrome	1	100	Risk Ratio (M-H, Fixed, 95% CI)	2.56 [0.28, 23.74]
9 Neonatal hypoglycaemia	1	100	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.50, 2.03]
10 Neonatal jaundice (hyperbilirubinaemia)	1	100	Risk Ratio (M-H, Fixed, 95% CI)	2.27 [0.64, 8.07]
11 Major anomalies	1	102	Risk Ratio (M-H, Fixed, 95% CI)	0.27 [0.03, 2.54]
12 Antenatal hospital admission	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.11, 0.33]
13 Feeding difficulties (not prespecified)	1	100	Risk Ratio (M-H, Fixed, 95% CI)	0.85 [0.41, 1.78]

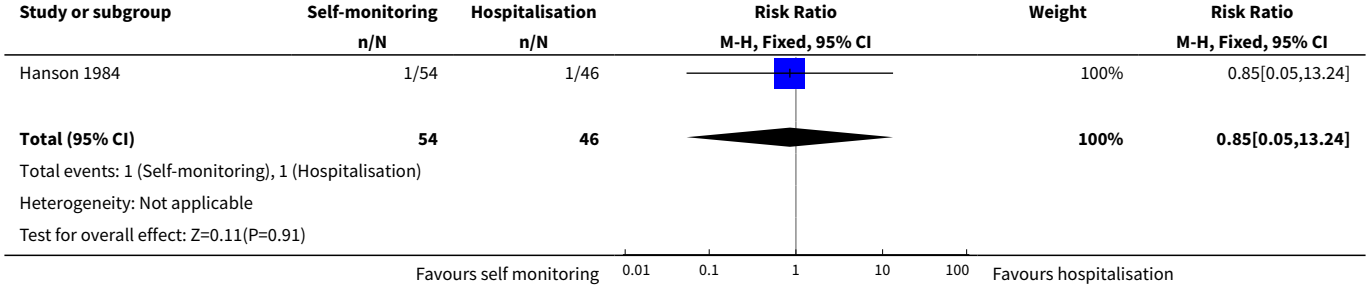
Analysis 3.1. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 1 Hypertensive disorders of pregnancy.



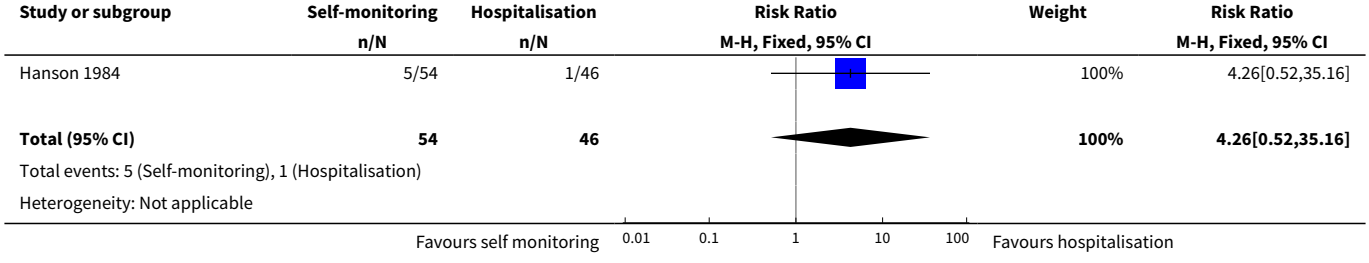
Analysis 3.2. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 2 Caesarean section.

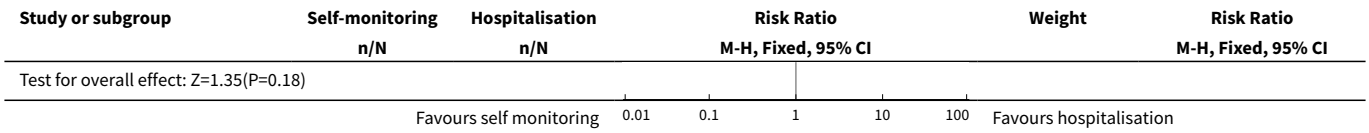


Analysis 3.3. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 3 Perinatal mortality (stillbirth and neonatal mortality).

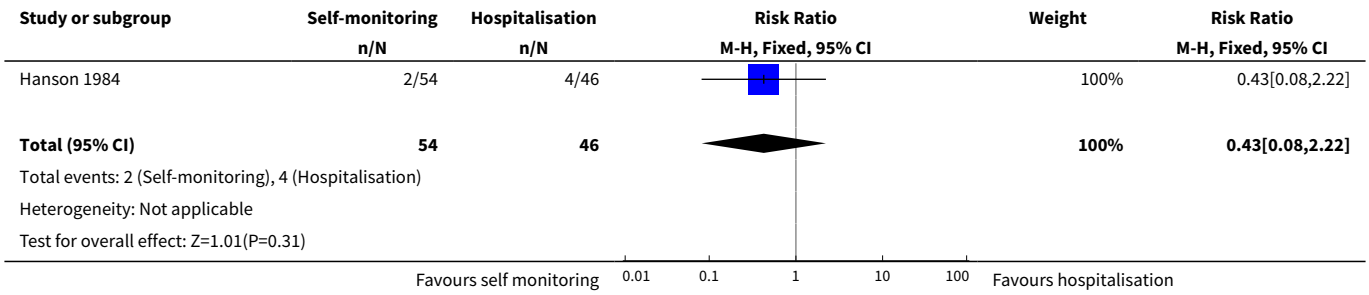


Analysis 3.4. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 4 Pre-eclampsia.

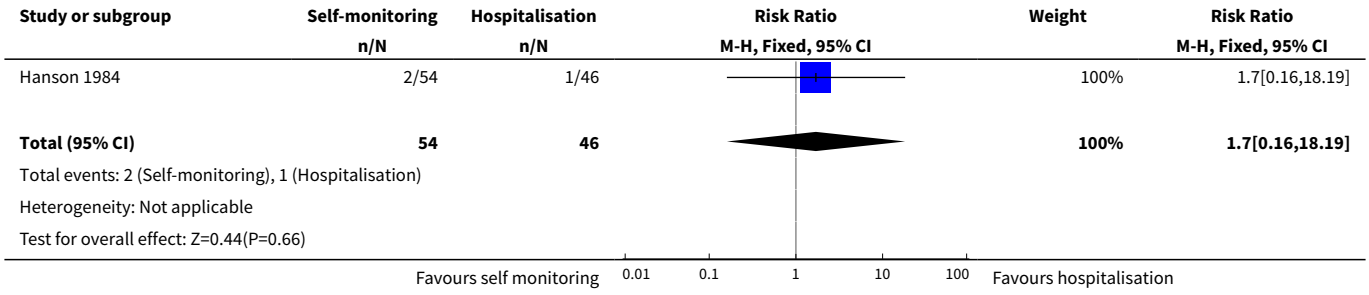




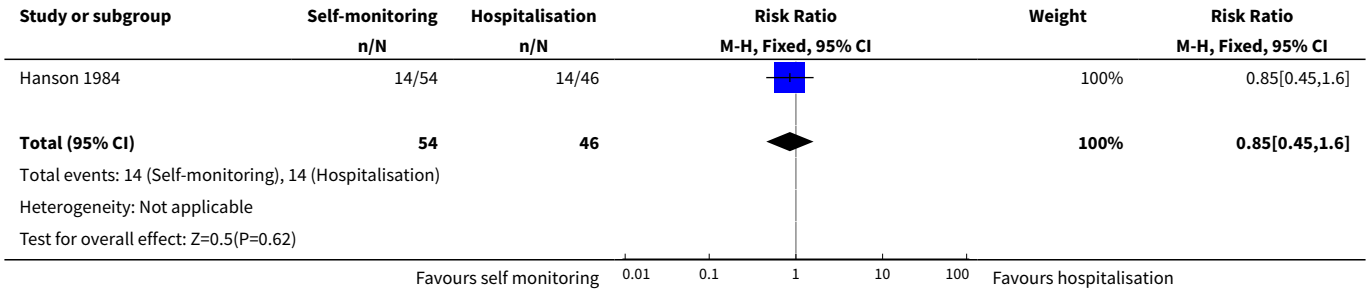
Analysis 3.5. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 5 Pregnancy-induced hypertension.



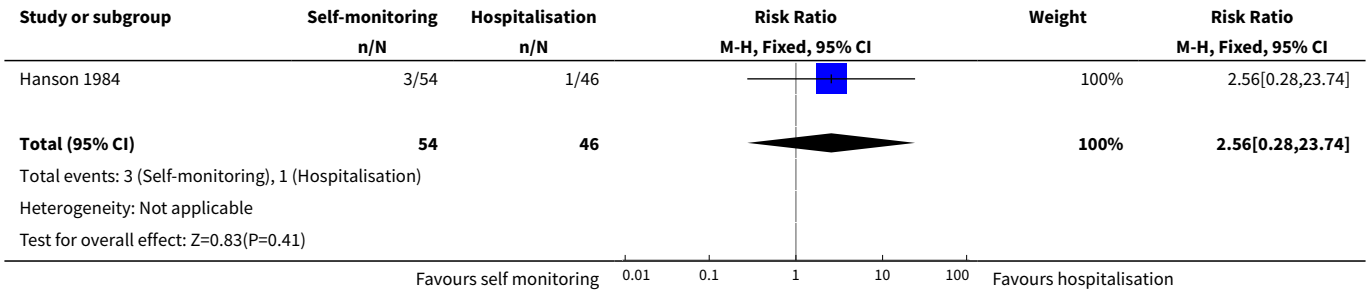
Analysis 3.6. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 6 Placental abruption.



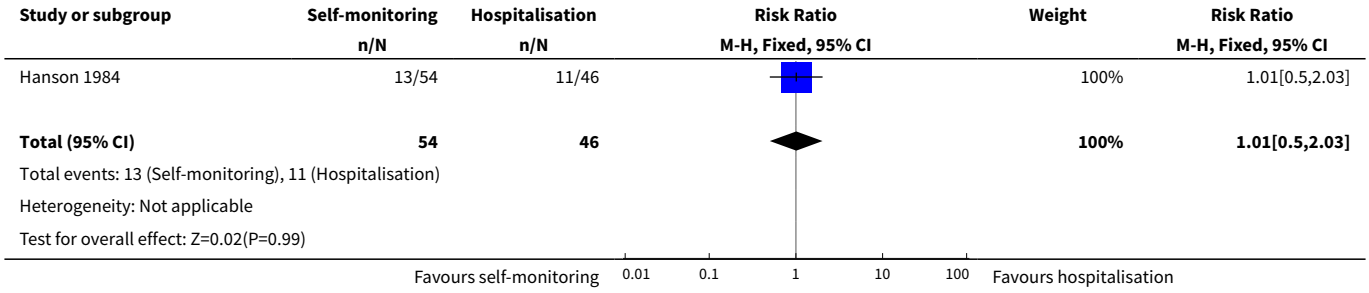
Analysis 3.7. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 7 Preterm birth < 37 weeks.



