Studies on induced labor
Bakker, J.J.H.

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Morning versus evening induction of labour for improving outcomes (Review)

Jannet J.H. Bakker
Birgit Y. van der Goes
Maria Pel
Ben Willem J. Mol
Joris A.M. van der Post

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ABSTRACT

Background Induction of labour is a common intervention in obstetric practice. Traditionally, in most hospitals induction of labour with medication starts early in the morning, with the start of the working day for the day shift. In human and animal studies spontaneous onset of labour is proven to have a circadian rhythm with a preference for start of labour in the evening. Moreover, when spontaneous labour starts in the evening, the total duration of labour and delivery shortens and fewer obstetric interventions are needed. Based on these observations one might assume that starting induction of labour in the evening, in harmony with the circadian rhythm of natural birth, is more beneficial for both mother and child.

Objectives To assess whether induction of labour starting in the evening, coinciding with the endogenous circadian rhythm, improves the outcome of labour compared with induction of labour starting in the early morning, organised to coincide with office hours.

Search methods We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group’s Trials Register (28 February 2012). In addition, we searched MEDLINE (1966 to 16 February 2012) and EMBASE (1980 to 16 February 2012).

Selection criteria We included all published and unpublished randomised controlled trials. We excluded trials that employed quasi-random methods of treatment allocation.

Data collection and analysis Two review authors independently assessed trials for inclusion and risk of bias. Two review authors independently extracted data. Data were checked for accuracy. Where necessary, we contacted study authors for additional information.

Main result The search resulted in 2693 articles that we screened on title and abstract for eligibility. Thirteen studies were selected for full text assessment. We included three randomised trials involving 1150 women. Two trials compared the administration of prostaglandins in the morning versus the evening in women with an unfavourable cervix, and one trial compared induction of labour in the morning versus the evening in women with a favourable cervix and/or ruptured membranes with intravenous oxytocin. Because of the different mechanism, we have reported results for these two comparisons separately. In the two trials comparing prostaglandins in the morning versus the evening there were few clinically significant differences between study groups for maternal or neonatal outcomes. One study reported a statistically significant preference by women to start induction of labour with prostaglandins in the morning. In the trial examining induction of labour with intravenous oxytocin, the number of neonatal admissions was statistically significantly increased in the group of women that started induction in the morning. This finding was unexpected, and while the trial authors offered some possible explanations for this, it is important that any future trials examine neonatal outcomes.
**Authors’ conclusions** Taking into account women’s preferences that favoured administration of prostaglandins in the morning, we conclude that caregivers should preferably consider administering prostaglandins in the morning. There is no strong evidence that induction of labour with intravenous oxytocin in the evening is more or less effective than induction in the morning. Consideration may be given to start induction of labour with oxytocin in the evening when indicated.

**BACKGROUND**

**Description of the condition**

Induction of labour is a common intervention in obstetric practice. In the Western world, labour is induced in one of every four pregnant women for reasons related to increasing risks for the mother, for example, hypertension, pre-eclampsia, diabetes or increasing risks for the fetus such as suspected fetal growth retardation. Moreover the rate of elective inductions i.e. induction without a medical indication, is rising rapidly, Reasons for wanting elective induction at term might include a woman’s physical discomfort, convenience of providers, or concern about the rapid progression of labour away from the hospital. Some clinicians may recommend elective induction due to concern about future complications. There are many different methods used to induce labour. Induction of labour with an unfavourable status of the cervix relies on a very different mechanism and time scale than induction of labour with a ripe favourable cervix and the possibility of artificially rupturing the membranes to induce contractions. In clinical situations medicinal and mechanical methods are used, including sweeping of membranes, the use of vaginal or intracervical prostaglandins, oestrogens, amniotomy, with or without intravenous oxytocin, corticosteroids, misoprostol and extra amniotic Foley catheters (Alfirevic 2006; Boulvain 2001; Boulvain 2005; Boulvain 2008; Bricker 2000; French 2001; Hofmeyr 2003; Howarth 2001; Hutton 2001; Kavanagh 2006a; Kavanagh 2006b; Kelly 2001b; Kelly 2001c; Kelly 2003; Luckas 2000; Muzonzini 2004; Neilson 2000; Thomas 2001). Many non-medical methods have traditionally been used to initiate labour, for example, sexual intercourse, enemas, breast stimulation, acupuncture, homeopathy and castor oil (Kavanagh 2005; Kelly 2001a; Smith 2003; Smith 2004). In most hospitals induction of labour with medication starts early in the morning, with the start of the working day for the day shift. The reason for the choice of this timing is probably the custom to schedule medical interventions and appointments in the morning, and the wish to plan the actual birth between office hours because of the availability of personnel.
Description of the intervention

The intervention was the timing of the start of the induction, in harmony with the circadian rhythm of natural birth, in the evening.

How the intervention might work

In human and animal studies spontaneous onset of labour is proven to have a circadian rhythm with a preference for start of labour in the evening (Backe 1991; Fraser 1989; Fraser 1989; Honnebier 1991; Honnebier 1994; Lindow 2000). The biological explanation for this phenomenon is the increased sensibility of oxytocin receptors in the myometrium of the uterus to maternal oxytocin in the night compared to the daytime. Myometrial contractibility is enhanced not only by increased sensitivity to oxytocin in the evening, but it is also related to an increase in oxytocin receptor concentration. Many other factors might also contribute to this increase of concentration and sensibility including the variation in concentration of steroid hormones in the blood where progesterone, oestrone, oestriol and oestradiol concentration reach their lowest point in the morning (Dodd2006a). So, when spontaneous contractions start in the evening, the total duration of labour and delivery shortens and less obstetric interventions are needed (Heres 2000). Based on these observations, one might assume that starting induction of labour in the evening is more beneficial for both mother and child.

