**Layer 1B starts**

CR Review formatting

Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants (Review)

rewritten to fit prototype format

September 10 2018

A review will have the following sections/pages:

Summary

Full text

Appendices

Related content

Messages for media

Article information

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# **Planned birth at or near term for improving health outcomes for pregnant women with pre-existing diabetes and their infants (Review)**

Cochrane Systematic Review – Intervention

Published date: 9 February 2018| Date of last search: 15 August 2017 (see what’s changed)

Authors: Biesty LM | Egan AM | Dunne F | Smith V | Meskell P | Dempsey E | Meabh Ni Bhuinneain G | Devane D |

View author’s declarations of interest

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

SUMMARY

# Objectives

This review aimed to assess the effect of planned birth (either by induction of labour or caesarean birth) at or near term (37 to 40 weeks' gestation) compared with an expectant approach for improving health outcomes for women with pre-existing diabetes and their infants.

# Main Findings

→ **Planned birth compared to an expectant approach:** We identified no eligible published trials for inclusion in this review.

# Background

For women with pre-existing diabetes, pregnancy is considered high risk as it is associated with increased rates of adverse outcomes for the mother and infant. Current clinical guidelines recommend elective birth, at or near term, because of increased perinatal mortality during the third trimester of pregnancy. An alternative is the expectant approach to the management of birth, which refers to waiting for the spontaneous onset of labour in the absence of any maternal or foetal issues that may necessitate birth. **This updated review aimed to assess whether planned birth compared with an expectant approach improve outcomes for women and their infants.** See more detail about planned birth for pregnant women with pre-existing diabetes.

# More detail about planned birth

## What is a planned birth?

A woman’s pregnancy is considered to be 'at term' when her pregnancy duration reaches 37 weeks. Planned birth involves the early birth of the infant either by induction of labour (artificially inducing labour) or caesarean section. This typically takes place between 37 and 40 weeks’ gestation.

## Who can use or administer a planned birth?

A planned birth requires clinical supervision in hospital. Planned birth can be by elective caesarean section or by induction of labour. Methods of induction vary according to local protocols and typically depend on cervical status. The process generally involves cervical ripening with misoprostol or prostaglandin E2 followed by amniotomy (cutting the membranes) and intravenous oxytocin infusion if labour has not started.

## What other options are there?

An expectant approach to birth includes continued antenatal surveillance and awaiting the spontaneous omset of labour in the absence of any maternal or foetal issues that may necessitate earlier birth. See systematic reviews of other options.

## How do people experience the intervention?

Women with pre-existing diabetes at higher risk of complications than women who do not have diabetes. For example, their babies may be larger and have a higher risk of death in the later weeks of pregnancy. Because of these risks, women with diabetes may select to have a planned birth rather than waiting for labour to start spontaneously. However, induction has the disadvantage of increasing the incidence of forceps or ventouse births, and women often find it difficult to cope with an induced labour. Caesarean section is a major operation which can lead to blood loss, infections and increased chance of problems with subsequence births. Early birth can increase the chance of breathing problems for babies.

## Is there anything else someone should know before using the intervention?

Current guidelines recommend planned birth for women with pre-existing diabetes but the evidence in support of this is currently lacking.

# What this review is based on

Cochrane Reviews are based on systematic and robust selection of relevant studies. We did not identify any completed trials comparing planned birth versus an expectant approach for women with pre-existing diabetes. See what studies we searched for and what we found.

1st link to standard description of what a Cochrane Review is.

2nd link leads to the text below, which is a narrative summary of the table in the Full text called “What review authors searched for and found”:

## What studies we searched for

We searched for randomised and non-randomised trials up until December 2016. Trials were to be included if they compared planned birth, at or near term, with an expectant approach for pregnant women with pre-existing diabetes.

## What we found

We did not identify any eligible published trials.

Standard sentences: See current Plain language summary guidance: http://www.cochrane.no/sites/cochrane.no/files/public/uploads/how\_to\_write\_a\_cochrane\_pls\_27th\_march\_2017.pdf

## Summary of findings 1

## **Summary of Findings should be numbered when there is more than one. Number 1 should be the one that appears in the summary. This will have consequences for the order of the comparisons listed in the full text.**

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Standard sentences: See current Plain language summary guidance: http://www.cochrane.no/sites/cochrane.no/files/public/uploads/how\_to\_write\_a\_cochrane\_pls\_27th\_march\_2017.pdf

# Authors’ conclusions

In the absence of randomised studies, we are unable to say if women with pre‐existing diabetes and their babies experience better health outcomes if they have a planned birth compared to waiting for labour to begin spontaneously or until 41 weeks' gestation if all is well. More research is needed to answer this question.

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

## Related content

* More information for patients and the public, health professionals and policy makers
* Cochrane Reviews of other options for birth for women with pre-existing diabetes

(Links leads to texts in ‘Related content’ section – see end of document, after Appendices)

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

## Messages for media

(Link leads to ‘Messages for media’ section, created for the most part by people other than authors.)

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

FULL TEXT

References in the text will be linked to reference lists in the final published version, but I have not bothered to recreate these links in the prototype sketches.

# Background

## Description of the condition

Pre-existing diabetes refers to maternal diabetes that existed prior to the pregnancy. This typically refers to Type 1 and Type 2 diabetes, however the term also encompasses rarer forms of diabetes, e.g. Maturity Onset Diabetes of the Young. Type 1 diabetes is characterised by autoimmune destruction of beta cells, usually leading to absolute insulin deficiency; Type 2 diabetes occurs due to a progressive loss of insulin secretion on a background of insulin resistance, and is likely to be the result of interactions between genetic, environmental and immunological factors (ADA 2016; Zaccardi 2016). Although estimates vary, it is believed that 0.5% to 0.9% of pregnancies are complicated by pre-existing diabetes (Correa 2015; NICE 2015). While the prevalence of both Type 1 and Type 2 diabetes has increased in recent years (NICE 2015), the rate of Type 2 diabetes in pregnant women in the USA more than quadrupled in the period from 1994 to 2004, overtaking the rates of pre-existing Type 1 diabetes (Albrecht 2010). This increase in prevalence of Type 2 diabetes is in line with the worldwide rise in obesity rates and advancing maternal age (ACOG 2005; Egan 2015; Zhu 2016).

In the setting of pre-existing diabetes, pregnancy is considered to be high risk and is associated with increased rates of adverse maternal and neonatal outcomes. Studies from the United Kingdom and Ireland reveal a congenital malformation rate twice that of the background population (24/1000), a five-fold increased risk of stillbirth (25/1000), and a three-fold increased risk of perinatal mortality and caesarean birth (25/1000) (Macintosh 2006; Dunne 2009; Egan 2015). During the third trimester, issues of significant concern are: late foetal death; complications necessitating premature birth; and the potential for birth trauma associated with foetal macrosomia (Cousins 1987; Hanson 1993; Dunne 2009). Although recent research has noted a higher risk of adverse neonatal outcomes including stillbirths and congenital abnormalities in offspring of women with Type 1 compared to Type 2 diabetes (Owens 2015), an earlier systematic review found perinatal mortality to be higher for women with Type 2 compared with Type 1 diabetes (Balsells 2009). It should be noted that women with Type 2 diabetes are more commonly from ethnic minorities and are often cared for in community settings with minimal access to specialist care (Murphy 2010). This makes them an especially vulnerable group.