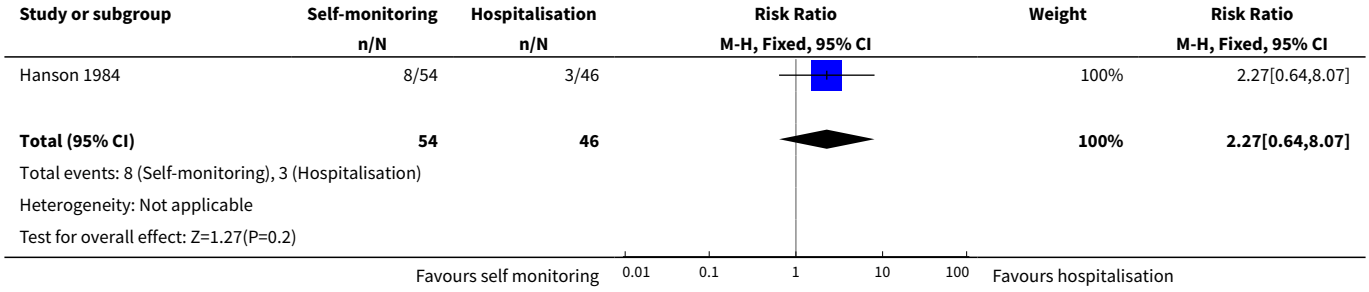
Analysis 3.8. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 8 Respiratory distress syndrome.



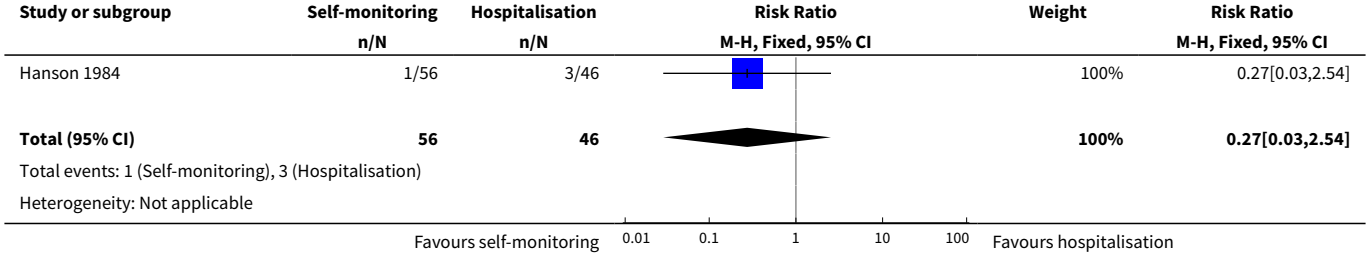
Analysis 3.9. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 9 Neonatal hypoglycaemia.

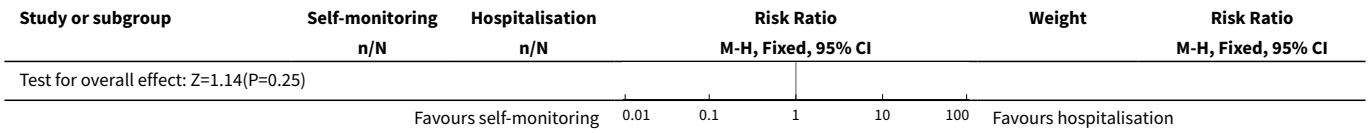


Analysis 3.10. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 10 Neonatal jaundice (hyperbilirubinaemia).

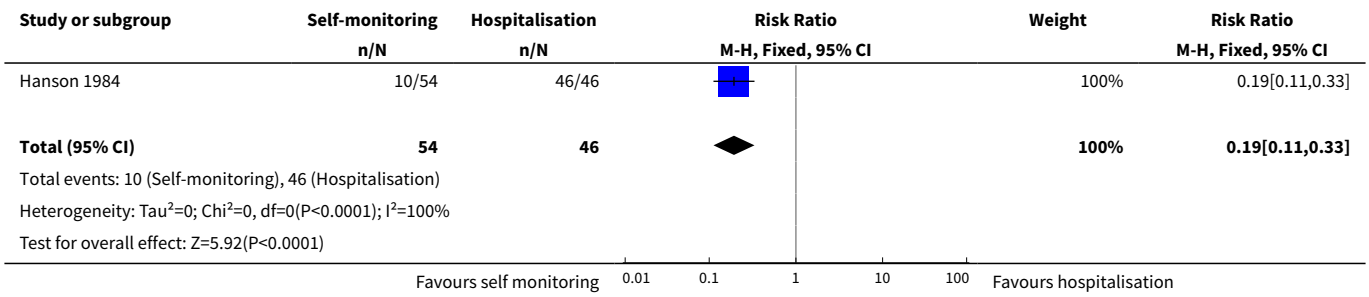


Analysis 3.11. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 11 Major anomalies.

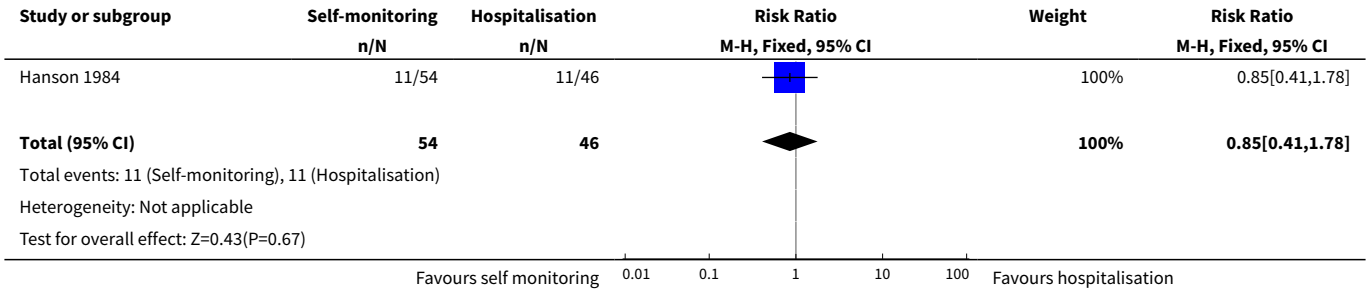




Analysis 3.12. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 12 Antenatal hospital admission.



Analysis 3.13. Comparison 3 Self-monitoring at home versus hospitalisation, Outcome 13 Feeding difficulties (not pre-specified).

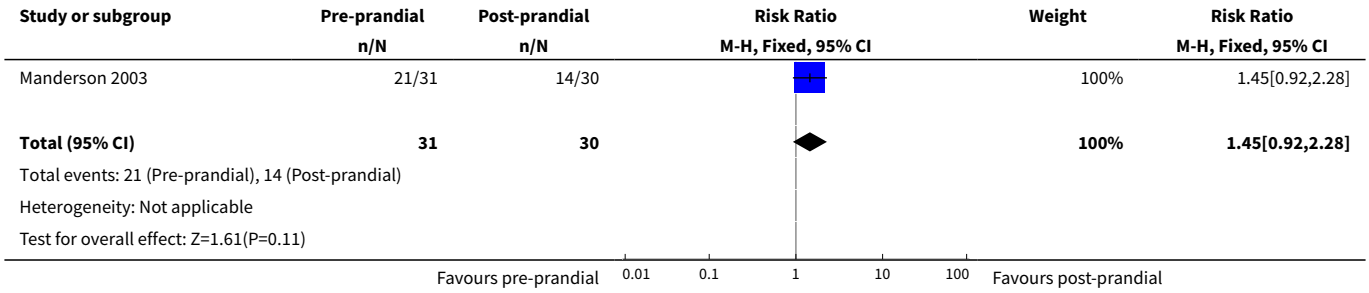


Comparison 4. Pre-prandial versus post-prandial glucose monitoring

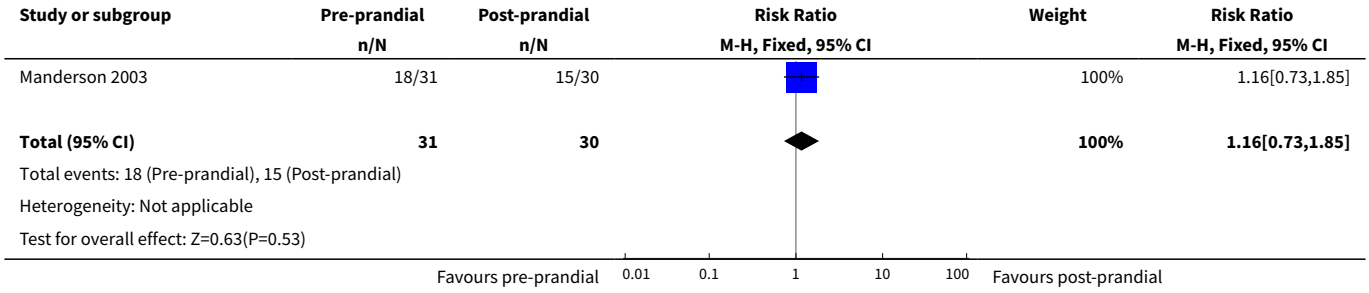
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.45 [0.92, 2.28]
2 Large-for-gestational age	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.73, 1.85]
3 Perinatal mortality (stillbirth and neonatal mortality)	1	61	Risk Ratio (M-H, Fixed, 95% CI)	2.91 [0.12, 68.66]
4 Pre-eclampsia	1	58	Risk Ratio (M-H, Fixed, 95% CI)	6.43 [0.82, 50.11]
5 Weight gain during pregnancy	1	61	Mean Difference (IV, Fixed, 95% CI)	-0.90 [-3.86, 2.06]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6 Insulin dose	1	61	Mean Difference (IV, Fixed, 95% CI)	-17.40 [-43.41, 8.61]
7 Glycaemic control - Insulin dose	1	61	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.45, 0.05]
8 Glycaemic control - HbA1c	1	61	Mean Difference (IV, Fixed, 95% CI)	0.30 [-0.08, 0.68]
9 Stillbirth	1	61	Risk Ratio (M-H, Fixed, 95% CI)	2.91 [0.12, 68.66]
10 Gestational age at birth	1	61	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.84, 1.24]
11 Preterm birth < 37 weeks	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.33 [0.62, 2.84]
12 Macrosomia	1	61	Risk Ratio (M-H, Fixed, 95% CI)	2.18 [0.75, 6.32]
13 Birthweight	1	61	Mean Difference (IV, Fixed, 95% CI)	0.24 [-0.10, 0.58]
14 Adiposity - Subscapula skinfold thickness	1	61	Mean Difference (IV, Fixed, 95% CI)	0.60 [-0.18, 1.38]
15 Adiposity - Triceps skinfold thickness	1	61	Mean Difference (IV, Fixed, 95% CI)	0.60 [0.04, 1.16]
16 Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite)	1	61	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.05, 5.06]
17 Respiratory distress syndrome	1	61	Risk Ratio (M-H, Fixed, 95% CI)	0.97 [0.06, 14.78]
18 Neonatal hypoglycaemia	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.48, 2.45]
19 Neonatal jaundice (hyperbilirubinaemia)	1	61	Risk Ratio (M-H, Fixed, 95% CI)	1.16 [0.40, 3.40]
20 Cord IGF-1	1	61	Mean Difference (IV, Fixed, 95% CI)	1.30 [-0.70, 3.30]
21 Neonatal glucose at age 1 hour (not pre-specified)	1	61	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-0.88, 0.48]
22 Transient tachypnea (not pre-specified)	1	61	Risk Ratio (M-H, Fixed, 95% CI)	2.58 [0.76, 8.81]
23 Neonatal intensive care admissions	1	59	Risk Ratio (M-H, Fixed, 95% CI)	1.04 [0.62, 1.74]