Why it is important to do this review

Starting induction in the evening, to coincide with the endogenous circadian rhythm, might improve the outcome of labour for both mother and child compared with starting induction in the early morning, organised to coincide with office hours. For hospitals staffed 24 hours a day with midwives and doctors, planning induction of labour both in the morning and the evening obviously opens possibilities for a more efficient use of hospital care resources in terms of the use of labour suites.

OBJECTIVES

To assess whether induction of labour starting in the evening improves the outcome of labour compared with induction of labour starting in the morning.
Chapter 3

METHODS

Criteria for considering studies for this review

Types of studies
We included all published and unpublished randomised controlled trials. We excluded trials that employed quasi-random methods of treatment allocation.

Types of participants
Pregnant women with the indication for induction of labour. All methods, medical, non medical or mechanical, used to induce labour could be included.

Types of interventions
The experimental group included women for whom induction was started in the evening compared with a control group of women for whom induction was started in the morning, using the same method of induction.

Types of outcome measures

Primary outcomes
The primary outcome of this review was perinatal mortality, defined as intrauterine deaths plus newborn deaths in the first week of life.

Secondary outcomes

Neonatal outcomes
1. Birth asphyxia as defined by trialist.
2. Admission to neonatal intensive care unit.
5. Use of anticonvulsants.
7. Meconium aspiration syndrome.
8. Pneumonia.
9. Neurodevelopment at childhood follow-up.

Maternal outcomes
1. Mode of delivery.
2. Analgesia used.
3. Perineal trauma.
4. Need for blood transfusion.
5. Use of antibiotics because of signs of intrauterine infection.
6. Duration of birth (as defined by trialist).
7. Prolonged labour (cut off used by trialist).
8. Patient satisfaction.
9. Postnatal depression.

Health services use
1. Length of maternal admission.
2. Length of neonatal admission.

Search methods for identification of studies

Electronic searches
We contacted the Trials Search Co-ordinator to search the Cochrane Pregnancy and Childbirth Group’s Trials Register (28 February 2012). The Cochrane Pregnancy and Childbirth Group’s Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:
1. monthly searches of the Cochrane Central Register of Controlled Trials CENTRAL;
2. weekly searches of MEDLINE;
3. weekly searches of EMBASE;
4. handsearches of 30 journals and the proceedings of major conferences;
5. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL, MEDLINE and EMBASE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the ‘Specialized Register’ section within the editorial information about the Cochrane Pregnancy and Childbirth Group.

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

We searched MEDLINE (1966 to 16 February 2012) and EMBASE (1980 to 16 February 2012).
We did not apply any restrictions on language or year of publication.

Data collection and analysis

Selection of studies
Two review authors (Birgit van der Goes (BG) and Jannet Bakker (JB)) independently assessed for inclusion all the potential studies we identified as a result of the search strategy. We resolved any disagreement through discussion. For the title in French another author (Maria Pel) was asked to confirm the non eligibility. For two titles, one in Japanese (Sekiba 1970) and one in Polish (Ostrowski 1984), we sought help for assessment from medical colleagues who are native speakers outside the team of authors.
Data extraction and management
We designed a form to extract data. For eligible studies, the review authors extracted the data using the agreed form. We resolved discrepancies through discussion. JB is an author of one of the included trials and was not involved in assessing eligibility, risk of bias or in data extraction for this study (Bakker 2009). We entered data into Review Manager software (RevMan 2011) and checked for accuracy.

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). We resolved any disagreement 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 the allocation sequence and determined 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; consecutive numbered sealed opaque envelopes);
- high risk of bias (open random allocation; unsealed or nonopaque 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 are at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results.
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 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. 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 prespecified; 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 sources of 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. We assessed 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.

(7) Overall risk of bias
We made explicit judgements about whether studies are at high risk of bias, according to the criteria given in the Handbook (Higgins 2011). With reference to (1) to (6) above, we assessed the likely magnitude and direction of the bias and whether we considered it is likely to impact on the findings.

Measures of treatment effect

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

Continuous data
For continuous data, we planned to use the mean difference if outcomes were measured in the same way between trials and the standardised mean difference to combine trials that measured the same outcome, but used different methods. As only one trial provided continuous data (Bakker 2009), we used mean difference.

Unit of analysis issues

Cluster-randomised trials
For interventions of this type it may be possible to randomise hospitals or labour wards rather than individual women, and we planned to include cluster-randomised trials in the analyses along with individually-randomised trials. In this version of the review we did not identify any cluster-randomised trials that were eligible for inclusion. In updates of the review if such trials are included we will adjust their sample sizes using the methods described in the Handbook (Higgins 2011) using an estimate of the intra-cluster 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.

Cross-over trials
We have not included cross-over trials as these are not an appropriate study design for the interventions in this review.
Dealing with missing data

For included studies, we noted levels of attrition. For all outcomes, we carried out analyses, 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, and all participants were analysed in the group to which they were allocated, regardless of whether or not they received the allocated intervention. 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 $T^2$, $I^2$ and Chi$^2$ statistics. We regard heterogeneity as substantial if the $I^2$ is greater than 30% and either the $T^2$ is greater than zero, or there is a low P value (less than 0.10) in the Chi$^2$ test for heterogeneity.

