

# Elective induction for pregnancies at or beyond 41 weeks of gestation and its impact on stillbirths: a systematic review with meta-analysis

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## Abstract

**Background** An important determinant of pregnancy outcome is the timely onset of labor and birth. Prolonged gestation complicates 5% to 10% of all pregnancies and confers increased risk to both the fetus and mother. The purpose of this review was to study the possible impact of induction of labour (IOL) for post-term pregnancies compared to expectant management on stillbirths.

**Methods** A systematic review of the published studies including randomized controlled trials, quasi-randomized trials and observational studies was conducted. Search engines used were PubMed, the Cochrane Library, the WHO regional databases and hand search of bibliographies. A standardized data abstraction sheet was used. Recommendations have been made for input to the Lives Saved Tool (LiST) model by following standardized guidelines developed by the Child Health Epidemiology Reference Group (CHERG).

**Results** A total of 25 studies were included in this review. Meta-analysis of 14 randomized controlled trials (RCTs) suggests that a policy of elective IOL for pregnancies at or beyond 41 weeks is associated with significantly fewer perinatal deaths (RR=0.31; 95% CI: 0.11-0.88) compared to expectant management, but no significant difference in the incidence of stillbirth (RR= 0.29; 95% CI: 0.06-1.38) was noted. The included trials evaluating this intervention were small, with few events in the intervention and control group. There was significant decrease in incidence of neonatal morbidity from meconium aspiration (RR = 0.43, 95% CI 0.23-0.79) and macrosomia (RR = 0.72; 95% CI: 0.54 – 0.98). Using CHERG rules, we recommended 69% reduction as a point estimate for the risk of stillbirth with IOL for prolonged gestation (> 41 weeks).

**Conclusions** Induction of labour appears to be an effective way of reducing perinatal morbidity and mortality associated with post-term pregnancies. It should be offered to women with post-term pregnancies after discussing the benefits and risks of induction of labor.

## Background

An important determinant of the pregnancy outcome is the timely onset of labor and birth. Both preterm and post-term births are associated with unfavorable maternal and neonatal outcomes. Prolonged gestation complicates 5% to 10% of all pregnancies and confers increased risk to both the fetus and mother [1,2]. In the United States, about 18% of all singleton pregnancies persist beyond 41 weeks, 10% (range, 3% to 14%) continue



those comparing induction at 41 weeks with induction at 42 weeks were excluded.

We graded the

the author(s). Summary estimates were described as risk ratios along with 95% confidence intervals. Fixed models were used for primary analyses. Statistical heterogeneity among trials was assessed by observing the overlap of the confidence intervals among the studies, Chi square value (P-value) of heterogeneity I

prolonged, nulliparous and uncomplicated pregnancies.

concluded that there was no need to consider the expectant management of the post-term pregnancies to be dangerous [41]. Similar conclusion was drawn by a retrospective analysis comparing the outcomes of post-term pregnancies managed actively by labour inductions beginning at 42 weeks with expectant management of