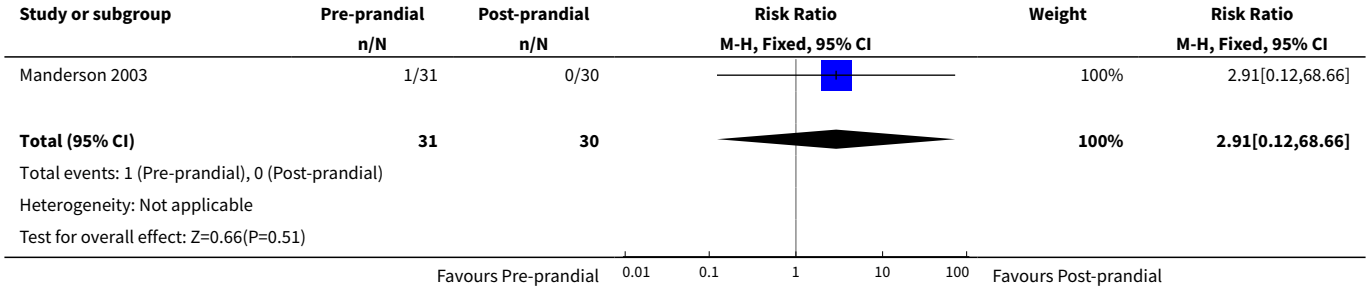
Analysis 4.1. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 1 Caesarean section.



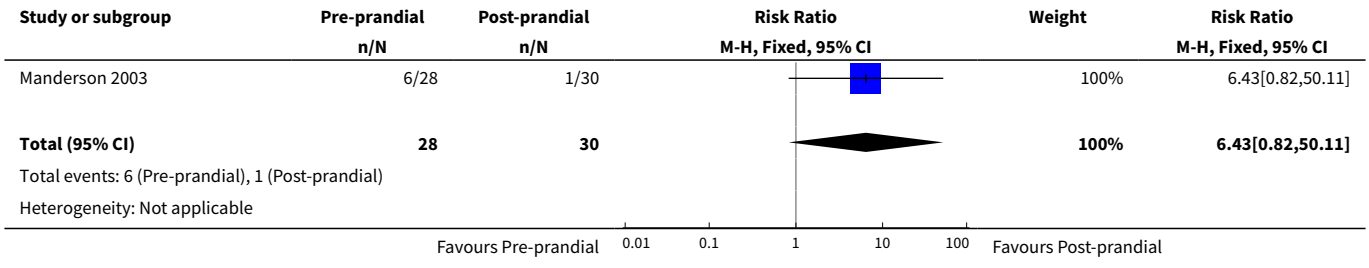
Analysis 4.2. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 2 Large-for-gestational age.

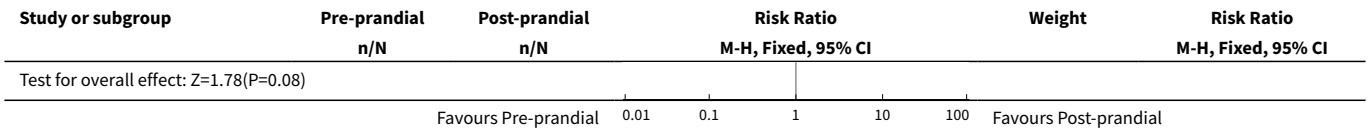


Analysis 4.3. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 3 Perinatal mortality (stillbirth and neonatal mortality).

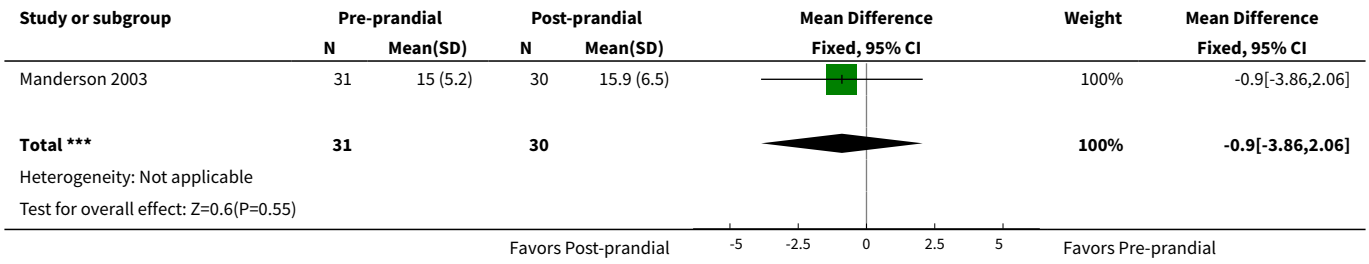


Analysis 4.4. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 4 Pre-eclampsia.

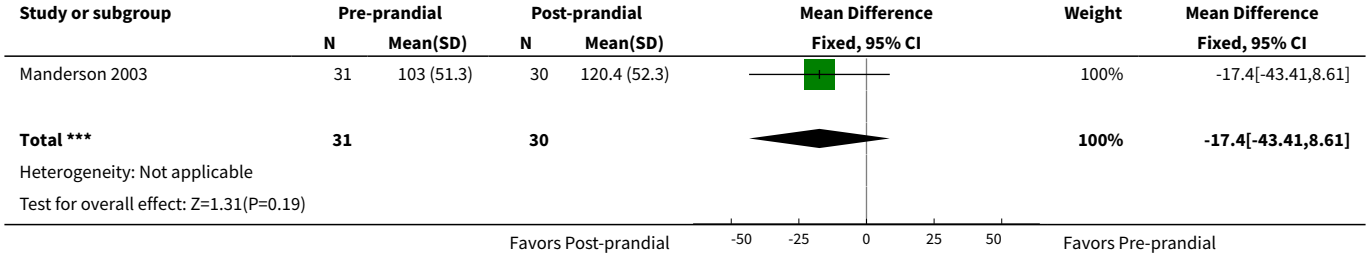




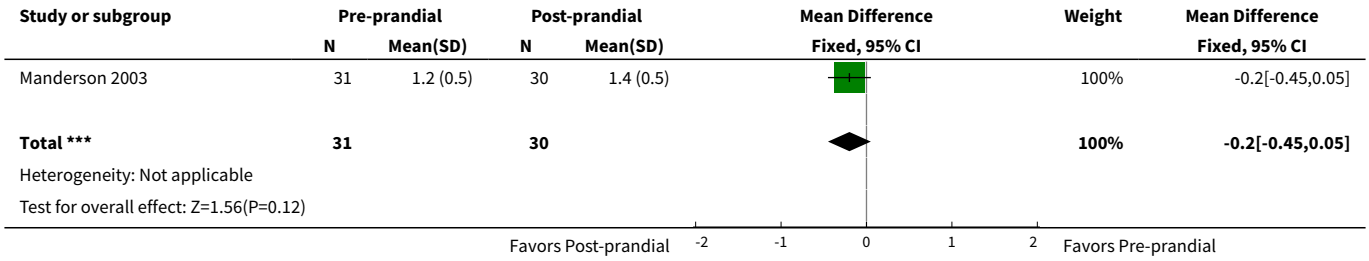
Analysis 4.5. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 5 Weight gain during pregnancy.



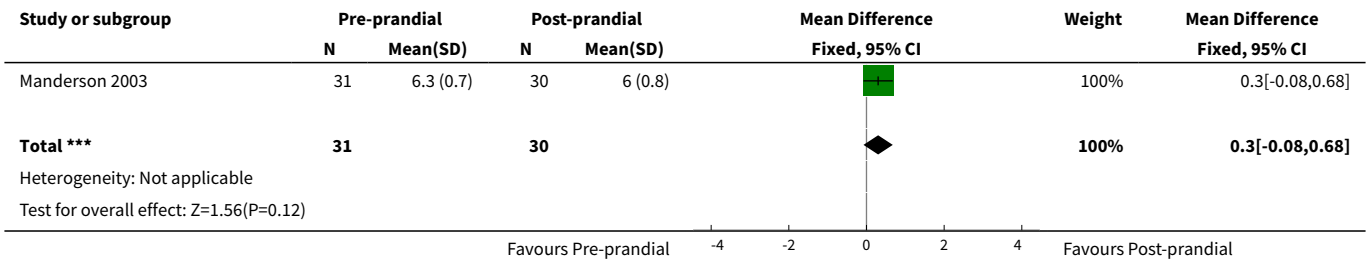
Analysis 4.6. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 6 Insulin dose.



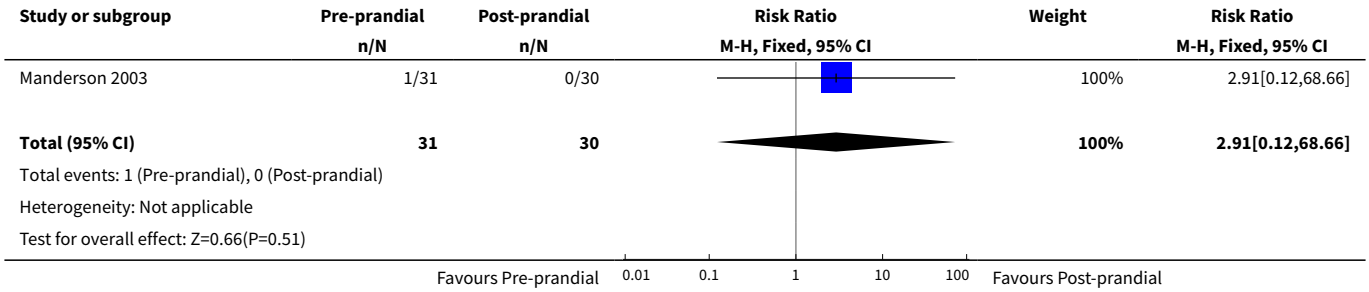
Analysis 4.7. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 7 Glycaemic control - Insulin dose.



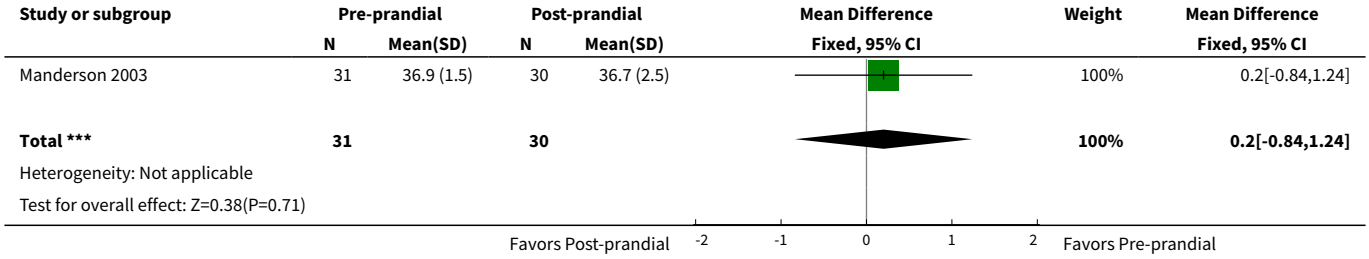
Analysis 4.8. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 8 Glycaemic control - HbA1c.