See Appendix 1 for detailed pathophysiology of pregnancy in women with pre-existing diabetes.

## Description of the intervention

A woman’s pregnancy is considered to be 'at term' when her pregnancy duration reaches 37 weeks (Gulmezoglu 2012). Planned birth involves the early birth of the infant either by induction of labour or caesarean section. This typically takes place between 37 and 40 weeks’ gestation. Methods of induction vary according to local protocols and typically depend on cervical status. The process generally involves cervical ripening with misoprostol or prostaglandin E2 followed by amniotomy and oxytocin infusion if labour has not started (Boulvain 2016). An alternative is the expectant approach to the management of birth, which refers to waiting for the spontaneous onset of labour in the absence of any maternal or fOetal issues that may necessitate birth (Bond 2017).

## Why it is important to do this review

In 1989, the St Vincent declaration called on governments and healthcare services to implement effective measures to achieve pregnancy outcomes in women with diabetes that approximate those of women without diabetes within five years (St Vincent Declaration 1990). While this goal was not achieved, it is important that we strive to identify any measures that may assist in meeting this target in our care for women with diabetes. Planned birth may have potential benefits, possibly reducing the risks of prolonged labour and elevated rates of caesarean section following induction of labour (Macer 1992). Birth by caesarean section, including elective caesarean, may increase the risk of maternal morbidity including postpartum infections, haemorrhage or uterine rupture during subsequent labour (Irion 1998). Induction of labour may lead to increased interventions during labour and birth and an increase in maternal morbidity (Khireddine 2013). Furthermore, early-term birth is associated with an increased risk of multiple neonatal morbidities including respiratory distress syndrome and the need for mechanical ventilation and admission to a neonatal intensive care unit (ACOG 2013). Women's views on elective birth versus continued antenatal surveillance should also be considered (Dodd 2014).

# Objectives

To assess the effect of planned birth compared with an expectant approach for pregnant women with pre-existing diabetes on maternal and perinatal mortality and morbidity.

# Methods

## Criteria for considering studies for this review

### Types of studies

We planned to include all published randomised trials (including those using a cluster-randomised design) and non-randomised trials which compared planned birth at or near term gestation, with an expectant approach for pregnant women with pre-existing diabetes.

Cross-over studies were not eligible for inclusion as this design is not appropriate for this intervention.

Studies published in abstract form only were eligible for inclusion where information on risk of bias and primary or secondary outcomes could be obtained.

### Types of participants

Pregnant women, at or near term gestation (37 to 40 weeks’ gestation), with pre-existing diabetes (Type 1 or Type 2) as diagnosed according to each included study.

Women with gestational diabetes are included in a different Cochrane review, 'Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants' (Biesty 2018).

We planned to exclude trials that included women both with gestational diabetes and pre-existing diabetes, where data could not be separated.

### Types of interventions

Planned birth (induction of labour or caesarean section) at or near term gestation (37 to 40 weeks’ gestation). Induction of labour was defined by trial authors and may include the use of prostaglandins, misoprostol, oxytocin, amniotomy or a combination of these.

The comparison was an expectant approach to the management of birth which refers to waiting for the spontaneous onset of labour in the absence of any maternal of foetal issues that may necessitate birth (Bond 2017) (or until 41 weeks' gestation or more, when induction of labour may be offered).

### Types of outcome measures

(isof.epistemonikos.org).

We adapted the core outcome set agreed by consensus between review authors of the Cochrane Pregnancy and Childbirth systematic reviews for prevention and treatment of gestational diabetes mellitus and pre-existing diabetes. The core outcome set was adapted to ensure that the outcome measures included were appropriate for this research question and all primary outcomes were included in the Summary of Findings Table.

The primary outcomes were:

**Maternal**

1. Maternal mortality or serious maternal morbidity (e.g. cardiac arrest, respiratory arrest, admission to intensive care unit)
2. Caesarean section
3. Instrumental vaginal birth (forceps or vacuum)

**Neonatal**

1. Perinatal mortality rate (corrected, i.e. stillbirth and early neonatal deaths excluding lethal congenital anomalies)
2. Shoulder dystocia
3. Large-for-gestational age (birthweight greater than the 90th centile or as defined by the trial authors)
4. Acidaemia (as evident by a pH of less than 7.0 or a base deficit greater than 12 mmol/L in umbilical arterial cord blood or neonatal blood sample within the first hour of life, or both)

The secondary outcomes were:

**Maternal**

1. Maternal death
2. Cardiac arrest
3. Respiratory arrest
4. Admission to Intensive Care Unit
5. Intact perineum
6. Uterine rupture
7. Postpartum haemorrhage (defined as 1000 mL or more)
8. Postnatal depression (as measured by either the Edinburgh Postnatal Depression Scale, the Postpartum Depression Screening Scale, the Beck Depression Inventory or other validated scales)
9. Maternal satisfaction (as measured by trial authors)
10. Intact perineum

**Neonatal**

1. Brachial plexus injury
2. Bone fracture at birth
3. Intracranial haemorrhage (all grades)
4. Hypoxic ischaemic encephalopathy
5. Respiratory distress syndrome
6. Neonatal hypoglycaemia (blood glucose concentrations below the normal range, investigator defined)
7. Neonatal hyperbilirubinaemia (blood bilirubin concentrations above the normal range, investigator defined)
8. Small-for-gestational age (birthweight below the third centile or as defined by the trial authors)
9. Admission to neonatal ICU
10. Neurosensory disability (defined by a standardised assessment tool at approximately two years of age)

**Health service outcomes**

1. Length of postnatal stay (mother)
2. Length of postnatal stay (baby)
3. Cost

## Methods for identifying studies

See: Additional details: Methods for identifying studies

## Methods for collecting and analysing data

See: Additional details: Methods for collecting and analysing data

# Results

## Results of the search

We did not identify any randomised or non-randomised trials from our searches. Below, Table 1 presents more detail about what we searched for and found. Figure 1 illustrates our inclusion and exclusion process in a study flow diagram. (See Additional Details for a list of all results tables and figures.)