Assessment of reporting biases

In this version of the review only three studies contributed data and we were not able to explore possible reporting biases. In updates, if more data become available, for those outcomes where there are 10 or more studies in the meta-analysis, we plan to investigate reporting biases (such as publication bias) by generating funnel plots. We will assess funnel plot asymmetry visually, and where there is any obvious asymmetry, we will use formal tests to test this. For continuous outcomes, we will use the test proposed by Egger 1997 and for dichotomous outcomes, we will use the test proposed by Harbord 2006. If asymmetry is detected in any of these tests, or 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 2011). We used 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 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 range of possible treatment effects and we discussed 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 were presented as the average treatment effect with its 95% confidence interval, and the estimates of $T^2$ and $I^2$. 


Subgroup analysis and investigation of heterogeneity

If we identified substantial heterogeneity, we investigated it using subgroup analyses and sensitivity analyses. We considered whether an overall summary was meaningful, and if it was, used random-effects analysis to produce it.

We planned to carry out the following subgroup analyses:
- primiparae;
- multiparae;
- for each method used to induce labour.

The following outcomes were used in subgroup analysis:
- perinatal mortality;
- mode of delivery;
- duration of labour.

We assessed differences between subgroups by interaction tests.

Sensitivity analysis

We carried out sensitivity analyses to explore the effect of trial quality for important outcomes in the review. Where there was risk of bias associated with a particular aspect of study quality (e.g. inadequate allocation concealment), this was explored by sensitivity analyses in order to assess for any substantive difference to the overall result.

RESULTS

Description of studies

The search of the Cochrane Pregnancy and Childbirth Group’s Trials Register found five trial reports and our additional search in MEDLINE provided 1715 records, EMBASE provided 2307 records. After removal of duplicates two review authors (BG and JB) assessed the remaining 2693 articles on title and abstract for eligibility. For the title in French one of the co-authors (Maria Pel) was asked to assess this study. For two titles, one in Japanese Sekiba 1970 and one in Polish Ostrowski 1984, we sought the help of medical professionals who are native speakers outside the team of authors. We selected 13 studies in total for full text assessment. Furthermore, we screened all references listed in the selected studies; we found no new hits. Two review authors (BG and JB) independently assessed all the potential studies identified as a result of the search strategy. Both review authors used a data form to assess the quality of the studies and to extract data from the included studies. There were three eligible randomised controlled trials. We found no unpublished or ongoing studies on this subject.
Included studies
We included three randomised controlled trials (Bakker 2009; Dodd 2006a; Oei 2000) involving 1150 women. All studies were performed in a hospital setting, two in the Netherlands and one in Australia. Two of them (Dodd 2006a; Oei 2000) used prostaglandins for priming and initiating labour in women with a Bishop’s score less than five or six. The Dodd 2006a trial was nested in the placebo-controlled Milo trial (Dodd 2006b) that randomised women for cervical priming with oral misoprostol solution (20 mcg at two-hour intervals with a maximum of six doses) with PGE2 gel at six-hour intervals with a maximum of six doses with vaginal PGE2 gel. Women who consented to the Milo trial were randomly allocated to admission in the morning or in the evening. The Bakker 2009 trial included women with a favourable cervix or with already ruptured membranes. Induction took place by amniotomy if the membranes were still intact and administration of intravenous oxytocin. All trials were stratified for woman’s parity and included prespecified subgroup analysis for parity.
We did not identify any eligible trials using traditional non clinical methods.
For details of included studies, see Characteristics of included studies.

Excluded studies
We excluded 10 studies. There were many prospective and retrospective cohort studies that focused solely on timing of birth in office hours and studies that compared, in a non randomised manner, timing of spontaneous labour with induced labour. The study of Kupietz 1994 compared women who were induced with prostaglandins in the morning and in the evening but divided the two groups by preference of the woman; we excluded this trial because of this allocation method.
For details of excluded studies, see Characteristics of excluded studies.

Risk of bias in included studies
The trial of Dodd 2006a reports no loss to follow-up. Before the date of scheduled induction, 20% women entered labour spontaneously. There was an unequal division between the groups; 64.5% of these women were scheduled for morning induction and 35.5% women scheduled for evening induction. This was unexpected and thought to reflect the increased ease in scheduling admission in the evening consistent with the unit’s policy and therefore increased time between randomisation and start of induction in the morning group. The authors state that data were analysed on an intention-to-treat basis; data for these women however, were not included in the analysis.
In the trial of Oei 2000, 20% of the randomised women entered into spontaneous labour or the cervix became ripe (Bishops’s score at least six) before the scheduled time of induction and were excluded from secondary analysis. These women were equally distributed over both groups. From the remaining women the authors report no cross-over and no loss to follow-up.
In the trial of Bakker 2009 no losses to follow-up were reported and four women were excluded after randomisation; one was wrongfully included and three women withdrew their consent. Women who entered labour at an earlier time than planned were included in the intention-to-treat analysis. This happened more often in the morning group. This was explained by the authors because of the significantly longer time interval between randomisation and the start of induction in the morning group. There were no women lost to follow-up. Assessment of this trial was done by BG as she was not involved in conducting the trial.

The principal outcome measures may have been affected in the trials that excluded participants following randomisation. Allocation concealment was adequately described in all three trials and concealment was ensured by means of sequentially numbered opaque sealed envelopes.

Due to the nature of the intervention, blinding of treatment allocation was not possible. Although we did not employ any language restrictions in our search for titles, and we considered existence of non published studies with a negative effect to be unlikely, publication bias remains a possibility. Due to the fact that we included only three studies, exploring the possibility of publication bias by generating a funnel plot did not seem sensible.