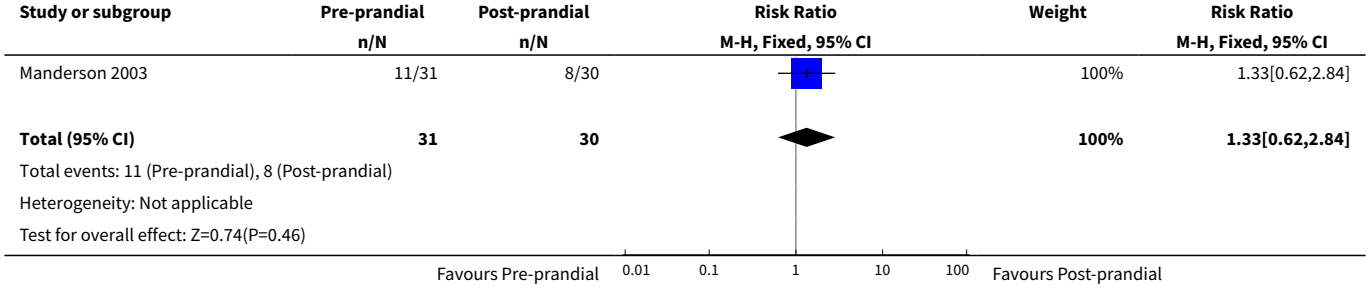
Analysis 4.9. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 9 Stillbirth.



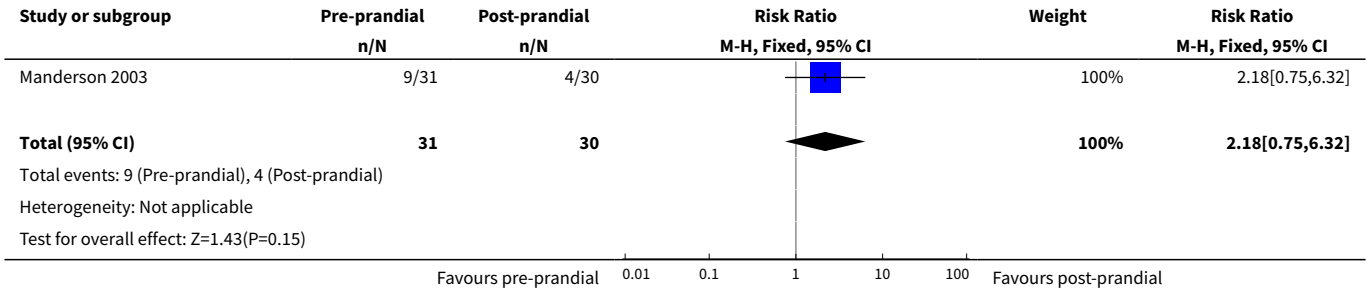
Analysis 4.10. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 10 Gestational age at birth.



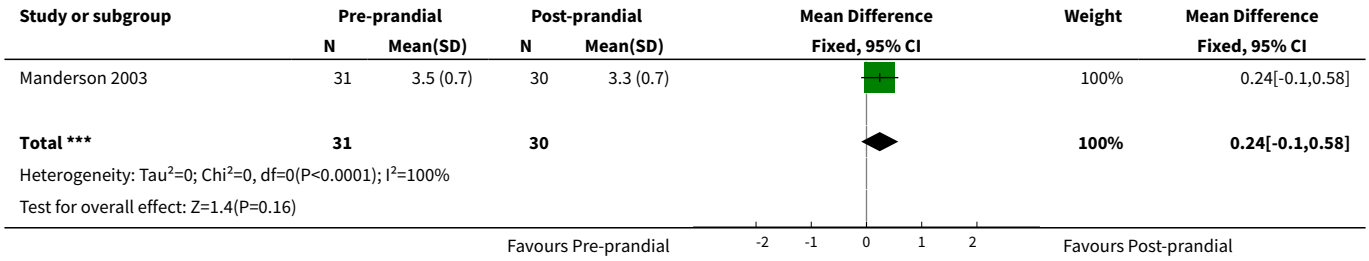
Analysis 4.11. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 11 Preterm birth < 37 weeks.



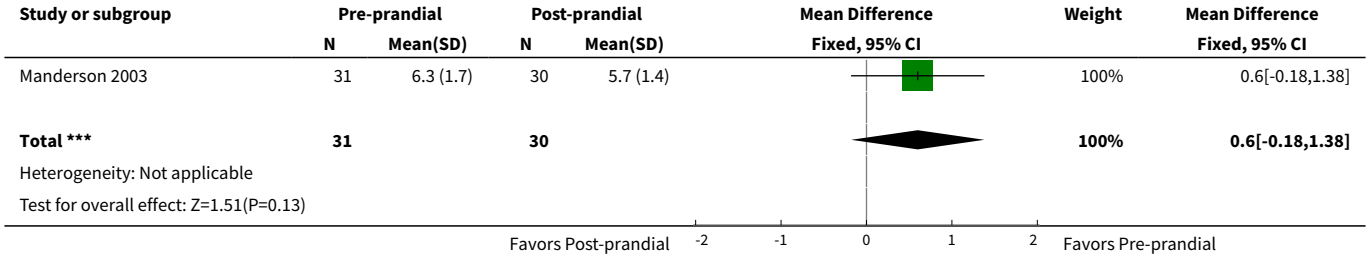
Analysis 4.12. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 12 Macrosomia.



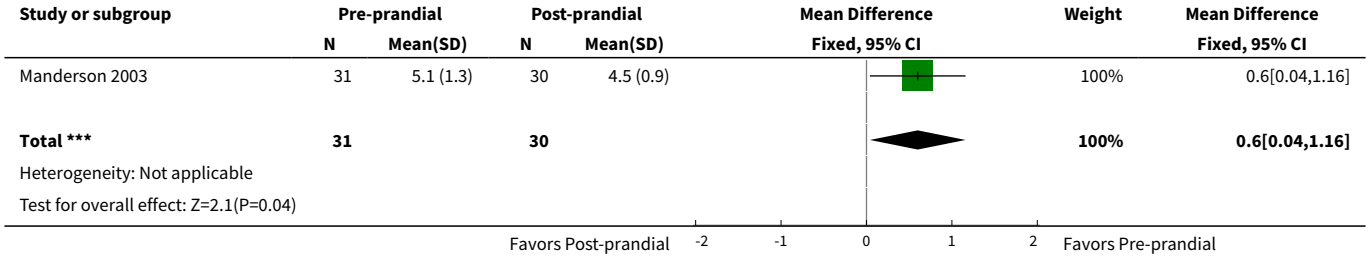
Analysis 4.13. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 13 Birthweight.



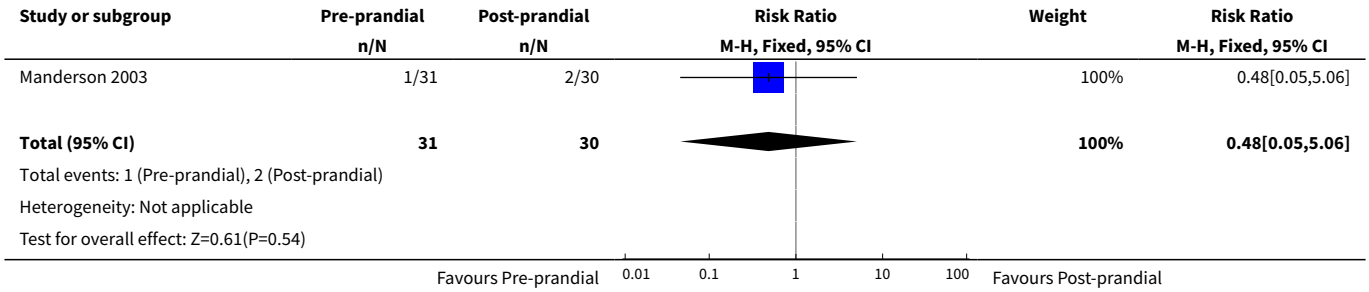
Analysis 4.14. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 14 Adiposity - Subscapula skinfold thickness.



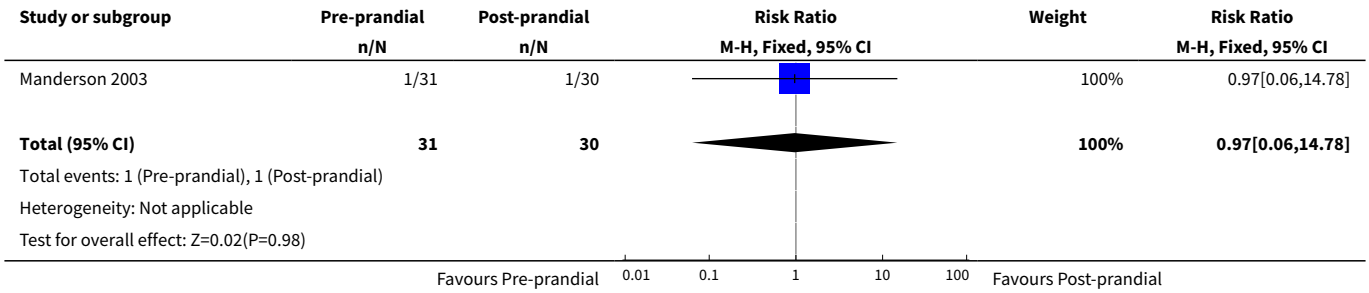
Analysis 4.15. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 15 Adiposity - Triceps skinfold thickness.



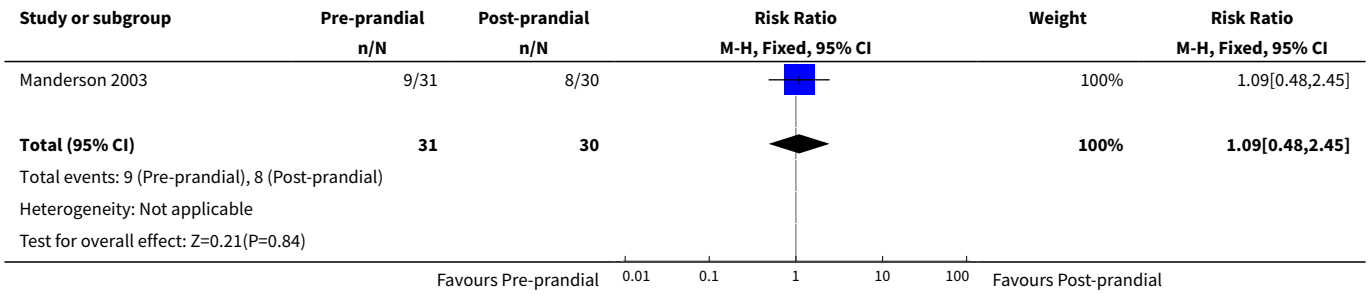
Analysis 4.16. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 16 Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite).