‘Figure 1’ link is the flow chart of included and excluded studies in Additional Details section 3

**Table 1: What review authors searched for and found**

|  |  |  |
| --- | --- | --- |
|  | **What the review authors searched for** | **What the review authors found** |
| ***Study designs*** | Randomised or non-randomised trials of the effects of planned birth versus an expectant approach. | We did not identify any eligible trials. |
| ***Interventions*** | Planned birth (induction of labour or caesarean section) at or near term gestation (37 to 40 weeks’ gestation). | We did not identify any eligible trials. |
| ***Participants*** | Pregnant women, at or near term gestation (37 to 40 weeks' gestation), with pre-existing diabetes (Type 1 or Type 2). | We did not identify any eligible trials. |
| ***Settings*** | Hospital settings in any country. | We did not identify any eligible trials. |
| ***Outcomes*** | *Primary outcomes*  *Maternal*   * Mortality or serious morbidity * Caesarean section * Instrumental vaginal birth (forceps or vacuum)   *Neonatal*   * Perinatal mortality rate (corrected, i.e. stillbirth and early neonatal deaths excluding lethal congenital anomalies) * Shoulder dystocia * Large-for-gestational age (birthweight greater than the 90th centile or as defined by the trial authors) * Acidaemia (as evident by a pH of less than 7.0 or a base deficit greater than 12 mmol/L in umbilical arterial cord blood or neonatal blood sample within the first hour of life, or both) | We did not identify any eligible trials. |

**Figure 1.** Study flow diagram of searches conducted for this update: How the authors selected the studies to be included in the review

**Table 2.** Characteristics of included studies: Details of the studies that the authors agreed to include in this review, according to the methods described for collecting and analysing data

**Table 3.** Characteristics of excluded studies: Details of the studies that the authors agreed to not include in this review

**Table 4.** Characteristics of ongoing studies

**Table 5.** Risk of bias of included studies: Details about the authors’ judgments about the risk of bias in the included studies

**Figure 2.** Risk of bias summary

## Effects of interventions

Effects according to outcome:

Summary of findings 1: *This table presents the effects of planned birth versus expectant approach for pregnant women with pre-existing diabetes*

Overview of analyses (with forestplots)

There were no eligible trials identified.

We identified one completed trial (Henry 1992) which is awaiting assessment. This trial was designed to compare elective induction of labour with expectant management for reducing the incidence of caesarean birth in pregnant women with insulin-requiring gestational diabetes or pre-existing diabetes. However, to date, published results do not separate the data of pregnant women with pre-existing diabetes and women with gestational diabetes.

# Discussion

## Key findings and certainty of the evidence

To date, no results from randomised trials have been published relating to the effect of planned birth at or near term gestation, compared with an expectant approach, for improving health outcomes for pregnant women with pre-existing diabetes and their babies. This review demonstrates the urgent need for such trials.

## Applicability of evidence

**Table 2:** *Applicability of evidence*

|  |  |
| --- | --- |
| Findings | *Interpretation* |
|  |  |
|  |  |
|  |  |
|  |  |

## Agreements and disagreements with other studies or reviews

**Table 3:** *Agreements and disagreements with other studies or reviews*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Author / Year | Effects reported? | Safety  reported? | Study types included | No. of  included studies | Summary of main findings |
|  |  |  |  |  |  |
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# Authors’ conclusions

## Implications for practice

There is no evidence from randomised trials to inform implications for practice. It is beyond the scope of this review to identify other sources of evidence, as they have not been considered for inclusion.

## Implications for research

**Table 6:** *Implications for research*

|  |  |
| --- | --- |
| **Trialists** | This review demonstrates the urgent need for high-quality trials evaluating the effectiveness of planned birth at or near term gestation for women with Type 1 or Type 2 diabetes, compared with an expectant approach. However, the equipoise on optimal approach must be considered when planning such trials and attention must be given to strategies to optimise the recruitment of women to such studies. |
| **Systematic  reviewers** | When new trials become available, there will be a need to synthesize the resultsin a systematic review. Trialists may consider adopting a 'living review' approach and conduct an individual patient data analysis of similar trials conducted around the world. |
| **Other researchers** | The needs, values and preferences of women with pre-existing diabetes with respect to their birth experiences requires further evaluation through qualitative research. |

# References

Jump to: Included studies | Excluded studies | Ongoing studies | Other references | Other published versions of this review

## Included studies

## Excluded studies

Alberico 2017

Alberico S, Erenbourg A, Hod M, Yogev Y, Hadar E, Neri F, et al. Immediate delivery or expectant management in gestational diabetes at term: the ginexmal randomised controlled trial. BJOG: an international journal of obstetrics and gynaecology 2017;124(4):669‐77.

Maso G, Alberico S, Wiesenfeld U, Ronfani L, Erenbourg A, Hadar E, et al. GINEXMAL RCT: induction of labour versus expectant management in gestational diabetes pregnancies. BMC Pregnancy and Childbirth 2011;11:31.

NCT01058772. GINEXMAL RCT: Induction of labour versus expectant management in gestational diabetes pregnancies. clinicaltrials.gov/ct2/show/NCT01058772 Vol. (first received 26 January 2010).

Dhaneshwor 2011

Dhaneshwor P, CTRI/2011/12/002290. Gestational diabetes well controlled on medical nutritional therapy: a randomized trial of active induction of labour compared with expectant management. ctri.nic.in/Clinicaltrials/pmaindet2.php?trialid=3618 (first received 26 December 2011).

Ghosh 1979

Ghosh S, Khakoo H, Pillari VT, Carmona RA, Rajegoda BK, Poliak A. Timing of delivery in rigidly controlled class B diabetes [abstract]. 9th World Congress of Gynecology and Obstetrics; 1979 October 26‐31; Tokyo, Japan. 1979:270-1.

Khojandi 1974

Khojandi M, Tsai AY/M, Tyson JE. Gestational diabetes: the dilemma of delivery. Obstetrics & Gynecology 1974;43:1‐6.

Worda 2017

Husslein P, NCT01256892. Insulin dependent gestational diabetes mellitus: randomized trial of induction of labour at 38 and 40 weeks of gestation. clinicaltrials.gov/ct2/show/NCT01256892 (first received 7 December 2010).

Worda K, Bancher-Todesca D, Husslein P, Worda C, Leipold H. Randomized controlled trial of induction at 38 weeks versus 40 weeks gestation on maternal and infant outcomes in women with insulin-controlled gestational diabetes. Wiener Klinische Wochenschrift 2017;129 (17-18):618-24.

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## Studies awaiting classification

Henry 1992

Henry OA, Kjos SL, Montoro M, Buchanan TA, Mestman JH. Randomized trial of elective induction vs expectant management in diabetics. American Journal of Obstetrics and Gynecology 1992;166: 304.

Kjos SL, Henry OA, Montoro M, Buchanan TA, Mestman JH. Insulin‐requiring diabetes in pregnancy: a randomized trial of active induction of labour and expectant management. American Journal of Obstetrics and Gynecology 1993;169: 611-5.

## Ongoing studies

## Other references

ACOG 2005

American College of Obstetricians and Gynecologists. Pregestational diabetes mellitus: ACOG Practice Bulletin Number 60. Obstetrics & Gynecology 2005;105(3):675-85.

ACOG 2013

American College of Obstetricians and Gynecologists Committee on Obstetric Practice. The society for Maternal-Fetal Medicine. Non-medically Indicated Early-Term Deliveries. Committee Opinion. Number 561 2013 (Reaffirmed 2015).