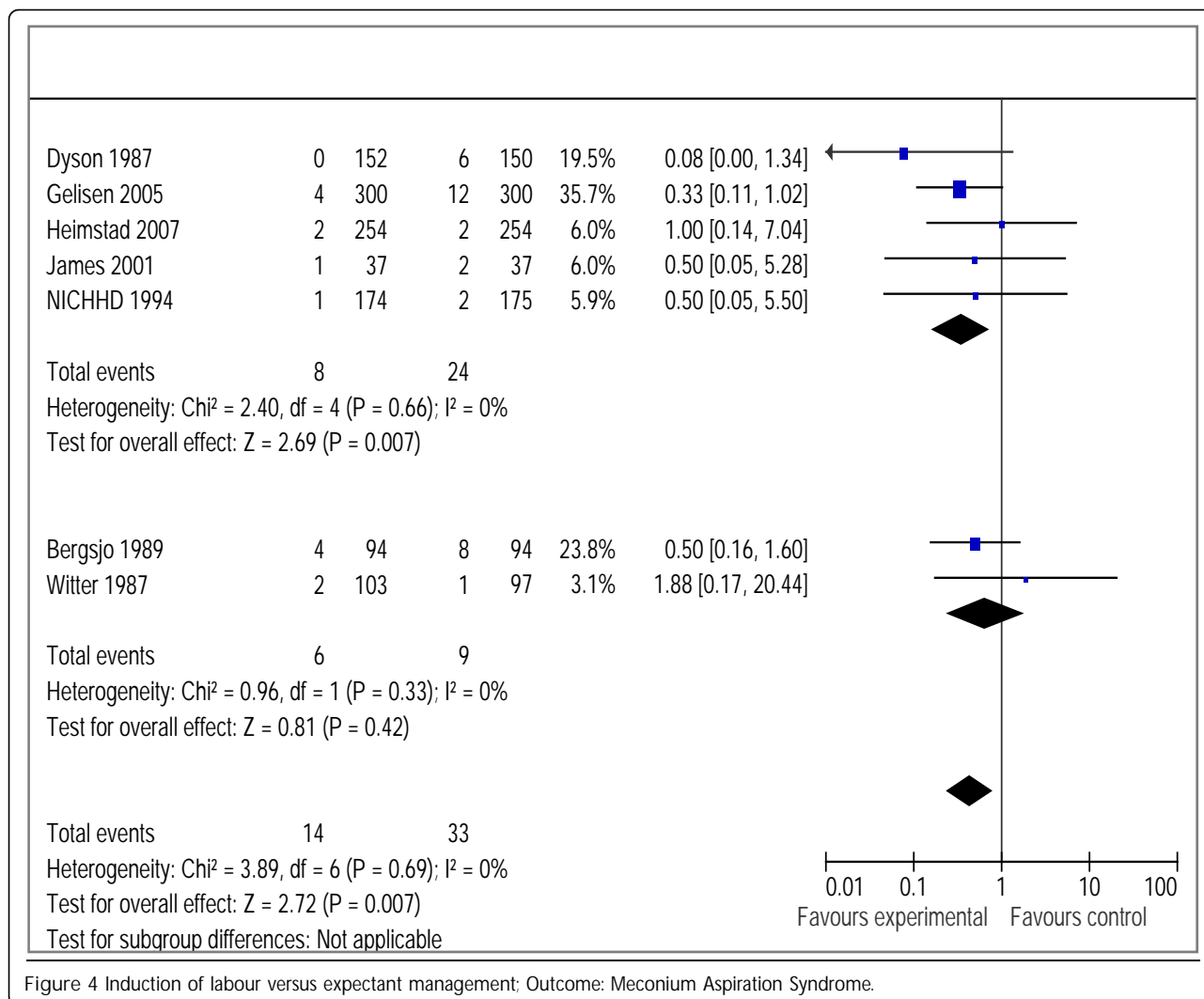


Figure 4 Induction of labour versus expectant management; Outcome: Meconium Aspiration Syndrome.

hospitals and provinces studied. The rate of stillbirth among deliveries at 41 or more weeks' gestation decreased significantly, from 2.8 per 1000 total births in 1980 to 0.9 per 1000 total births in 1995 ( $p < 0.001$ ). The study concluded that the increased rate of labour induction at 41 or more weeks' gestation may have contributed to the decreased stillbirth rates [42]. An observational study compared the impact of IOL with spontaneous onset of labour among post term pregnancies ( $>$  or  $=$  294 days) between July 1980 -December 1984 at Chicago Lying-In Hospital. The study comprised of 12,930 deliveries from which 707 gestations were prolonged (5.5%). Labor started spontaneously in 62%, and 38% underwent induction; the perinatal mortality was 20.5/1000 among those with spontaneous onset of labor while no deaths occurred among those in whom labour was induced. The study concluded that prolonged gestation had a high perinatal morbidity and mortality rate and "active management" (induction at 42 weeks)

prevented perinatal deaths in this group thereby justifying an active approach for post-term pregnancies [43].

#### Discussion

Meta-analyses of randomized controlled trials demonstrate that a policy of induction of labour for pregnancies at or beyond 41 weeks as compared to expectant management of gestation is associated with fewer perinatal deaths, but no significant difference in the rate of stillbirth. The above mentioned results are in accordance to the findings of the Cochrane review by Gulmezoglu et al 2009 [10]. This review included a total of 12 trials and reported a non-significant reduction in stillbirth risk (RR = 0.28, 95% CI: 0.05–1.67), but a statistically significant reduction in perinatal mortality (RR = 0.30, 95% CI: 0.09–0.99). An update of this Cochrane review having 14 trials reports similar results [Stillbirth: 41 complete weeks (RR = 0.29; 95% CI: 0.06 – 1.38), 42 complete weeks (not estimable); perinatal death: 41 complete

weeks (RR = 0.27; 95% CI: 0.08 – 0.98), 42 complete  
weeks (RR = 0.41; 95% CI: 0.06 – 2.73) (Gulmezoglu M



Chanrachkul 2003  
Heimstad 2007

Total events

Heterogeneity: Chi<sup>2</sup> = 0.11, df = 1 (I<sup>2</sup> = 0%)

Gulmezoglu or Sanchez-Ramos review. We have excluded any non-english article that was not translated and for which the abstract did not provide adequate data. The same approach was used by Wennerholm et al. The reviews by Sanchez Ramos et al. or Gulmezoglu et al. did not exclude studies based on this criterion. However, there were no additional studies in either of the latter reviews that were not included in our review. Hence, it is unlikely that we have missed out any clinical trial because it was published in a language other than English.

Table 1 shows the qualitative assessment of overall evidence regarding induction of labor at 41 weeks and beyond. The pooled estimate from 14 randomized controlled trials showed a non-significant reduction in stillbirths [RR = 0.29, 95 % CI 0.06-1.38] and a significant reduction in perinatal mortality [RR = 0.31, 95 % CI 0.11-0.88]. We graded the overall quality of evidence for stillbirths and perinatal mortality as 'moderate'. This assessment was based on the fact that most of the studies were conducted in developed country settings and numbers of events were relatively few in the intervention and control groups. Using CHERG rules, we recommend a reduction in perinatal mortality (i.e. 69 %

as a surrogate for reduction in stillbirths. The reason for recommending perinatal mortality as surrogate for stillbirths was based on the fact most of the studies do not report disaggregated data for stillbirths but do so for perinatal mortality. In order to further support this assumption we pooled the data for early neonatal mortality in the included studies and the results showed a non-significant (RR = 0.37; 95% CI: 0.10 – 1.38) reduction in early neonatal mortality (data not shown). We suggest that the main effect of IOL in the combined outcome of 'perinatal mortality' could be due to stillbirths. Further evidence of effectiveness of IOL at 41 weeks comes from the fact that this approach reduces incidence of morbidities like meconium aspiration syndrome (RR=0.43 95% CI 0.23- 0.79) and macrosomia (RR=0.72 95% CI 0.54-0.98).

As the number of stillbirths in the randomized trials was relatively small, we also included observational studies in our review. Although the quality of evidence derived from observational studies is generally considered poor, it is worth considering data from these studies. The evidence from observational studies included is variable, half of the studies showed a significant difference in the rate of stillbirth and perinatal death for active versus expectant management, thereby advocating the use of