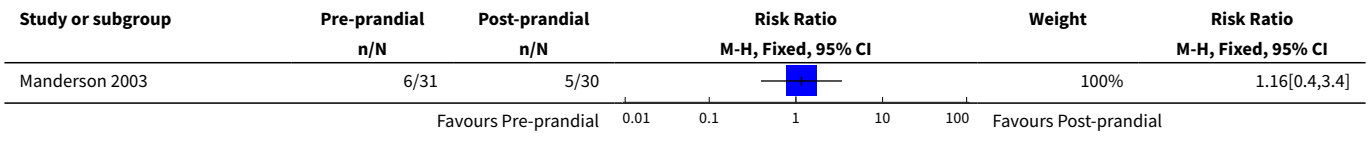
Analysis 4.17. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 17 Respiratory distress syndrome.

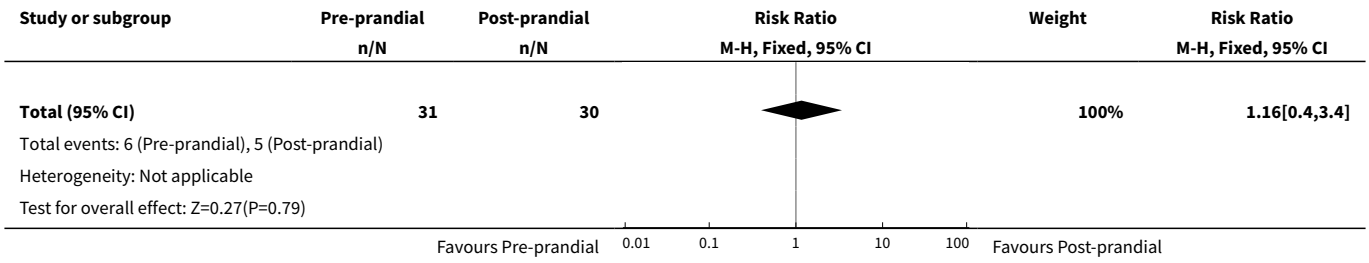


Analysis 4.18. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 18 Neonatal hypoglycaemia.

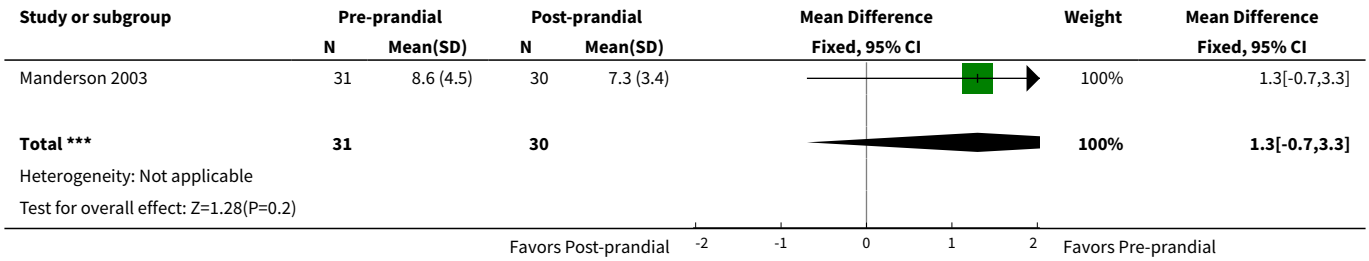


Analysis 4.19. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 19 Neonatal jaundice (hyperbilirubinaemia).

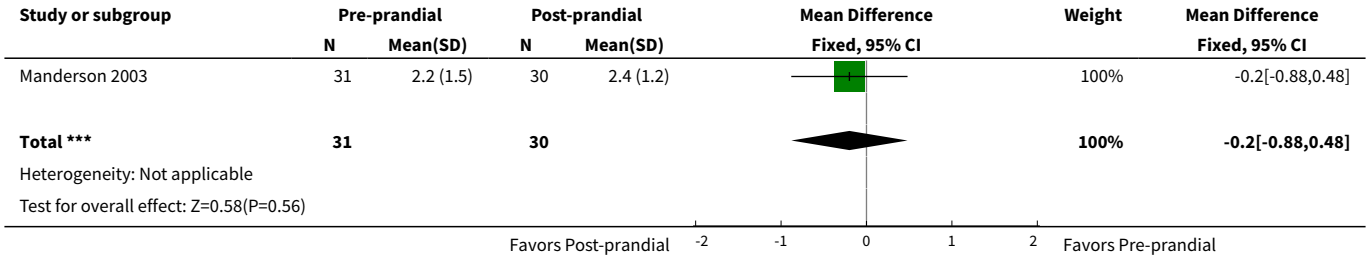




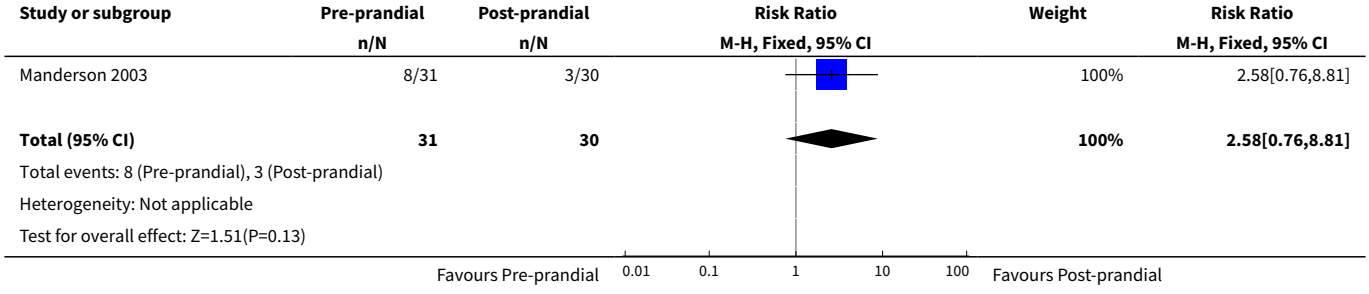
Analysis 4.20. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 20 Cord IGF-1.



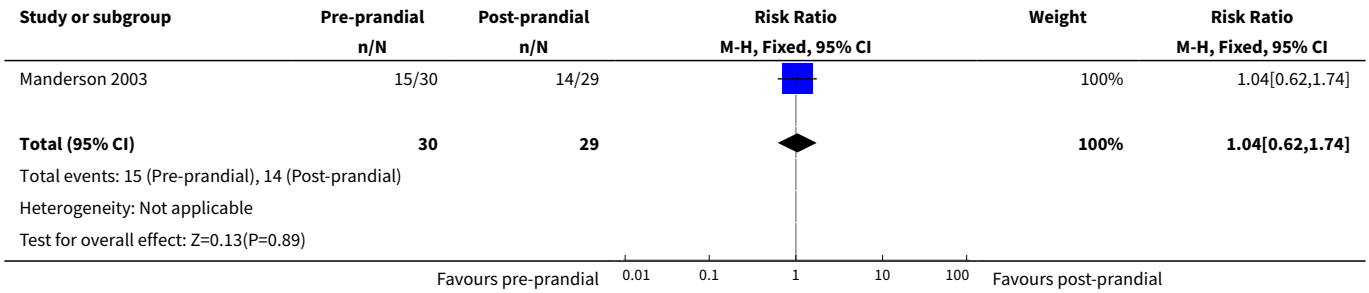
Analysis 4.21. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 21 Neonatal glucose at age 1 hour (not pre-specified).



Analysis 4.22. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 22 Transient tachypnea (not pre-specified).



Analysis 4.23. Comparison 4 Pre-prandial versus post-prandial glucose monitoring, Outcome 23 Neonatal intensive care admissions.

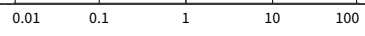


Comparison 5. Automated telemedicine monitoring versus conventional

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	32	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.62, 1.48]
2 Neonatal morbidity composite	1	32	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.53, 2.62]
3 Gestational age at birth	3	84	Mean Difference (IV, Fixed, 95% CI)	0.24 [-0.39, 0.88]
4 Use of additional insulin therapy	1	32	Risk Ratio (M-H, Fixed, 95% CI)	1.0 [0.89, 1.12]
5 Insulin requirement at end of study	1	20	Mean Difference (IV, Fixed, 95% CI)	18.4 [12.88, 23.92]
6 Glycaemic control - Maternal fasting blood glucose: before breakfast	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.0 [-1.22, -0.78]
7 Glycaemic control - Maternal fasting blood glucose: before lunch	1	20	Mean Difference (IV, Fixed, 95% CI)	-1.10 [-1.32, -0.88]
8 Glycaemic control - Maternal HbA1c	3	82	Mean Difference (IV, Random, 95% CI)	-0.17 [-0.82, 0.48]
9 Glycaemic control - Maternal post-prandial blood glucose	2	50	Mean Difference (IV, Random, 95% CI)	-0.80 [-1.67, 0.08]
10 Weight gain during pregnancy [kg]	1	32	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-4.95, 3.55]
11 Macrosomia	1	32	Risk Ratio (M-H, Fixed, 95% CI)	1.18 [0.31, 4.43]
12 Birthweight	1	32	Mean Difference (IV, Fixed, 95% CI)	-0.16 [-0.64, 0.32]

Analysis 5.1. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 1 Caesarean section.

Study or subgroup	Telemedicine n/N	Conventional n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dalfrà 2009	12/17	11/15		100%	0.96[0.62,1.48]
Total (95% CI)	**17**	**15**		**100%**	**0.96[0.62,1.48]**
Total events: 12 (Telemedicine), 11 (Conventional)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.17(P=0.86)					



Favours telemedicine — Favours conventional

Analysis 5.2. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 2 Neonatal morbidity composite.

Study or subgroup	Telemedicine n/N	Conventional n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dalfrà 2009	8/17	6/15		100%	1.18[0.53,2.62]
Total (95% CI)	**17**	**15**		**100%**	**1.18[0.53,2.62]**
Total events: 8 (Telemedicine), 6 (Conventional)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.4(P=0.69)					

Favours telemedicine — Favours conventional

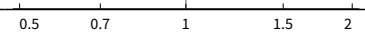
Analysis 5.3. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 3 Gestational age at birth.

Study or subgroup	Telemedicine N	Telemedicine Mean(SD)	Conventional N	Conventional Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Dalfrà 2009	17	36.1 (1.9)	15	35.1 (1.7)		25.71%	1[-0.25,2.25]
di Biase 1997	10	37.8 (0.6)	10	37.7 (1.3)		52.47%	0.1[-0.77,0.97]
Wojcicki 2001	17	37 (2.2)	15	37.3 (1.7)		21.81%	-0.3[-1.65,1.05]
Total ***	**44**		**40**			**100%**	**0.24[-0.39,0.88]**
Heterogeneity: Tau²=0; Chi²=2.14, df=2(P=0.34); I²=6.35%							
Test for overall effect: Z=0.76(P=0.45)							

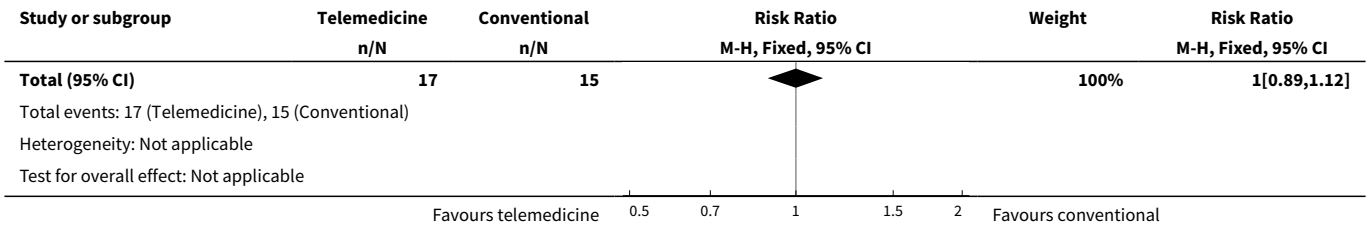
Favours Conventional — Favours Telemedicine

Analysis 5.4. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 4 Use of additional insulin therapy.