ADA 2016

American Diabetes Association. Classification and diagnosis of diabetes. Sec. 2 In Standards of Medical Care in Diabetes. Diabetes Care 2016;39(Suppl 1):S13-S22.

Albrecht 2010

Albrecht SS, Kuklina EV, Bansil P, Jamieson DJ, Whiteman MK, Kourtis AP, et al. Diabetes trends among delivery hospitalizations in the US, 1994-2004. Diabetes Care 2010;33:768-73.

Balsells 2009

Balsells M, Garcia-Patterson A, Gich I, Corcoy R. Maternal and fetal outcome in women with type 2 versus type 1 diabetes: a systematic review and metaanalysis. Journal of Clinical Endocrinology and Metabolism 2009;94(11):4284-91.

Biesty 2018

Biesty LM, Egan AM, Dunne F, Dempsey E, Meskell P, Smith V, et al. Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012910. DOI: 10.1002/14651858.CD012910.

Bond 2017

Bond DM, Middleton P, Levett KM, van der Ham DP, Crowther CA, Buchanan SL, et al. Planned early birth versus expectant management for women with preterm prelabour rupture of membranes prior to 37 weeks' gestation for improving pregnancy outcome. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD004735. DOI: 10.1002/14651858.CD004735.pub4.

Boulvain 2016

Boulvain M, Irion O, Dowswell T, Thornton JG. Induction of labour at or near term for suspected fetal macrosomia. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD000938. DOI: 10.1002/14651858.CD000938.pub2.

Brudenell 1989

Brudenell M, Doddridge M. Delivering the infant. In: Lind T, editor(s). Current Reviews in Obstetrics and Gynecology. Diabetic Pregnancy. Vol. 13. New York: Churchill Livingstone, 1989:70-83.

Bytoft 2016

Bytoft B, Knorr S, Vlachova Z, Jensen RB, Mathiesen ER, Beck-Nielsen H, et al. Long-term cognitive implications of intrauterine hyperglycaemia in adolescent offspring of women with Type I Diabetes (The EPICOM Study). Diabetes Care 2016;39(8):1356-63.

Catalano 2011

Catalano PM, Hauguel-de Mouzon S. Is it time to revisit the Pedersenhypothesis in the face of the obesity epidemic? American Journal of Obstetrics and Gynecology 2011;204(6):479-87.

Correa 2015

Correa A, Bardenheier B, Elixhauser A, Geiss LS, Gregg E. Trends in prevalence of diabetes among delivery hospitalizations, United States, 1993–2009. Maternal and Child Health Journal 2015;19:635-42.

Cousins 1987

Cousins L. Pregnancy complications among diabetic women: review 1965-1985. Obstetrical & Gynecological Survey 1987;42:140-9.

Dabelea 2000

Dabelea D, Knowler WC, Pettitt DJ. Effect of diabetes in pregnancy on offspring: follow-up research in the Pima Indians. Journal of Maternal-Fetal Medicine 2000;9(1):83-8.

Dodd 2014

Dodd JM, Deussen AR, Grivell RM, Crowther CA. Elective birth at 37 weeks’ gestation for women with an uncomplicated twin pregnancy. Cochrane Database of Systematic Reviews 2014, Issue 2. Art. No.: CD003582. DOI: 10.1002/14651858.CD003582.pub2.

Dunne 2009

Dunne FP, Avalos G, Durkan M, Mitchell Y, Gallacher T, Keenan M, et al. ATLANTIC DIP: pregnancy outcome for women with pregestational diabetes along the Irish Atlantic seaboard. Diabetes Care 2009;32(7):1205-6.

Egan 2015

Egan AM, Murphy HR, Dunne FP. The management of Type I and Type II diabetes in pregnancy. Quarterly Journal of Medicine 2015;108(12):923-7.

EPOC 2016

Effective Practice and Organisation of Care (EPOC). What study designs should be included in an EPOC review? EPOC Resources for review authors 2016;Oslo: Norwegian Knowledge Centre for the Health Services.

Evers 2002

Evers IM, de Valk HW, Mol BW, ter Braak EW, Visser GH. Macrosomia despite good glycaemic control in Type I diabetic pregnancy; results of a nationwide study in the Netherlands. Diabetologia 2002;45:1484-9.

Farrar 2016

Farrar D, Tuffnell DJ, West J, West HM. Continuous subcutaneous insulin infusion versus multiple daily injections of insulin for pregnant women with diabetes. Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD005542. DOI: 10.1002/14651858.CD005542.pub3.

Feig 2015

Feig DS, Corcoy R, Jensen DM, Kautzky-Willer A, Nolan CJ, Oats JJ, et al. International Association of Diabetes in Pregnancy Study Group (IADPSG) Working Group on Outcome Definitions. Diabetes/metabolism Research and Reviews 2015;31(7):680-90.

Gulmezoglu 2012

Gülmezoglu AM, Crowther CA, Middleton P, Heatley E. Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD004945. DOI: 10.1002/14651858.CD004945.pub3.

Hanson 1993

Hanson U, Persson B. Outcome of pregnancies complicated by type 1 insulin-dependent diabetes in Sweden: acute pregnancy complications, neonatal mortality and morbidity. American Journal of Perinatology 1993;10:330-3.

Higgins 2011

Higgins JP, Green S, editor(s). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook-5-1.cochrane.org.

Hunter 1989

Hunter DJS. Diabetes in Pregnancy. In: Chalmers I, Enkin MW, Keirse MJNC, editor(s). Effective Care in Pregnancy and Childbirth. Oxford: Oxford University Press, 1989.

Inkster 2006

Inkster ME, Fahey TP, Donnan PT, Leese GP, Mires GJ, Murphy DJ. Poor glycated haemoglobin control and adverse pregnancy outcomes in type 1 and type 2 diabetes mellitus: systematic review of observational studies. BMC Pregnancy and Childbirth 2006;6:30.

Irion 1998

Irion O, Boulvain M. Induction of labour for suspected fetal macrosomia. Cochrane Database of Systematic Reviews 1998, Issue 2. Art. No.: CD000938. DOI: 10.1002/14651858.CD000938.

Ju 2009

Ju H, Chadha Y, Donovan T, O'Rourke P. Fetal macrosomia and pregnancy outcomes. Australian & New Zealand Journal of Obstetrics & Gynaecology 2009;49(5):504-9.

Khireddine 2013

Khireddine I, Le Ray C, Dupont C, Rudigoz RC, Bouvier-Colle MH, Deneux-Tharaux C. Induction of labor and risk of postpartum hemorrhage in low risk parturients. PLOS One 2013;8(1):e54858.

Macer 1992

Macer JA, Macer CL, Chan LS. Elective induction versus spontaneous labor: a retrospective study of complications and outcome. American Journal of Obstetrics and Gynecology 1992;166:1690-7.