Effects of interventions

Induction of labour with an unfavourable cervix and a Bishop score lower than five relies on a very different mechanism and time scale than induction of labour with intravenous oxytocin when the woman has a ripe cervix and ruptured membranes. The primary goal of use of prostaglandins is to ripen the cervix which makes it possible to artificially rupture the membranes and induce contractions. Therefore, we reported the outcomes of these two comparisons separately.

Comparison 1. Morning versus evening start of induction with prostaglandins

Two trials with a total of 746 women contributed to this comparison (Dodd 2006a; Oei 2000). The study by Oei 2000 included women with a unfavourable cervix and a Bishop’s score of ≤ five; and primed with PGE2 (0.5 mg) endocervical gel, second administration when needed was after 10 hours and third administration after 48 hours. The trial by Dodd 2006a included women with a Bishops’ score ≤ 6 who consented to the Milo trial (Dodd 2006b); a randomised controlled trial that compared oral misoprostol (20 mcg at two-hour intervals with a maximum of six doses) with PGE2 gel at six-hour intervals with a maximum of six doses. Both trials included women with a vital singleton pregnancy, a gestational age greater than 36+6 weeks, cephalic presentation and a fetus in good condition. Women with any contraindication to vaginal birth, previous uterine surgery (including caesarean section), or ruptured membranes were excluded. Since misoprostol is an E1 prostaglandin analogue we judged it appropriate to combine both trials in the analysis.
The primary outcome of this review was perinatal mortality, defined as intrauterine deaths plus newborn deaths in the first week of life. No such adverse events were reported in the included trials.

Secondary neonatal outcomes
Birth asphyxia was defined by trialists in both included trials as an Apgar score below seven at five minutes. There was no statistical difference between study groups; only one of the trials contributed estimable data (Dodd 2006a) (risk ratio (RR) 0.20, 95% confidence interval (CI) 0.02 to 1.67) Analysis 1.1. Admission to neonatal intensive care was reported in both trials, there was no statistical difference between study groups. There was estimable data for only one of the trials (Dodd 2006a) (RR 0.40, 95% CI 0.04 to 3.87) Analysis 1.2.

The following prespecified secondary neonatal outcomes of this review were not reported: convulsions, encephalopathy, use of anticonvulsants, neonatal admissions, meconium aspiration syndrome, pneumonia and neurodevelopment at childhood follow-up.

Secondary maternal outcomes
Mode of delivery: rates of caesarean section and vaginal instrumental delivery were reported in both trials. Because these variables can interfere with each other and there was substantial heterogeneity ($I^2$: 51% for caesarean section and 86% for instrumental vaginal delivery), we decided not to pool these variables. Possibly, the different basic intervention rates between the Australian population in the study of Dodd 2006a, (24.4% caesarean sections), and the Dutch population in the study of Oei 2000, (15.1% caesarean sections) partly accounts for this heterogeneity. There was no evidence of a difference in the risk for caesarean section between study groups in either of these studies Oei 2000 (RR 1.61, 95% CI 0.70 to 37.4) and Dodd 2006a (RR 0.85, 95% CI 0.64 to 1.12) Analysis 1.3. Although the risk for a instrumental vaginal delivery was statistically significantly higher in the evening group in the trial of Oei 2000 (RR 0.25, 95% CI 0.10 to 0.63), this was not confirmed by the outcome in the larger trial of Dodd 2006a (RR 0.92, 95% CI 0.65 to 1.30) (Analysis 1.4).

In the study by Dodd 2006a, use of epidural anaesthesia was much more common, more than 64% versus 13.5% of the women in the study by Oei 2000. This is in concordance with the difference in daily practices in obstetrics between Australia and the Netherlands. Because of substantial statistical heterogeneity ($I^2$ 61%), we decided not to pool results for this outcome; there was no evidence of a difference in the studies between the morning and the evening group (Oei 2000 (RR 0.49, 95% CI 0.18 to 1.31), Dodd 2006a (RR 1.10, 95% CI 0.98 to 1.24)) Analysis 1.5.

Perineal trauma was not reported in either of the trials.
Need for blood transfusion was only reported in the study by Dodd 2006a, and there was no strong evidence of any difference between groups (RR 0.91, 95% CI 0.32 to 2.59) Analysis
1.6. Use of antibiotics because of signs of intrauterine infection was not reported in either of these trials.

Duration of labour was not reported in these two studies. Because the primary outcome measure of the Dodd 2006a trial was “vaginal birth not achieved within 24 hours”, we decided to report this non-prespecified outcome here. There was no evidence of a difference between study groups; in the subgroup of primiparae (RR 1.00, 95% CI 0.84 to 1.20), and in multiparae (RR 0.92, 95% CI 0.60 to 1.43) Analysis 1.7. The study of Oei 2000 chose “delivery outside office hours” (08:00 to 18:00) as a primary outcome. The number of deliveries outside office hours was similar for women in both groups (RR 1.17, 95% CI 0.83 to 1.65) Analysis 1.8. In this study the authors reported that in nulliparous women, the chance of delivery at night was slightly reduced when endocervical prostaglandin E2 was administered in the evening (RR 0.65, 95% CI 0.29 to 1.5), while in multiparous women the chance of delivery in the evening was significantly reduced (RR 0, 95% CI 0 to 0.71) with no effect on the probability to deliver at night (data not shown in data and analyses tables). Delivery outside office hours was not reported by Dodd 2006a.

Prolonged labour was not reported in either of the trials.