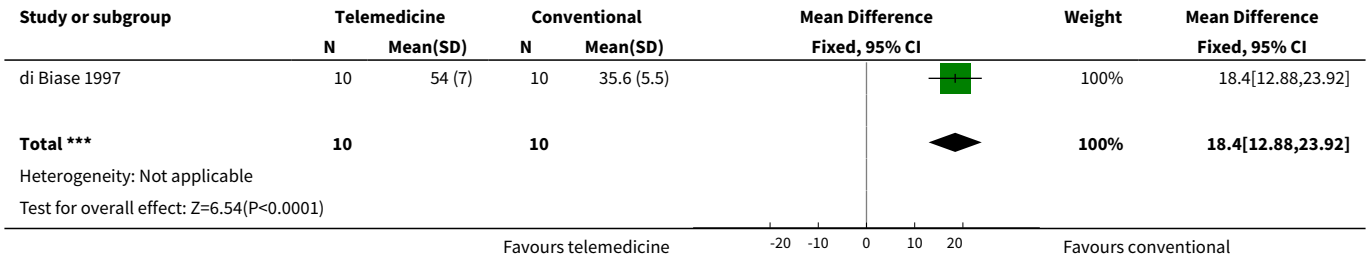
Study or subgroup	Telemedicine n/N	Conventional n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dalfrà 2009	17/17	15/15		100%	1[0.89,1.12]



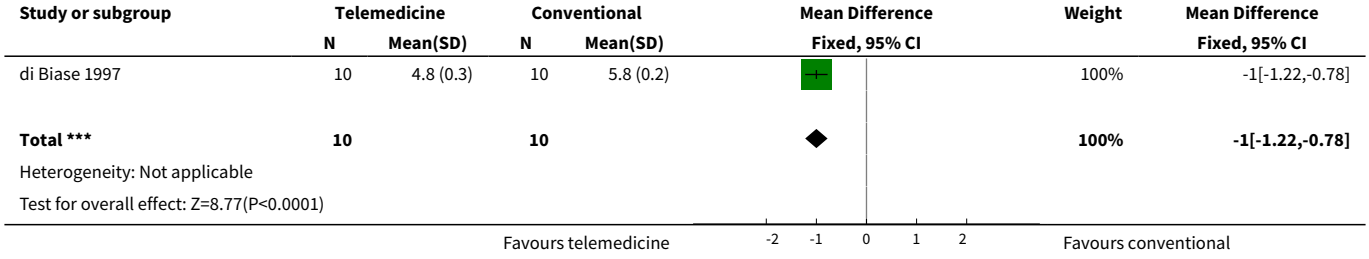
Favours telemedicine — Favours conventional



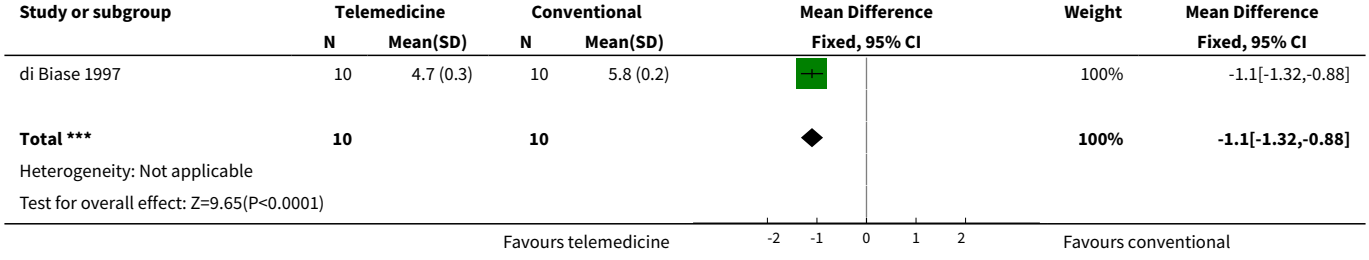
Analysis 5.5. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 5 Insulin requirement at end of study.



Analysis 5.6. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 6 Glycaemic control - Maternal fasting blood glucose: before breakfast.

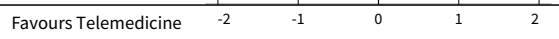


Analysis 5.7. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 7 Glycaemic control - Maternal fasting blood glucose: before lunch.



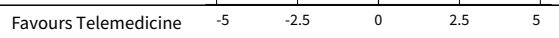
Analysis 5.8. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 8 Glycaemic control - Maternal HbA1c.

Study or subgroup	Telemedicine N	Telemedicine Mean(SD)	Conventional N	Conventional Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Dalfrà 2009	17	6.7 (0.7)	15	6.5 (0.8)		32.66%	0.2[-0.32,0.72]
di Biase 1997	10	5 (0.4)	10	5.7 (0.3)		37.86%	-0.7[-1.01,-0.39]
Wojcicki 2001	15	6.8 (0.9)	15	6.7 (0.9)		29.48%	0.1[-0.54,0.74]
Total ***	**42**		**40**			**100%**	**-0.17[-0.82,0.48]**
Heterogeneity: Tau^2=0.27; Chi^2=10.93, df=2(P=0); I^2=81.71%							
Test for overall effect: Z=0.51(P=0.61)							



Analysis 5.9. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 9 Glycaemic control - Maternal post-prandial blood glucose.

Study or subgroup	Telemedicine N	Telemedicine Mean(SD)	Conventional N	Conventional Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
di Biase 1997	10	5.7 (0.3)	10	6.9 (0.3)		55.02%	-1.2[-1.46,-0.94]
Wojcicki 2001	15	7.3 (0.7)	15	7.6 (1)		44.98%	-0.3[-0.92,0.32]
Total ***	**25**		**25**			**100%**	**-0.8[-1.67,0.08]**
Heterogeneity: Tau^2=0.35; Chi^2=6.9, df=1(P=0.01); I^2=85.51%							
Test for overall effect: Z=1.78(P=0.08)							

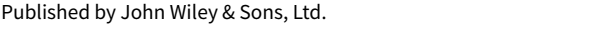


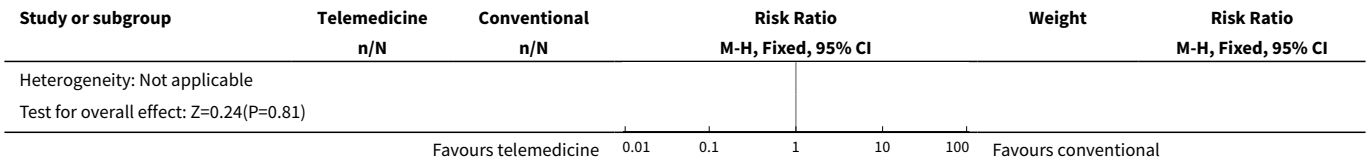
Analysis 5.10. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 10 Weight gain during pregnancy [kg].

Study or subgroup	Telemedicine N	Telemedicine Mean(SD)	Conventional N	Conventional Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Dalfrà 2009	17	11 (4)	15	11.7 (7.5)		100%	-0.7[-4.95,3.55]
Total ***	**17**		**15**			**100%**	**-0.7[-4.95,3.55]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.32(P=0.75)							

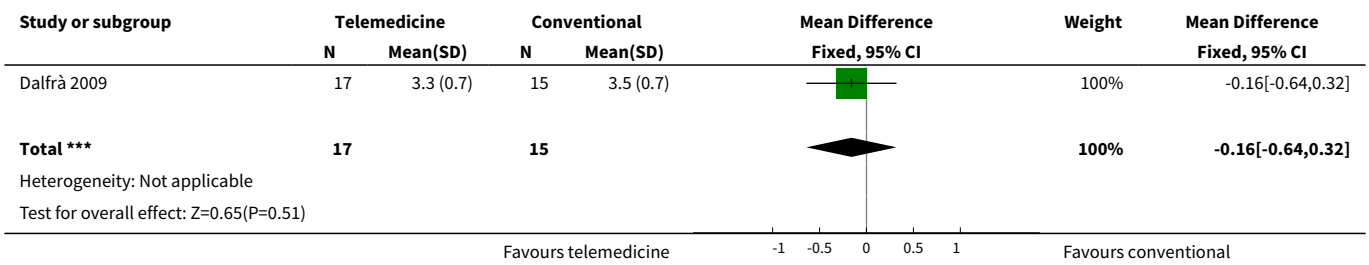
Analysis 5.11. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 11 Macrosomia.

Study or subgroup	Telemedicine n/N	Conventional n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Dalfrà 2009	4/17	3/15		100%	1.18[0.31,4.43]
Total (95% CI)	**17**	**15**		**100%**	**1.18[0.31,4.43]**
Total events: 4 (Telemedicine), 3 (Conventional)					





Analysis 5.12. Comparison 5 Automated telemedicine monitoring versus conventional, Outcome 12 Birthweight.



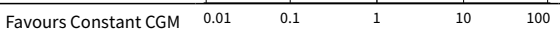
Comparison 6. Constant CGM versus intermittent CGM

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Caesarean section	1	25	Risk Ratio (M-H, Fixed, 95% CI)	0.77 [0.33, 1.79]
2 Weight gain during pregnancy	1	25	Mean Difference (IV, Fixed, 95% CI)	0.5 [-1.82, 2.82]
3 Insulin dosage, 3rd trimester (IU/kg/day)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.03 [-1.30, 1.24]
4 Glycaemic control - Maternal blood glucose (1st trimester)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-2.70, 1.70]
5 Glycaemic control - Maternal blood glucose (3rd trimester)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-2.00, 1.72]
6 Glycaemic control - Maternal HbA1c (1st trimester)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.13, 0.53]
7 Glycaemic control - Maternal HbA1c (3rd trimester)	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.09 [-0.69, 0.51]
8 Maternal hypoglycemia	1	25	Risk Ratio (M-H, Fixed, 95% CI)	0.54 [0.06, 5.24]
9 Diabetic ketoacidosis (not pre-specified)	1	25	Risk Ratio (M-H, Fixed, 95% CI)	0.36 [0.02, 8.05]
10 Preterm birth < 37 weeks	1	25	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.08, 15.46]
11 Macrosomia	1	25	Risk Ratio (M-H, Fixed, 95% CI)	1.08 [0.08, 15.46]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12 Neonatal hypoglycaemia	1	25	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]

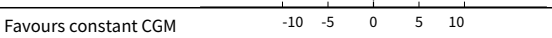
Analysis 6.1. Comparison 6 Constant CGM versus intermittent CGM, Outcome 1 Caesarean section.