Macintosh 2006

Macintosh MC, Fleming KM, Bailey JA, Doyle P, Modder J, Acolet D, et al. Perinatal mortality and congenital anomalies in babies of women with type 1 or type 2 diabetes in England, Wales, and Northern Ireland: population based study. BMJ 2006;333(7560):177.

Maresh 2015

Maresh MJ, Holmes VA, Patterson CC, Young IS, Pearson DW, Walker JD, et al. Diabetes and pre-eclampsia Intervention Trial Study Group. Glycaemic targets in the second and third trimester of pregnancy for women with Type I diabetes. Diabetes Care 2015;38(1):34-42.

Middleton 2016

Middleton P, Crowther CA, Simmonds L. Different intensities of glycaemic control for pregnant women with pre-existing diabetes. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD008540. DOI: 10.1002/14651858.CD008540.pub4.

Murphy 2010

Murphy HR, Roland JM, Skinner TC, Simmons D, Gurnell E, Morrish J, et al. Effectiveness of a regional prepregnancy care program in women with Type I and Type II diabetes: benefits beyond glycaemic control. Diabetes Care 2010;33(12):2514-20.

NICE 2015

National Institute for Health and Care Excellence (NICE) and National Collaborating Centre for Women and Children's Health Project Team. Diabetes in pregnancy: Management of diabetes and its complications from pre-conception to the postnatal period. NICE guideline (NG3). Available from nice.org.uk/guidance/ng3 2015.

Owens 2015

Owens LA, Sedar J, Carmody L, Dunne F. Comparing type 1 and type 2 diabetes in pregnancy- similar conditions or is a separate approach required? BMC Pregnancy and Childbirth 2015;15:69.

Pedersen 1952

Pedersen J. Diabetes and pregnancy: Blood sugar of newborn infants. Ph.D Thesis, Danish Science Press; Copenhagen 1952.

Pedersen 1967

Pedersen J. The pregnant diabetic and her newborn: problems and management. In: The Pregnant Diabetic and Her Newborn. Baltimore: Wiliams & Wilkins, 1967:128-37.

Perlow 1996

Perlow JH, Wigton T, Hart J, Strassner HT, Nageotte MP, Wolk BM. Birth trauma: a five-year review of incidence and associated perinatal factors. Journal of Reproductive Medicine 1996;41:754-60.

RevMan 2014

Review Manager 5 (RevMan 5) [Computer program]. Version 5.3. Copenhagen: Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

St Vincent Declaration 1990

World Health Organization (Europe) and International Diabetes Federation (Europe). Diabetes care and research in Europe: the Saint Vincent Declaration. Diabetic Medicine 1990;7(4):360.

WHO 2014

World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy: a World Health Organization Guideline. Diabetes Research and Clinical Practice 2014;103(3):341-63.

Zaccardi 2016

Zaccardi F, Webb DR, Yates T, Davies MJ. Pathophysiology of type 1 and type 2 diabetes mellitus: a 90-year perspective. Postgraduate Medical Journal 2016;92(1084):63-9.

Zhu 2016

Zhu Y, Zhang C. Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective. Current Diabetes Reports 2016;6:7.

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

## ADDITIONAL DETAILS

1. Methods details
   1. Methods for identifying studies
      1. Electronic searches
      2. Searching other resources

## Methods for collecting and analysing data

* 1. Selection of studies
  2. Data extraction and management
  3. Assessment of risk of bias in included studies
  4. Measures of treatment effect
  5. Unit of analysis issues
  6. Dealing with missing data
  7. Assessment of heterogeneity
  8. Data synthesis
  9. Subgroup analysis and investigation of heterogeneity
  10. Sensitivity analysis
  11. Summary of findings table

1. Study characteristics
   1. Table 1. What the review authors searched for and found
   2. Figure 1. Study flow diagram of searches conducted for this update
   3. Table 2. Characteristics of included studies
   4. Table 3. Characteristics of excluded studies
   5. Table 4. Characteristics of ongoing studies
2. Risk of Bias
   1. Table 5. Risk of bias of included studies
   2. Figure 2. Risk of bias summary
3. Evidence tables
   1. Summary of Findings table
   2. GRADE Evidence Profile
4. Analyses with forest plots
5. Appendices
   1. Appendix 1: Pathophysiology of pre-existing diabetes
   2. Appendix 2: Search terms for ICTRP and ClinicalTrials.gov

# 1. Methods details

## a. Methods for identifying studies

*Electronic searches*

We searched Cochrane Pregnancy and Childbirth’s Trials Register by contacting their Information Specialist (15 August 2017).

The Register is a database containing over 24,000 reports of controlled trials in the field of pregnancy and childbirth. For full 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 to the editorial information about the Cochrane Pregnancy and Childbirth in the Cochrane Library and select the 'Specialized Register' section from the options on the left side of the screen.

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

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

Two people screen the search results and review the full text of all relevant trial reports identified through the searching activities described above. 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 (Excluded studies; Studies awaiting classification).

In addition, we searched ClinicalTrials.gov and the WHO International Clinical Trials Registry Platform (ICTRP) for unpublished, planned and ongoing trial reports using the search methods detailed in Appendix 2.

* + 1. *Searching other resources*

We searched the reference lists of retrieved studies. We did not apply any language or date restrictions.

# Methods for collecting and analysing data

## Selection of studies

Two review authors (LB, DD) independently assessed for inclusion all potential eligible studies identified by our search strategy. We planned to resolve any disagreement through discussion or, if required, we planned to consult a third person.

We created a study flow diagram to map out the number of records identified, included and excluded.

There were no studies identified as eligible for inclusion in this review. In future updates, if there are any eligible studies identified for inclusion, we will use the   
following methods.

## Data extraction and management

We will design a form to extract data. For eligible studies, two review authors will extract the data independently using the agreed form. We will resolve discrepancies through discussion or, if required, we will consult a third person. We will pilot test the data extraction tool on two papers prior to the conduct of the full review and amend as necessary.

One review author will enter all data into Review Manager 5 (RevMan 2014) software which will be checked for accuracy against the data extraction sheets by a second review author. Where additional information is needed, we will try to contact authors of the original reports to provide further details. When information regarding any of the above is unclear, we will attempt to contact authors of the original reports to provide further details and will note this contact in the 'Characteristics of included studies' tables.

## Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012948/references#CD012948-bbs2-0030)). We will resolve any disagreement by discussion or by involving a third assessor. The following sections refer to individually randomised trials. If cluster‐randomised trials are included we will use appropriate methods for assessing bias in these designs, as outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012948/references#CD012948-bbs2-0030)). Where information on risk of bias relates to unpublished data or correspondence with trialists, this will be noted in the 'Risk of bias' table.

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

We will describe 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 will assess the method as being at:

* Low risk of bias: e.g. a table of random numbers or computer-generated random numbers.
* High risk of bias: e.g. alternation, date of birth, day of the week, or case record number.
* Unclear risk of bias: if insufficient information was provided.