Both studies assessed patient satisfaction by asking the participating women to complete questionnaires for assessment of patient preferences. In the study by Dodd 2006a, all women completed the forms, and in the study by Oei 2000 86% of all women filled in the forms. In the morning group in the study of Oei 2000 2/48 (4.2%) of the women were dissatisfied with the timing of induction versus 12/60 (20%) of the women of the evening group. This was a statistically significant difference (RR 0.21, 95% CI 0.05 to 0.89) Analysis 1.9. Both studies questioned women about the quality of their sleep during the night before delivery. Significantly more women in the evening group reported a bad quality of sleep (average RR 0.24, 95% CI 0.04 to 1.46) Analysis 1.10. There was substantial heterogeneity (I² 69%) so we decided to use the random-effects model.

Postnatal depression was not reported in the trials.

Health service use
Length of maternal or neonatal admission was not reported in the included studies.

Comparison 2. Morning versus evening start of induction with intravenous oxytocin

One study Bakker 2009 with 371 women contributed to this comparison. Women beyond a gestational age of 36 weeks and with a favourable cervix (Bishop score greater than six) or ruptured membranes, with an indication for induction of labour, were randomised to either the evening group (a start of induction of labour at 21:00 hours) or the morning group (start at 07:00 hours).

When the membranes were still intact, they were artificially ruptured. Oxytocin was administered by an intravenous pump infusion. The dosage was raised stepwise according to the protocol, starting with 3.3 mIU oxytocin/minute and a maximum of 33.3 mIU oxytocin/minute, until regular contractions occurred every three to four minutes. Exclusion criteria
were intrauterine fetal death, non reassuring fetal status, contraindication for amniotomy (e.g. HIV positive women), maternal age below 18 years or a history of secondary caesarean section (failed vaginal delivery). Data are presented both by the authors according to the intention-to-treat principle as well as according to the on-protocol principle and for the strata primiparity and multiparity separately. For this review, we used the aggregated data of primi- and multiparae in the intention-to-treat analysis.

**The primary outcome** of this review was perinatal mortality; no such adverse events were reported in this trial.

**Secondary neonatal outcomes**
Birth asphyxia was not statistically significantly different between the study groups; 4/187 children in the morning group versus 2/184 children in the evening group (RR 1.97, 95% CI 0.36 to 10.61) Analysis 2.1.
Admission to the neonatal intensive care unit was not reported separately. Neonatal convulsions, neonatal encephalopathy and use of anti-convulsants were not reported in the trial.
Neonatal admission (defined by trialists as neonatal admissions to the maternity ward, the neonatal medium care or neonatal intensive care) occurred statistically significantly more often when the induction of labour started in the morning; 54/187 children in the morning group versus 36/184 children in the evening group (RR 1.48, 95% CI 1.02 to 2.14 ) Analysis 2.2. Meconium aspiration syndrome, pneumonia and neurodevelopment at childhood follow-up were not reported in the trial.

**Secondary maternal outcomes**
No evidence of a difference in mode of delivery was found between study groups; 23/187 women in the morning group versus 20/184 women in the evening group gave birth with a caesarean section (RR 1.13, 95% CI 0.64 to 1.99) Analysis 2.3 and 26/187 women in the morning group had a vaginal instrumental delivery versus 23/184 women in the evening group (RR 1.11, 95% CI 0.66 to 1.88) Analysis 2.4.
Epidural anaesthesia was not different between study groups; 22/187 women in the morning group versus 25/184 women in the evening group (RR 0.87, 95% CI 0.51 to 1.48) Analysis 2.5.
Perineal trauma and need for blood transfusion were not reported in the trial.
There was no evidence of a difference in rates of use of antibiotics during labour because of signs of intrauterine infection between study groups; 4/187 women in the morning group versus 1/184 women in the evening group (RR 1.97, 95% CI 0.36 to 10.61) Analysis 2.6.
Duration of labour, defined as time between start of labour and time of birth, was the primary outcome of the only study in this comparison Bakker 2009. The intention-to-treat analysis showed no evidence of a difference in both subgroups (primiparae n=242: morning 12 hours and eight minutes versus evening 11 hours and 22 minutes, P value 0.29;
multiparae n = 129: morning seven hours and 34 minutes versus evening seven hours and 46 minutes, P value 0.70) Analysis 2.7. Prolonged labour was not reported in the trial.

In this study patient satisfaction was measured by a postpartum questionnaire. The results showed no evidence of a difference between the study groups, all women in both groups showed signs of fatigue at the start of the induction with Likert scores of 6.6 for the morning group and 7.1 for the evening group on a scale ranging from 1 (extreme fatigue) to 10 (no fatigue at all). All other items, provision of information, level of attendance and care of nurses and staff, scored on average between 8 and 9.

Postnatal depression was not reported in the trial.

Health service use
Length of maternal or neonatal admission was not reported in this included study.

DISCUSSION

Summary of main results

Administering prostaglandins in the morning or the evening showed no clear evidence of a difference for neonatal or maternal outcomes in the two of the included (Dodd 2006a; Oei 2000). This review shows a small but non-significant increased risk for instrumental vaginal delivery after administration of gel in the evening. It is unclear whether this reflects physiologic variations in diurnal rhythm in the onset of labour and timing of spontaneous birth, or reflects the bad quality of sleep of the mother the night before or whether they are a result of diurnal variations in clinical practice. The significantly increased additional use of oxytocin and slightly increased rates of vaginal instrumental deliveries in the evening group may reflect a degree of impatience and pressure to have women give birth at a time more convenient for caregivers during office hours. The only study that looked at timing of delivery during office hours was the study of Oei 2000. They concluded that there was a slight but non-significant reduction of the chance of delivery at night after endocervical administration of prostaglandin E2 in the evening in nulliparous women. The impact on the workload will however be rather limited, especially if one takes into account that administration of the gel itself will increase the workload in the evening and at night. In multiparous women there was a significant reduction in the chance of delivery in the evening after priming in the evening, but there was no effect on the chance of delivery at night. The majority of women were more satisfied with administration of prostaglandins in the morning and reported a better quality of sleep the night before the start of the induction than women admitted in the evening.