Study or subgroup	Constant CGM n/N	Intermittent CGM n/N	Risk Ratio M-H, Fixed, 95% CI	Weight	Risk Ratio M-H, Fixed, 95% CI
Petrovski 2011	5/12	7/13		100%	0.77[0.33,1.79]
Total (95% CI)	**12**	**13**		**100%**	**0.77[0.33,1.79]**
Total events: 5 (Constant CGM), 7 (Intermittent CGM)					
Heterogeneity: Not applicable					
Test for overall effect: Z=0.6(P=0.55)					



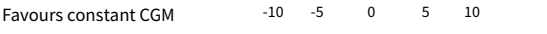
Analysis 6.2. Comparison 6 Constant CGM versus intermittent CGM, Outcome 2 Weight gain during pregnancy.

Study or subgroup	Constant CGM N	Mean(SD)	Intermittent CGM N	Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Petrovski 2011	12	13.4 (3.1)	13	12.9 (2.8)		100%	0.5[-1.82,2.82]
Total ***	**12**		**13**			**100%**	**0.5[-1.82,2.82]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.42(P=0.67)							

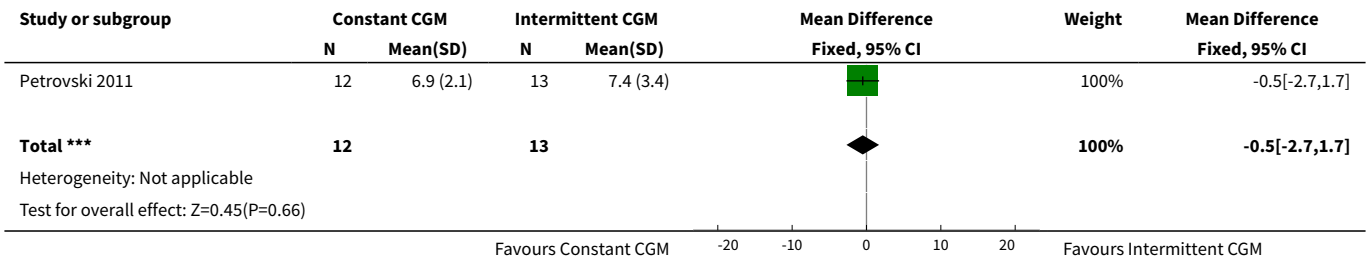


Analysis 6.3. Comparison 6 Constant CGM versus intermittent CGM, Outcome 3 Insulin dosage, 3rd trimester (IU/kg/day).

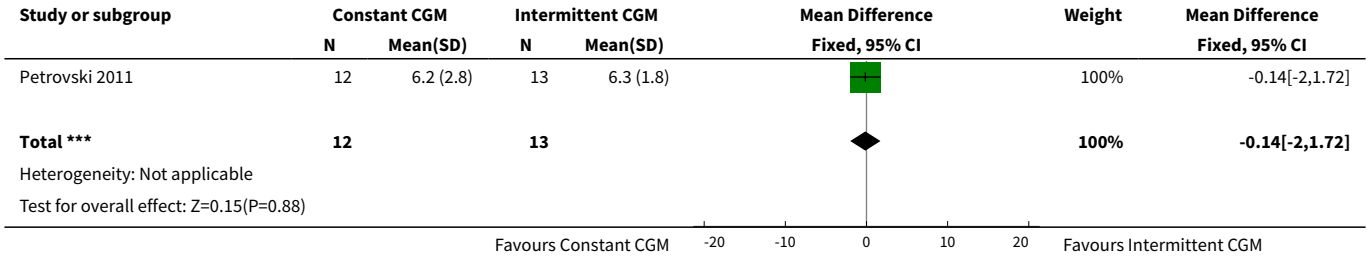
Study or subgroup	Constant CGM N	Mean(SD)	Intermittent CGM N	Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
Petrovski 2011	12	0.9 (1.3)	13	0.9 (1.9)		100%	-0.03[-1.3,1.24]
Total ***	**12**		**13**			**100%**	**-0.03[-1.3,1.24]**
Heterogeneity: Not applicable							
Test for overall effect: Z=0.05(P=0.96)							



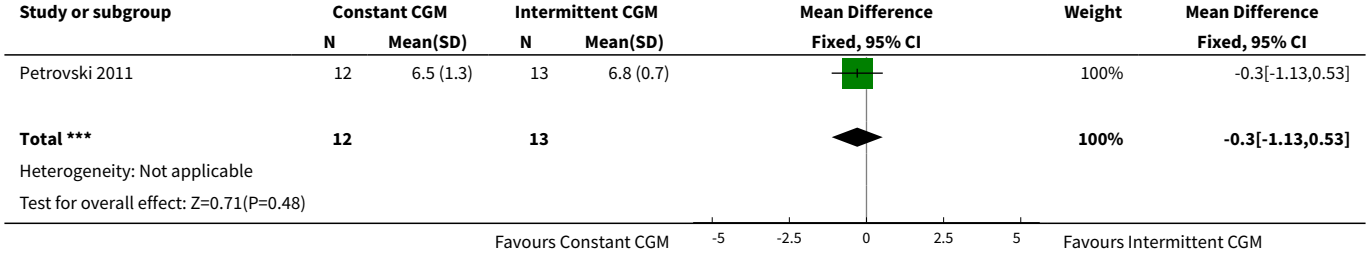
Analysis 6.4. Comparison 6 Constant CGM versus intermittent CGM, Outcome 4 Glycaemic control - Maternal blood glucose (1st trimester).



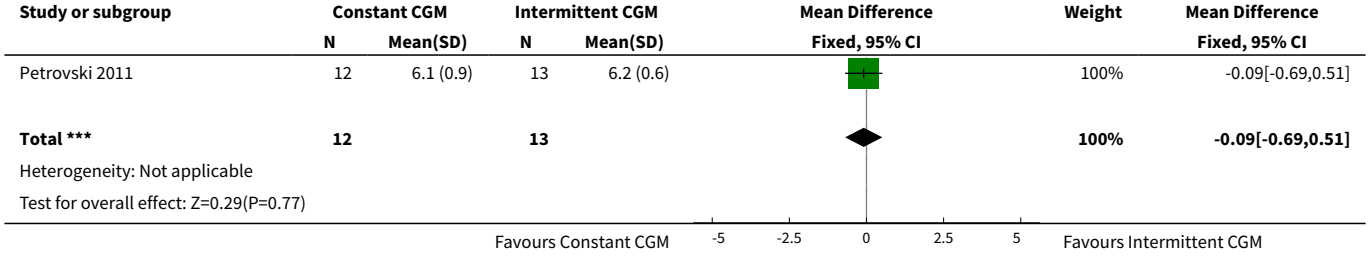
Analysis 6.5. Comparison 6 Constant CGM versus intermittent CGM, Outcome 5 Glycaemic control - Maternal blood glucose (3rd trimester).



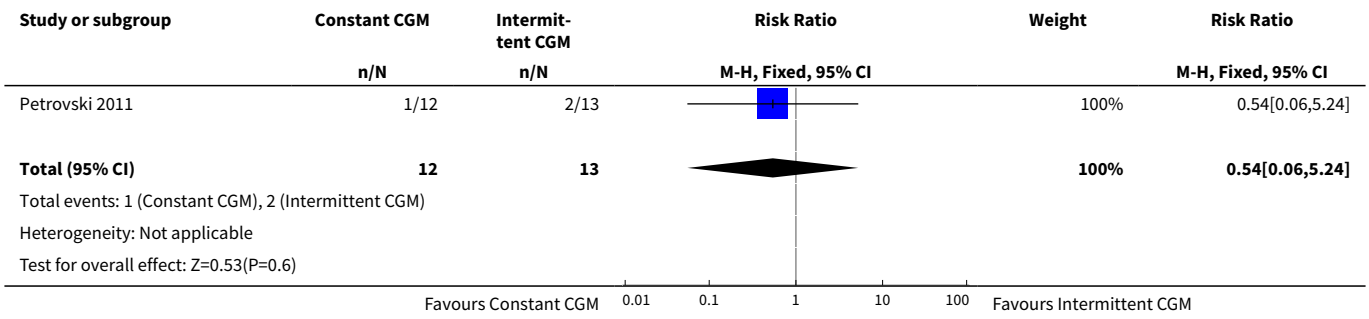
Analysis 6.6. Comparison 6 Constant CGM versus intermittent CGM, Outcome 6 Glycaemic control - Maternal HbA1c (1st trimester).



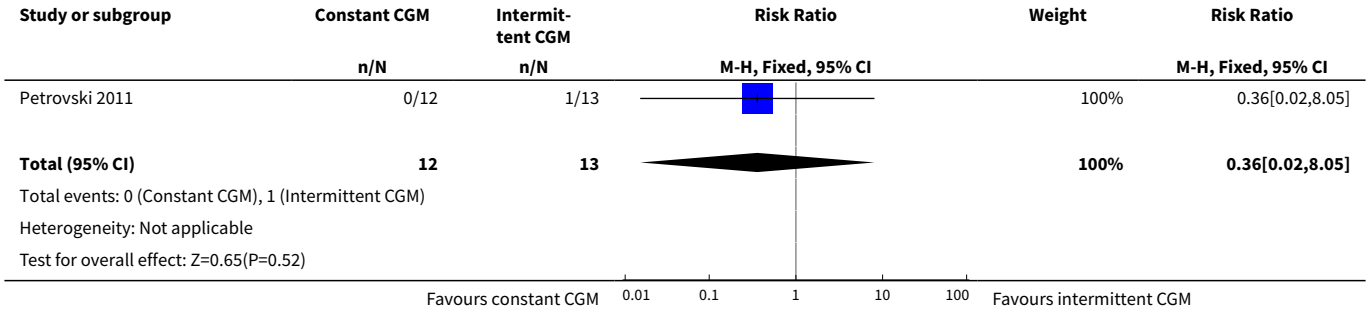
Analysis 6.7. Comparison 6 Constant CGM versus intermittent CGM, Outcome 7 Glycaemic control - Maternal HbA1c (3rd trimester).



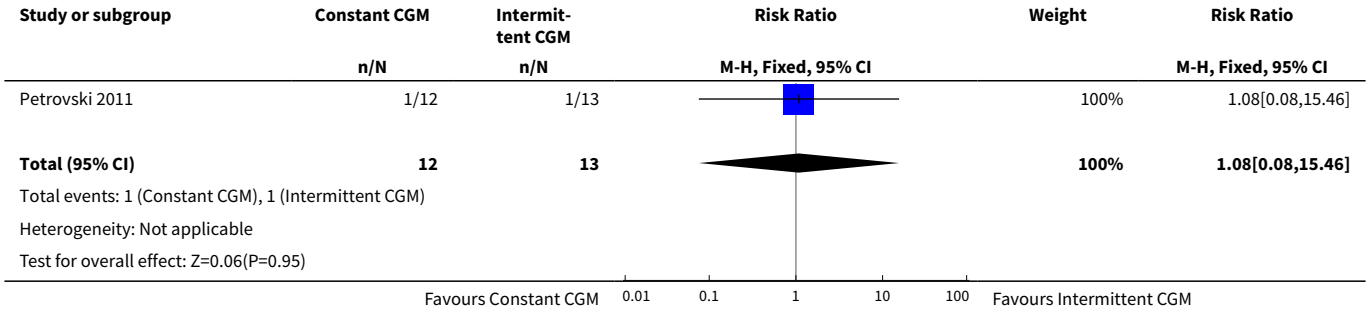
Analysis 6.8. Comparison 6 Constant CGM versus intermittent CGM, Outcome 8 Maternal hypoglycemia.