*Allocation concealment (checking for possible selection bias)*

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

We will assess the methods as being at:

* Low risk of bias: e.g. telephone or central randomisation, consecutively numbered, opaque, sealed envelopes)
* High risk of bias: e.g. open random allocation, unsealed or non-opaque envelopes, alternation, date of birth)
* Unclear risk of bias.

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

We will describe for each included study the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We will consider that studies are at low risk of bias if they were blinded, or if we judge that the lack of blinding would be unlikely to affect results. We will assess risk of detection bias for self‐reported and objective outcome measurement. We will assess the methods as being at:

* Low, high, or unclear risk for participants
* Low, high, or unclear risk for personnel

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

We will describe for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We will consider blinding separately for different outcomes where appropriate (for example, blinding may have the potential to differently affect subjective versus objective outcome measures).

We will assess methods used to blind outcome assessment as being at low, high or unclear risk of bias.

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

We will describe for each included study, and for each outcome or class of outcomes, the completeness of data including attrition and exclusions from the analysis. We will state whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomised women), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information is reported, or can be supplied by the trial authors, we will re-include missing data in the analyses which we undertake. We will assess risk of attrition bias for self-reported and objective outcome measurement.

We will assess methods as being at:

* Low risk of bias (e.g. no missing outcome data; missing outcome data balanced across groups, the proportion of missing data were less than the effect size, i.e. unlikely to overturn the results);
* High risk of bias (For self-reporting outcomes of maternal depression and satisfaction we will judge attrition of > 20% as high risk of bias. For other outcomes, we will explore if numbers or reasons for missing data imbalance across groups; ‘as treated’ analysis done with substantial departure of intervention received from that assigned at randomisation and judge based on these findings);
* Unclear risk of bias

*Selective reporting (checking for reporting bias)*

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

We will assess the methods as being at:

* Low risk of bias (where 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.

*Other bias (checking for bias due to problems not covered by the above)*

We will describe for each included study any important concerns we have about other possible sources of bias.

We will assess whether each study was free of other problems that could put it at risk of bias:

* Low risk of other bias;
* High risk of other bias;
* Unclear whether there is risk of other bias.

*Overall risk of bias*

We will make explicit judgements about whether studies are at high risk of bias, according to the criteria given in the *Handbook* ([Higgins 2011](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012948/references#CD012948-bbs2-0030)). With reference to the above domains, we will assess the likely magnitude and direction of the bias and whether we consider it is likely to impact on the findings. We will explore the impact of the level of bias through undertaking sensitivity analyses ‐ see [Sensitivity analysis](https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012948/full#CD012948-sec3-0017).

## Measures of treatment effect

*Dichotomous data*

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

*Continuous data*

For continuous data, we will use the mean difference if outcomes are measured in the same way between trials. We will use the standardised mean difference to combine trials that measure the same outcome, but use different methods. We will report mean and standardised mean differences with 95% confidence intervals.

## Unit of analysis issues

*Cluster-randomised trials*

We will include cluster-randomised trials 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 (section 16.3.4 or 16.3.6) (Higgins 2011) 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 unlikely.

We will also acknowledge heterogeneity in the randomisation unit and perform a sensitivity analysis to investigate the effects of the randomisation unit.

*Studies with multiple arms*

For studies with multiple treatment arms, we will combine all relevant experimental intervention groups in the study (e.g. groups with different methods for induction of labour) into a single group and all comparable relevant control intervention groups into a single control group and perform a single pair-wise comparison, as recommended in the Cochrane Handbook for Systematic Reviews of Interventions (section 16.5.4) (Higgins 2011).

## Dealing with missing data

For included studies, we will note levels of attrition. We will explore the impact of including studies with high levels of missing data (more than 20%) in the overall assessment of treatment effect by using sensitivity analysis.

For all outcomes, we will carry out analyses, as far as possible, on an intention-to-treat basis, i.e. we will attempt to include all participants randomised to each group in the analyses, and all participants will be analysed in the group to which they were allocated, regardless of whether they received the allocated intervention. The denominator for each outcome in each trial will be the number randomised minus any participants whose outcomes are known to be missing.

## Assessment of heterogeneity

We will assess statistical heterogeneity in each meta-analysis using the Tau2, I2 and Chi2 statistics. We will regard inconsistency as important if I2 is greater than 30% and either Tau2 is greater than zero, or there is a low P value (less than 0.10) in the Chi2 test for heterogeneity.

## Data synthesis

We will carry out statistical analysis using Review Manager 5 (RevMan 2014). We will use fixed-effect meta-analysis for combining data where it is reasonable to assume that studies are estimating the same underlying treatment effect, i.e. where trials are examining the same intervention, and the trials’ populations and methods are judged to be sufficiently similar. If there is clinical heterogeneity sufficient to expect that the underlying treatment effects differ between trials, or if substantial statistical heterogeneity is detected, we will use random-effects meta-analysis to produce an overall summary if an average treatment effect across trials is considered clinically meaningful. The random-effects summary will be treated as the average of the range of possible treatment effects and we will discuss the clinical implications of treatment effects differing between trials. If the average treatment effect is not clinically meaningful we will not combine trials.

If we use random-effects analyses, the results will be presented as the average treatment effect with 95% confidence intervals, and the estimates of Tau2 and I2.

## Subgroup analysis and investigation of heterogeneity

If we identify substantial heterogeneity, we will investigate it using subgroup analyses and sensitivity analyses. We will consider whether an overall summary is meaningful, and if it is, use random-effects analysis to produce it.

We plan to carry out the following subgroup analyses.

1. Women with Type I diabetes versus women with Type 2 diabetes
2. Parity: primiparous women versus multiparous women
3. Birth by planned caesarean section versus planned elective induction of labour

The following outcomes will be used in subgroup analysis.

**Maternal**

1. Maternal mortality or serious maternal morbidity (e.g. cardiac arrest, respiratory arrest, admission to ICU)
2. Caesarean section
3. Instrumental vaginal birth (forceps or vacuum)

**Neonatal**

1. Corrected perinatal mortality rate (stillbirths and early neonatal deaths, excluding lethal congenital anomalies)
2. Shoulder dystocia
3. Large‐for‐gestational age (birthweight greater than the 90th centile or as defined by the trial authors)
4. Acidaemia (as evident by a pH of less than 7.0 or a base deficit greater than 12 mmol/L in umbilical arterial cord blood or neonatal blood sample within the first hour of life, or both

We will assess subgroup differences using interaction tests available within Review Manager 5 (RevMan 2014). We will report the results of subgroup analyses quoting the Chi2 statistic and P value, and the interaction test I2 value.

## Sensitivity analysis

We will conduct a sensitivity analysis based on risk of bias in trials. We will exclude all studies at high or unclear risk of bias for either sequence generation or allocation concealment to see if this makes any difference to the overall results. This is based on growing empirical evidence that these factors are a particularly important potential source of bias (Higgins 2011). We will limit sensitivity analyses to primary outcomes.