The single included study that compared induction of labour with oxytocin in the morning or the evening coinciding with the endogenous circadian rhythm revealed no strong evidence
of differences for maternal and most neonatal outcomes (Bakker 2009). There were no clinically relevant differences in duration of labour, caesarean section or instrumental vaginal delivery rates. Neonatal admission among children of primiparae in the morning group occurred more often, and significantly more of these children were admitted with indications solely provoked by birth, such as asphyxia or signs of infection. The authors give a possible explanation for this unexpected better neonatal outcome for the women induced in the evening; the combination of non-significant factors including reduced amount of oxytocin used, shorter second stage of labour and a reduction in the amount of obstetric intervention needed, might account for this effect. The oxytocin protocol used in this study was a stepwise raised drip, starting with 3.3 mIU oxytocin/minute and a maximum of 33.3 mIU oxytocin/-minute; a different oxytocin regimen might have a different effect on outcomes. Timing of delivery within office hours was not reported in the trial, however, the trial authors concluded that hospitals staffed 24 hours a day with midwives and doctors might benefit by planning induction of labour with oxytocin both in the morning and in the evening so as to make more efficient use of hospital care resources in terms of use of labour suites.

Overall completeness and applicability of evidence
Only three studies with two different comparisons could be included in this review, generating insufficient data to decide in favour of either morning or evening for starting induction of labour.

Quality of the evidence
The methodological quality of the trials was considered good. However, the total of weight of the studies did not provide enough evidence to conclude in favour for a start of induction in the morning or in the evening in either of the comparisons.

Potential biases in the review process
We acknowledge that there is always a possibility of introducing bias at every stage of the reviewing process. We attempted to minimise bias in a number of ways; two review authors assessed independently eligibility for inclusion, carried out data extraction and assessed risk of bias, moreover we did not apply any language restrictions.

Agreements and disagreements with other studies or reviews
To our knowledge there are no other published reviews on this subject. The results of the excluded studies were not in disagreement with the outcomes of this review. In more detail: administering prostaglandins in the morning versus the evening was also studied by Kupietz 1994. This study, with 50 women in each group, had to be excluded from this review because group allocation was not random but by women’s preference. The study focused on duration of labour. The conclusion of this study was, that induction
with prostaglandin PGE2 intra-cervically was more effective in the evening group with a shortening of the first stage by two hours in primiparous women without increasing the rate of complications. The retrospective cohort study of Thorsell 2011, excluded because of the design, involved 1950 women. The time of start of cervical ripening with prostaglandins did not affect the risk of giving birth in the night in primiparous women. For multiparous women, on the other hand, induction in the morning reduced the risk of night-time deliveries. Matijevic 1991 reported results of a case control study with a historical control group. They found significantly fewer out of hours deliveries in primiparous women with a start in the evening (21/32 versus 32/33; P < 0.01) without a difference in rate of complications.

**AUTHORS’ CONCLUSIONS**

**Implications for practice**

Although the women preferred a start in the morning, there was no clear benefit in starting induction of labour with prostaglandin E2 in the evening, compared with starting in the morning. There was no strong evidence that induction of labour with intravenous oxytocin in the evening was any more or less effective than induction in the morning.

**Implications for research**

In the trial examining induction of labour with intravenous oxytocin, the finding that paediatric involvement was increased in the group of women that started induction in the morning was unexpected. The trial authors offered some possible explanations for this, however, any future trials should be sufficiently well powered to address substantive indices of neonatal outcome.

**ACKNOWLEDGEMENT**

We would like to thank Sonja Henderson and her team in Liverpool for all their ongoing technical support and encouragement with completing this review. We thank Rene Spijker, Medical Information Specialist Dutch Cochrane Centre, for performing the additional search in MEDLINE and EMBASE. We would like to acknowledge Dr CR Kowalik for assessment of the Polish reference and Dr Erika Ota for assessment of the Japanese reference.

As part of the pre-publication editorial process, this review has been commented on by four peers (an editor and three referees who are external to the editorial team), a member
of the Pregnancy and Childbirth Group’s international panel of consumers and the Group’s Statistical Adviser.

Cochrane Reviews are regularly updated as new evidence emerges and in response to comments and criticisms, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the Review.’

REFERENCES TO STUDIES INCLUDED IN THIS REVIEW


REFERENCES TO STUDIES EXCLUDED FROM THIS REVIEW


ADDITIONAL REFERENCES


### CHARACTERISTICS OF STUDIES

Characteristics of included studies *ordered by study ID*

**Bakker 2009**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants</td>
<td>371 term pregnant women with an indication for induction of labour with intravenous oxytocin</td>
</tr>
<tr>
<td>Interventions</td>
<td>Start of induction in the evening (21:00 hours). Outcomes</td>
</tr>
<tr>
<td>Duration of labour.</td>
<td></td>
</tr>
<tr>
<td>Instrumental delivery rate.</td>
<td></td>
</tr>
<tr>
<td><strong>Adverse neonatal outcome.</strong></td>
<td></td>
</tr>
<tr>
<td>Indications for paediatric consultations and neonatal admissions</td>
<td></td>
</tr>
<tr>
<td>Duration second stage. Intrapartum infections. Use of pain relief. Patient’s satisfaction.</td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td>Stratification on parity.</td>
</tr>
</tbody>
</table>