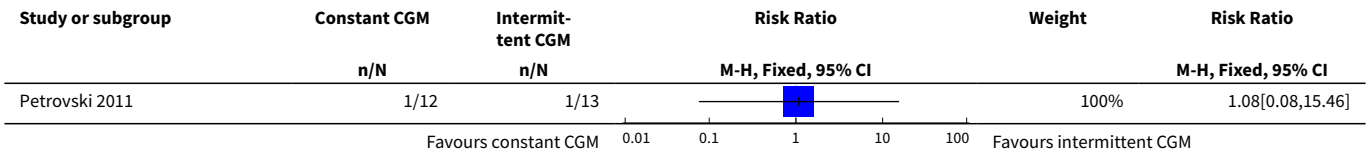
Analysis 6.9. Comparison 6 Constant CGM versus intermittent CGM, Outcome 9 Diabetic ketoacidosis (not pre-specified).

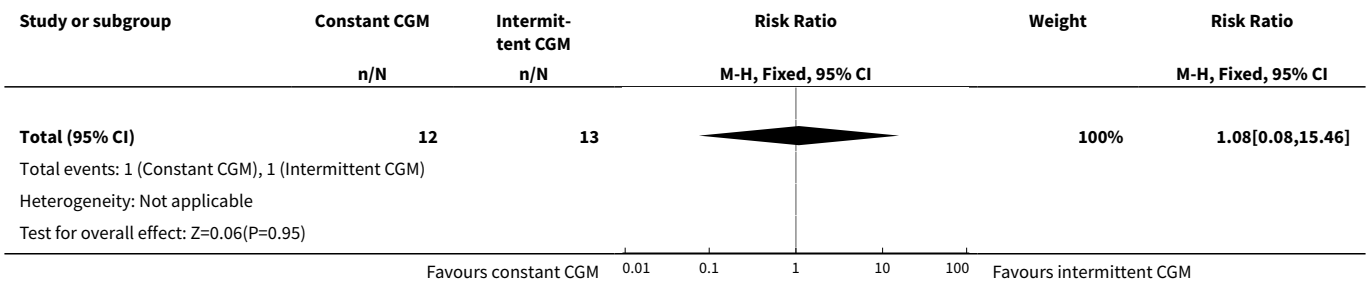


Analysis 6.10. Comparison 6 Constant CGM versus intermittent CGM, Outcome 10 Preterm birth < 37 weeks.

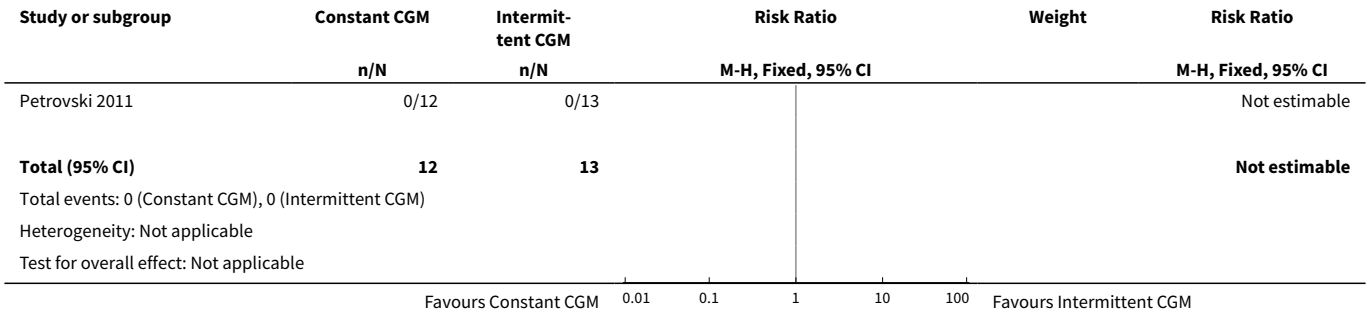


Analysis 6.11. Comparison 6 Constant CGM versus intermittent CGM, Outcome 11 Macrosomia.





Analysis 6.12. Comparison 6 Constant CGM versus intermittent CGM, Outcome 12 Neonatal hypoglycaemia.



APPENDICES

Appendix 1. Search methods for ClinicalTrials.gov and ICTRP

Each line was run separately

ICTRP

diabetes AND pregnancy AND monitoring

diabetes AND pregnant AND monitoring

diabetic AND pregnancy AND glucose

diabetic AND pregnant AND glucose

ClinicalTrials.gov

Advanced search

pregnancy | Interventional Studies | Diabetes | Glucose Control | Studies with Female Participants

pregnant | Interventional Studies | Diabetes | monitoring | Studies with Female Participants

pregnancy | Interventional Studies | Diabetes | blood glucose | Studies with Female Participants

WHAT'S NEW

Date	Event	Description
3 June 2019	Amended	We have edited the numbers of participants to clarify the number of women with type 1 or type 2 diabetes. We have also clarified that in two trials (171 women) the data were not presented separately for type 1 or type 2 diabetes.

HISTORY

Protocol first published: Issue 2, 2012
Review first published: Issue 4, 2014

Date	Event	Description
1 November 2018	New citation required but conclusions have not changed	The overall conclusions have not changed. There are data from two new studies, which adds some data to one of the six comparisons: 'Continuous glucose monitoring (CGM) versus intermittent glucose monitoring'. There is now evidence to suggest that CGM may reduce hypertensive disorders of pregnancy, although the results were less clear for the single outcome of pre-eclampsia. CGM may reduce neonatal hypoglycaemia.
1 November 2018	New search has been performed	Search updated and six studies were assessed for eligibility. Two studies have been included (Feig 2017; Voormolen 2018), two are ongoing (Link 2018; Logan 2011), one is an additional study report of an already included study (di Biase 1997), and one is an additional report of an already excluded study (Bartholomew 2011).
30 November 2016	New citation required but conclusions have not changed	One new trial added and the conclusions remain unchanged.
30 November 2016	New search has been performed	Search updated, seven trial reports identified. One new trial added for this update from ongoing studies (Dalfrà 2009). The review now includes 10 trials. 'Risk of bias' assessments for blinding have been updated to include assessments of both performance and detection bias. 'Summary of findings' tables have been incorporated.

CONTRIBUTIONS OF AUTHORS

Foong Ming Moy (FMM), the contact person, is the guarantor of the review. Leanne Jones drafted the review update, extracted additional data, assessed study quality, undertook data entry and analysis in Review Manager, and prepared the 'Summary of findings' table for comparison 5. Three review authors (FMM, Amita Ray and Brian S Buckely) commented on drafts of the review update.

DECLARATIONS OF INTEREST

Foong Ming Moy: none known.

Amita Ray: none known.

Brian Buckley: none known.

Leanne Jones: is employed by the University of Liverpool as an Associate Editor/Deputy Managing Editor with Cochrane Pregnancy and Childbirth. Her employment is supported by the National Institute for Health Research, via Cochrane Infrastructure funding to Cochrane

Pregnancy and Childbirth. She had no involvement with the editorial processes for this review update. Cochrane Pregnancy and Childbirth received an award from UK NIHR Cochrane Reviews of NICE Priority: Project Ref NIHR 128651, to update this review.

SOURCES OF SUPPORT

Internal sources

- University of Malaya, Malaysia.
- (LVJ) Cochrane Pregnancy and Childbirth Group, Department of Women's and Children's Health, The University of Liverpool, Liverpool, UK.

External sources

- High Impact Research Grant (E000010-20001), Malaysia.

  Funding in providing the Cochrane Library data base and support in retrieving full text articles
- NIHR Cochrane Programme Grant Project: 13/89/05 – Pregnancy and childbirth systematic reviews to support clinical guidelines, UK.

  2017 update
- National Institute of Health Research (NIHR) UK, UK.

  NIHR Cochrane Reviews of NICE Priority: Project Ref NIHR 128651 (2019 update)

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

For the 2017 update, in order to improve consistency across reviews, we used the Cochrane Pregnancy and Childbirth core outcome set for reviews of diabetes in pregnancy, developed by the Cochrane Pregnancy and Childbirth Australasian satellite.

The outcomes specified in the last version of the review have been expanded to incorporate the core outcome set, but were as follows.

Primary outcomes

Maternal

1. Glycaemic control (HbA1c, fructosamine, fasting blood glucose, post-prandial blood glucose)

Infant

1. Birthweight
2. Macrosomia greater than 4.5 kg

Secondary outcomes

Maternal

1. Frequency of hypoglycaemia
2. Antenatal hospital stay (percentage requiring admission, length of stay)
3. Induction of labour
4. Caesarean section rates
5. Miscarriage

Infant

1. Gestational age (at birth) or preterm birth less than 37/less than 34 weeks
2. Frequency of neonatal hypoglycaemia
3. Shoulder dystocia
4. Major and minor anomalies
5. Neonatal intensive care admissions
6. Death of baby including stillbirth/neonatal death

to the following.

The following outcomes were not pre-specified in our protocol.

1. Birth trauma (shoulder dystocia, bone fracture, nerve palsy) (not pre-specified as a composite)
2. Neonatal glucose at age one hour

3. Transient tachypnoea
4. Diabetic ketoacidosis
5. Feeding difficulties

We have added 'Summary of findings' tables and an assessment of the quality of the evidence using the GRADE approach.

For this update (2019)

We added in a search of ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports. We have also included two new outcomes (instrumental delivery, and neonatal intensive care unit length of stay greater than 24 hours). We now include information about trial dates, sources of trial funding, and trial authors' declarations of interest.

We have two new secondary outcomes to the review:

1. Instrumental vaginal birth
2. Neonatal intensive care unit length of stay greater than 24 hours

In response to referee feedback, the following changes have been made.

GRADE outcomes have now been limited to primary outcomes of the review, so that Glycaemic control during/end of treatment (as defined by trialists) (e.g. HbA1c, fructosamine, fasting blood glucose, post-prandial blood glucose) and preterm birth (less that 37 weeks' gestation and less than 34 weeks' gestation) have been removed from the 'Summary of findings' tables.

We have added pre-eclampsia, pregnancy-induced hypertension and eclampsia as secondary outcomes. They form part of the composite outcome 'hypertensive disorders of pregnancy' but had not been listed separately as individual secondary outcomes.

We have re-ordered the comparisons so that comparison 5 is now comparison 1.

INDEX TERMS

Medical Subject Headings (MeSH)

Blood Glucose [*metabolism]; Blood Glucose Self-Monitoring [*methods]; Canada; Diabetes Mellitus, Type 1 [*blood]; Diabetes Mellitus, Type 2 [*blood]; Europe; Hypertension [prevention & control]; Hypoglycemia [chemically induced]; Perinatal Mortality; Pre-Eclampsia [prevention & control]; United States

MeSH check words

Adult; Female; Humans; Infant, Newborn; Pregnancy