## Summary of findings table

We will assess 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 the comparisons of planned birth (induction of labour or caesarean section), at or near term gestation versus an expectation approach.

1. Maternal mortality or serious maternal morbidity (e.g. cardiac arrest, respiratory arrest, admission to ICU)
2. Caesarean section
3. Instrumental vaginal birth (forceps or vacuum)
4. Perinatal mortality rate (corrected, i.e. stillbirth and early neonatal deaths excluding lethal congenital anomalies)
5. Shoulder dystocia
6. Large‐for‐gestational age (birthweight greater than the 90th centile or as defined by the trial authors)
7. Acidaemia (as evident by a pH of less than 7.0 or a base deficit greater than 12 mmol/L in umbilical arterial cord blood or neonatal blood sample within the first hour of life, or both)

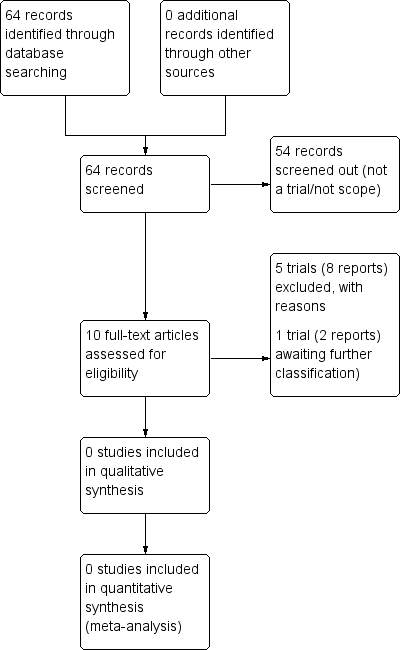
We will use the GRADEpro Guideline Development Tool to import data from Review Manager 5 (RevMan 2014) to create 'Summary of findings' tables. A summary of the intervention effect and a measure of quality for each of the above outcomes will be produced using the GRADE approach. The GRADE approach uses 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 limitations (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.

# Study Characteristics

**Table 1:** *What review authors searched for and found*

Same as above in Full text

**Figure 1.** *Study flow diagram of searches conducted for this review*



**Table 2.** *Characteristics of included studies*

**Key features of the included studies**

No trials were identified for inclusion in this review.

Sort tables by: comparison | study design

***Randomized controlled trials***

| **Study /setting**  **(RCT)** | **Participants** | | | **Interventions and comparisons** | **Outcomes** |
| --- | --- | --- | --- | --- | --- |
| **Inclusion  criteria** | **Exclusion  criteria** | **Enrolled** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

***Observational studies***

| **Study /setting**  **(design)** | **Participants** | | | **Interventions and comparisons** | **Outcomes** |
| --- | --- | --- | --- | --- | --- |
| **Inclusion  criteria** | **Exclusion  criteria** | **Enrolled** |
|  |  |  |  |  |  |
|  |  |  |  |  |  |

**Table 3.** *Characteristics of excluded studies (ordered by study ID)*

|  |  |
| --- | --- |
| **Study** | **Reason for exclusion** |
| Alberico 2017 | This study explores immediate birth versus expectant management for women with gestational diabetes at term. |
| Dhaneshwor 2011 | This study compares expectant management versus induction of labour for women with gestational diabetes. |
| Ghosh 1979 | No further details or publication in the intervening period (38 years). |
| Khojandi 1974 | The focus of this study was women with gestational diabetes. |
| Worda 2017 | This study evaluates the impact of induction of labour on maternal and fetal outcomes in women with insulin-dependent gestational diabetes. |

**Table 4.** *Characteristics of ongoing studies*

| **Study /setting**  **(RCT)** | **Participants** | | | **Interventions and comparisons** | **Outcomes** |
| --- | --- | --- | --- | --- | --- |
| **Inclusion  criteria** | **Exclusion  criteria** | **Enrolled** |
| Henry 1992  Hospital  USA | Women diagnosed before pregnancy with insulin-dependent diabetes mellitus or non-insulin-dependent diabetes mellitus without vascular complications or with gestational diabetes requiring insulin treatment during pregnancy, and with good metabolic control of blood glucose levels.  38 completed weeks gestation (266 days), good compliance with clinical appointments and home blood glucose monitoring, no abnormalities in the twice weekly antepartum assessment with nonstress testing and amniotic fluid volume measurement performed from 34 weeks onward, singleton gestation and cephalic presentation, clinical and ultrasonographic estimation of fetal weight <3800gm at 38 completed weeks with no evidence of intrauterine growth retardation, no other medical or obstetric complications, a candidate for trial of vaginal delivery (no more than 2 previous C-sections). |  | Total N = 200. | Planned birth: labour was induced with intravenous oxytocin in women with favourable Bishops Score (<4), unscarred uteri and normal amniotic fluid indexes (>5.0cms), up to 3 applications of vaginal prostaglandin (3 mg) were used for cervical ripening before oxytocin treatment.  Expectant approach: expectant management consisted of daily split dose insulin therapy and home blood glucose monitoring, weekly antenatal clinic visits, and twice-weekly antepartum testing. Induction of labour indicated by: suspected foetal distress, pre-eclampsia, maternal hyperglycaemia, estimated foetal weight > 4200gm, 42 weeks gestation. | * Mode of delivery * Iinfant birthweight * Macrosomia * Large-for-gestational age * Shoulder dystocia * Birth trauma (bone fracture, Erbs palsy) * Hypoglycaemia * Mortality |

# Risk of Bias

**Figure 2.** *Risk of bias summary*

**Table 5.** *Risk of bias table*

# Evidence tables

* 1. **Summary of findings 1**

Interactive table: isof.epistemonikos.org

Or see:

Isof.epistemonikos.org

For examples

**Table 6.** GRADE evidence profile

# Analyses with forest plots

* 1. *Overview of analyses*

# Appendices

**Appendix 1: Pathophysiology of pre-existing diabetes and pregnancy**

The hyperglycaemia-hyperinsulinaemia hypothesis, also known as the Pederson Hypothesis, aims to explain the underlying pathology that leads to the disordered fetal growth associated with the diabetic pregnancy. It states that "maternal hyperglycaemia results in foetal hyperglycaemia and, hence, in hypertrophy of foetal islet tissue with insulin-hypersecretion. This again means a greater foetal utilisation of glucose" (Pedersen 1952; Pedersen 1967). More recently, it has been suggested that additional factors such as alterations in lipid metabolism and inflammatory change may contribute to the abnormal metabolic environment associated with diabetic pregnancies, particularly when obesity co-exists (Catalano 2011). Such metabolic disruptions can affect organogenesis in early pregnancy, and cardiac malformations in particular are more common in infants of women with diabetes (Inkster 2006). As the pregnancy progresses, this abnormal intrauterine environment may result in the aforementioned neonatal morbidity, including being large-for-gestational age; having neonatal hypoglycaemia, hyperbilirubinaemia, hypocalcaemia; and increased need for admission to an intensive care unit (Macintosh 2006; Dunne 2009; Middleton 2016). It is becoming increasingly evident that exposure to maternal diabetes in utero may also have a longer-term negative impact on the offspring, with one recent study noting that adolescent offspring of women with Type 1 diabetes have lower cognitive function compared with a control group even after adjusting for confounders (Bytoft 2016). In addition, long-term follow up of offspring of women with diabetes reveal that they have elevated rates of obesity and Type 2 diabetes later in life (Dabelea 2000).