#### Bias

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Randomisation was conducted by drawing sequentially numbered sealed opaque envelopes, containing the allocation code, on a two-folded paper, provided by the Data Management Services of the Academic Medical Centre with permuted block randomisation in a 1:1 ratio.”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Quote: “Randomisation was conducted by drawing sequentially numbered sealed opaque envelopes, containing the allocation code, on a two-folded paper, provided by the Data Management Services of the Academic Medical Centre with permuted block randomisation in a 1:1 ratio.”</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Due to the nature of the intervention participants and personnel were not blinded. Staff behaviour may have been affected by the time of induction</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Unclear risk</td>
<td>Due to the nature of the outcome assessor/ statistician was not blinded</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias) All outcomes</td>
<td>Low risk</td>
<td>The data were analysed according to the intention-to-treat principle, there were no withdrawals</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Low risk</td>
<td>All of the study’s pre-specified outcomes and all expected outcomes of interest to the review have been reported. 4 women were excluded after randomisation, selected reporting is however, not likely due to the low numbers</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear risk</td>
<td>None</td>
</tr>
</tbody>
</table>
### Dodd 2006a

<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>620 term pregnant women and an indication for induction with prostaglandins (misoprostol or PGE2)</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Start induction in the evening (20:00 hours).</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Vaginal birth not achieved within 24 hours.</td>
</tr>
<tr>
<td><strong>Neonatal and maternal complications.</strong></td>
<td>Uterine hyperstimulation with associated fetal heart rate changes</td>
</tr>
<tr>
<td><strong>Mode of delivery.</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Stratification on parity.</td>
</tr>
<tr>
<td></td>
<td>Nested trial.</td>
</tr>
<tr>
<td></td>
<td>Randomisation for timing of start induction and type of prostaglandin (misoprostol versus PGE2)</td>
</tr>
</tbody>
</table>

#### Risk of bias

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Support for judgement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “The randomisation schedule was generated by a non clinical researcher using a computer-generated sequence.”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>The allocation was written on a card, folded, and placed inside sequentially numbered, sealed opaque envelopes</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias) All outcomes</td>
<td>High risk</td>
<td>Due to the nature of the intervention participants and personnel were not blinded, staff behaviour may have been affected by the time of induction</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias) All outcomes</td>
<td>Low risk</td>
<td>Due to the nature of the intervention the outcome assessor was not blinded, the statistician was blind to the allocated time of induction</td>
</tr>
</tbody>
</table>

### Oei 2000

<table>
<thead>
<tr>
<th><strong>Methods</strong></th>
<th>Randomised controlled trial.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>158 term pregnant women and an indication for induction with prostaglandins (PGE2)</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>Start induction in the evening (22:00 hours).</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td>Delivery during evening or night hours.</td>
</tr>
<tr>
<td></td>
<td>Time to delivery.</td>
</tr>
<tr>
<td></td>
<td>Use of pain relief.</td>
</tr>
<tr>
<td></td>
<td>Mode of delivery.</td>
</tr>
<tr>
<td></td>
<td>Patient’s preference.</td>
</tr>
<tr>
<td><strong>Notes</strong></td>
<td>Stratification on parity.</td>
</tr>
</tbody>
</table>

#### Risk of bias

<table>
<thead>
<tr>
<th><strong>Bias</strong></th>
<th><strong>Authors’ judgement</strong></th>
<th><strong>Support for judgement</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Quote: “we used simple randomisation with random table numbers.”</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>Concealment was ensured by using of sequentially numbered opaque sealed envelopes</td>
</tr>
</tbody>
</table>
Blinding of participants and personnel (performance bias) All outcomes: High risk. Due to the nature of the intervention participants and personnel were not blinded, staff behaviour may have been affected by the time of induction.

Blinding of outcome assessment (detection bias) All outcomes: Unclear risk. Due to the nature of the outcome assessor/statistician was not blinded.

Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fraser 1989</td>
<td>No comparison; prospective cohort study examining timing start of spontaneous labour</td>
</tr>
<tr>
<td>Kato 1987</td>
<td>Randomised comparison of spontaneous versus induced labour.</td>
</tr>
<tr>
<td>Kupietz 1994</td>
<td>Comparison of 2 groups who were induced with prostaglandins in the morning and in the eveniing</td>
</tr>
<tr>
<td>Levey 2010</td>
<td>No randomisation; comparison of 2 hospital protocols of induction of labour with Prostin</td>
</tr>
<tr>
<td>Matijevic 1991</td>
<td>Case control study, 32 women induced with prostaglandin E2 in the evening were matched with 33 women induced in the morning</td>
</tr>
<tr>
<td>Ostrowski 1984</td>
<td>Non randomised comparison of 2 groups women with different patient characteristics</td>
</tr>
</tbody>
</table>