Due to the association between hyperglycaemia and poor pregnancy outcomes, pregnant women with diabetes are advised to keep blood glucose levels as close to normal as possible. Frequent capillary blood-glucose monitoring and tight targets such as fasting glucose of less than 5.3 mmol/L (96 mg/dL) and one-hour post prandial of less than 7.8 mmol/L (140 mg/dL) are typically recommended (NICE 2015). While HbA1c is not entirely reliable in pregnancy, higher levels (HbA1c more than 6.0% to 6.5% or more than 42 to 48 mmol/mol) may still be used as a marker of poor glycaemic control and a higher risk pregnancy (Egan 2015; Maresh 2015). In early pregnancy, there is increased insulin sensitivity, lower glucose levels and lower insulin requirements in women with Type 1 diabetes (ADA 2016). During the second and early third trimesters, physiological insulin resistance increases to facilitate the transfer of glucose across the placenta to the fetus and ensure adequate growth and development (Farrar 2016). This creates a significant challenge for women with diabetes who must adjust their treatments regularly to match these increasing insulin requirements and achieve their therapeutic goals. Typically, care of these women involves significant input from a multidisciplinary team of specialists, with intensive monitoring throughout the pregnancy, including frequent ultrasound surveillance of fetal growth (NICE 2015). Unfortunately, the prevalence of large-for-gestational age or macrosomia (or both) remains high in infants of women with diabetes, even in pregnancies that are considered 'well-controlled' (Evers 2002). In the past, some authors have proposed to perform birth before full term in women with pre-existing diabetes, because of increased perinatal mortality during the third trimester (Hunter 1989). This viewpoint is also reflected in current clinical guidelines (NICE 2015).

**Appendix 2: Search terms for ICTRP and ClinicalTrials.gov**

Search strategies to go here – reviewers sometimes present as tables or as text, so this should be clear in the guidance or allow for flexibility

WHO International Clinical Trials Registry Platform (ICTRP)

(we ran each line and alternative spelling separately and then de-duplicated)

GDM AND c(a)esarean

diabetes AND c(a)esarean

diabetic AND c(a)esarean

planned AND birth AND GDM

planned AND birth AND diabetes

planned AND birth AND diabetic

elective AND birth AND GDM

elective AND birth AND diabetes

elective AND birth AND diabetic

induction AND labo(u)r AND diabetes

induction AND labo(u)r AND GDM

Induction AND labo(u)r AND diabetic

expectant AND birth AND GDM

expectant AND birth AND diabetic

expectant AND birth AND diabetes

ClinicalTrials.gov

(we ran each search separately and then de-duplicated)

Advanced search

1.

diabetes OR diabetic OR GDM - Condition

cesarean OR caesarean – Intervention

2.

diabetic OR diabetes OR GDM - Condition

(planned OR elective OR expectant) AND (birth OR delivery) - Intervention

3.

diabetes OR diabetic OR GDM - Condition

induction AND (labour OR labor)

## **\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_**

Additional sections

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## **Authors’ contributions**

Aoife Egan (AE) and Fidelma Dunne (FD) drafted the background section. All other authors contributed to editing the background text. All authors contributed to the drafting of the inclusion criteria for the review. Linda Biesty (LB) and Declan Devane (DD) drafted the methodology and all authors read and commented on this. LB and DD abstracted data including risk of bias. LB wrote the results section, discussion and implications sections with input from all authors. LB is the guarantor of this review.

# Declarations

## **Authors’ declarations of interest**

## Linda M Biesty: none known.

## Aoife M Egan: none known.

## Fidelma Dunne: none known.

## Eugene Dempsey: none known.

## Pauline Meskell: none known.

## Valerie Smith: none known.

## Méabh Ní Bhuinneáin: none known.

## Declan Devane: none known.

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# History

## **Version history**



## **Search history**

## **What’s changed**

## **Difference between protocol and review**

The title has changed from 'Planned elective birth at or near term for improving health outcomes for pregnant women with gestational diabetes', to 'Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants'.

The protocol for this Cochrane review was published in PROSPERO on 16 August 2017 — see http://www.crd.york.ac.uk/PROSPERO/display\_record.asp?ID=CRD42017072476. The protocol was not published in theCochrane Library.

# Messages for Media

# Information for decision-makers

# For patients and the public

## What is a planned birth?

A woman’s pregnancy is considered to be 'at term' when her pregnancy duration reaches 37 weeks. Planned birth involves the early birth of the infant either by induction of labour (artificially inducing labour) or caesarean section. This typically takes place between 37 and 40 weeks’ gestation.

## Who can use or administer a planned birth?

A planned birth requires clinical supervision in hospital. Planned birth can be by elective caesarean section or by induction of labour. Methods of induction vary according to local protocols and typically depend on cervical status. The process generally involves cervical ripening with misoprostol or prostaglandin E2 followed by amniotomy (cutting the membranes) and intravenous oxytocin infusion if labour has not started.

## What other options are there?

An expectant approach to birth includes continued antenatal surveillance and awaiting the spontaneous omset of labour in the absence of any maternal or foetal issues that may necessitate earlier birth. See systematic reviews of other options.

## How do people experience the intervention?

Women with pre-existing diabetes at higher risk of complications than women who do not have diabetes. For example, their babies may be larger and have a higher risk of death in the later weeks of pregnancy. Because of these risks, women with diabetes may select to have a planned birth rather than waiting for labour to start spontaneously. However, induction has the disadvantage of increasing the incidence of forceps or ventouse births, and women often find it difficult to cope with an induced labour. Caesarean section is a major operation which can lead to blood loss, infections and increased chance of problems with subsequence births. Early birth can increase the chance of breathing problems for babies.

## Is there anything else someone should know before using the intervention?

Current guidelines recommend planned birth for women with pre-existing diabetes but the evidence in support of this is currently lacking.What are influenza vaccines?

# For clinical decisions

## Indications and contraindications

## Delivery

## Cautions

## Counselling patients

# For policy decisions

## Policy options

## Equity considerations

## Economic considerations

## Monitoring and evaluation

# Other options

## **Cochrane Reviews of other options for women with pre-existing diabetes**

## **Related systematic reviews**

Planned birth at or near term for improving health outcomes for pregnant women with gestational diabetes and their infants

Linda M Biesty, Aoife M Egan, Fidelma Dunne, Eugene Dempsey, Pauline Meskell, Valerie Smith, G Meabh Ni Bhuinneain, Declan Devane | 5 January 2018

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