### DATA AND ANALYSES

**Comparison 1. Morning versus evening start of induction with prostaglandins**

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Apgar less than 7 at 5 minutes</td>
<td>2</td>
<td>746</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.20 [0.02, 1.67]</td>
</tr>
<tr>
<td>2 Admission to NICU</td>
<td>2</td>
<td>746</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.40 [0.04, 3.87]</td>
</tr>
<tr>
<td>3 Caesarean section</td>
<td>2</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>4 Instrumental vaginal delivery</td>
<td>2</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>5 Use of epidural anaesthesia</td>
<td>2</td>
<td></td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>Totals not selected</td>
</tr>
<tr>
<td>6 Need for blood transfusion</td>
<td>1</td>
<td>620</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.91 [0.32, 2.59]</td>
</tr>
<tr>
<td>7 Vaginal birth not achieved 24 hours</td>
<td>1</td>
<td>620</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.98 [0.83, 1.17]</td>
</tr>
<tr>
<td>7.1 Primiparae</td>
<td>1</td>
<td>365</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.00 [0.84, 1.20]</td>
</tr>
<tr>
<td>7.2 Multiparae</td>
<td>1</td>
<td>255</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.92 [0.60, 1.43]</td>
</tr>
<tr>
<td>8 Delivery outside office hours</td>
<td>1</td>
<td>126</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.17 [0.83, 1.65]</td>
</tr>
<tr>
<td>9 Dissatisfaction with time start</td>
<td>1</td>
<td>108</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.21 [0.05, 0.89]</td>
</tr>
<tr>
<td>10 Bad quality of sleep</td>
<td>2</td>
<td>728</td>
<td>Risk Ratio (M-H, Random, 95% CI)</td>
<td>0.24 [0.04, 1.46]</td>
</tr>
</tbody>
</table>
**Comparison 2.** Morning versus evening start of induction with intravenous oxytocin

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apgar score less than 7 at 5</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.97 [0.36, 10.61]</td>
</tr>
<tr>
<td>Neonatal admission</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.48 [1.02, 2.14]</td>
</tr>
<tr>
<td>Caesarean section</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.13 [0.64, 1.99]</td>
</tr>
<tr>
<td>Instrumental vaginal delivery</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.11 [0.66, 1.88]</td>
</tr>
<tr>
<td>Use of epidural anaesthesia</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>0.87 [0.51, 1.48]</td>
</tr>
<tr>
<td>Use of antibiotics because of</td>
<td>1</td>
<td>371</td>
<td>Risk Ratio (M-H, Fixed, 95% CI)</td>
<td>1.97 [0.36, 10.61]</td>
</tr>
<tr>
<td>Duration of labour (minutes)</td>
<td>1</td>
<td>371</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-12.68 [-61.67, 36.31]</td>
</tr>
<tr>
<td>1.1 Primiparae</td>
<td>1</td>
<td>242</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-14.0 [-98.17, 70.17]</td>
</tr>
<tr>
<td>7.2 Multiparae</td>
<td>1</td>
<td>129</td>
<td>Mean Difference (IV, Fixed, 95% CI)</td>
<td>-12.0 [-72.24, 48.24]</td>
</tr>
</tbody>
</table>

**Comparison 1 Prostaglandins for induction of labour, Outcome 1.1 Apgar less than 7 after 5 minutes**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Morning</th>
<th>Evening</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dodd 2006a</td>
<td>62</td>
<td>89</td>
<td>0.80 [0.55, 1.16]</td>
</tr>
<tr>
<td>Oei 2000</td>
<td>11</td>
<td>8</td>
<td>1.76 [0.65, 4.71]</td>
</tr>
</tbody>
</table>

**Comparison 1 Prostaglandins for induction of labour, Outcome 1.3 Caesarean section**

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Morning</th>
<th>Evening</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dodd 2006a</td>
<td>47</td>
<td>62</td>
<td>0.92 [0.65, 1.30]</td>
</tr>
<tr>
<td>Oei 2000</td>
<td>5</td>
<td>23</td>
<td>0.25 [0.10, 0.63]</td>
</tr>
</tbody>
</table>

**Comparison 1 Prostaglandins for induction of labour, Outcome 1.4 Vaginal instrumental delivery**

---

Chapter 3
## Comparison 1: Prostaglandins for Induction of Labour, Outcome 1.7 Vaginal Birth Not Achieved in 24 Hours

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Morning</th>
<th>Evening</th>
<th>Weight</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>0.98 [0.83, 1.17]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **1.7.1 Primiparae**
  - Dodd 2006a
    - Events: 94, Total: 164
  - Subtotal (95% CI)
    - Event: 16, Total: 201
  - Total events: 94
  - Heterogeneity: Not applicable
  - Test for overall effect: Z = 0.02 (P = 0.98)

- **1.7.2 Multiparae**
  - Dodd 2006a
    - Events: 27, Total: 116
  - Subtotal (95% CI)
    - Event: 35, Total: 139
  - Total events: 27
  - Heterogeneity: Not applicable
  - Test for overall effect: Z = 0.35 (P = 0.72)

## Comparison 1: Prostaglandins for Induction of Labour, Outcome 1.10 Bas Quality of Sleep

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Morning</th>
<th>Evening</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>0.24 [0.04, 1.46]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Dodd 2006a**
  - Events: 1, Total: 280
  - Total: 280
  - Heterogeneity: Chi² = 1.26; df = 1 (P = 0.73); I² = 0%
  - Test for overall effect: Z = 1.54 (P = 0.12)
  - Test for subgroup differences: Chi² = 0.11, df = 1 (P = 0.74), I² = 0%

- **Oei 2000**
  - Events: 16, Total: 48
  - Total: 64.0%
  - Heterogeneity: Chi² = 3.27, df = 1 (P = 0.07); I² = 69%
  - Test for overall effect: Z = 1.54 (P = 0.12)

- **Total (95% CI)**
  - Event: 17, Total: 328
  - Total: 100.0%
  - Heterogeneity: Tau² = 1.26; Chi² = 3.27, df = 1 (P = 0.07); I² = 69%
  - Test for overall effect: Z = 1.54 (P = 0.12)

Favours morning Favours evening