NICE National Institute for Health and Care Excellence

Appendices A, B and C

Implementation support
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Contents

Appendix A: Risks associated with different induction of labour timing strategies

Where has this data come from?

The information used to generate the data below comes from randomised controlled trials (RCTs) published between 1987 and 2019. RCTs that compared 2 or more induction timing strategies, including those that compared expectant management to a specified time point at which induction then occurred (for example, induction at 40 weeks versus 42 weeks or induction at 39 weeks versus expectant management until 41 weeks) were included. However, studies that compared induction of labour with expectant management with insufficient information to determine the timing of eventual induction in the expectant management group were not included. For full information on each primary study, see evidence review C.

What does this data represent?

This data represents the estimated risks (in other words, the expected increase in actual outcomes) associated with different induction of labour timing strategies, reported by studies that compared 2 timings of induction using any methods broadly in line with those recommended in this guideline. In addition, outcomes that are likely to be the same with different induction of labour timing strategies have also been included.

This information is intended to aid understanding of the evidence reviewed and to support discussions that rely on shared decision making, however the committee did not review the entire body of evidence that could inform a full discussion of the risks at each week (for example non-comparative cohort or cross-sectional studies that report adverse event incidence at each week), therefore this information could not be included here.

Does this mean that continuing pregnancy beyond 41+0 weeks can cause these outcomes?

This data comes from RCTs, which is a study type in which a number of similar people are randomly assigned to 2 (or more) groups to test a specific intervention. Randomisation reduces bias and balances known and unknown participants' characteristics, allowing the attribution of any differences in outcome to the interventions under study. However, this should not be taken as definitive evidence based on the limitations of the included studies. In addition, while the committee agreed that the risk of perinatal mortality, NICU admission, and caesarean birth increases over time with a prolonged pregnancy, the absolute risk remains low.

What were the main limitations of the included studies?

Although all included studies were conducted in high-income countries, they were conducted in a variety of countries (not just the United Kingdom) where healthcare is mainly accessible through private funding and where there are usually fewer midwives available to support women during birth, such as the US. This may have led to an overestimation of certain outcomes, such as caesarean birth. However, the committee agreed that overall the evidence was broadly applicable to the current UK context. Most trials had a large sample size, but were not powered to detect differences in infrequent outcomes, such as adverse neonatal outcomes, which are relatively uncommon. Therefore, the certainty of these outcomes remains unclear.

One included study (SWEPIS study, Wennerholm 2019) was powered for a much larger sample, but was terminated early for ethical reasons due to a significantly higher perinatal death rate in the expectant management (delayed induction) group. The strengths of this study include its large size and relevance to this question. However, the fact that the study was terminated early due to ethical concerns and never reached the sample size intended to power its primary endpoint was a limitation, which may have led to an overestimation of the treatment effect in the intervention group and decreased the precision of the results.

The included studies were also at risk of bias as it was not possible to blind participants or personnel to their allocation. However, for mortality outcomes it was deemed unlikely to bias the results. Evidence was downgraded for imprecision due to wide confidence intervals or small sample size.

These limitations were reflected in the overall quality of the evidence of the studies, acknowledged by the committee and taken into consideration when interpreting the evidence.

Why is there specific data on nulliparous women only but not data on multiparous women only?

One of the included studies (Grobman 2018) included nulliparous women only (defined as no previous pregnancy beyond 20+0 weeks), but the remaining studies included both nulliparous and multiparous women, therefore the data could not be reported for multiparous women only.

Table 1: Outcomes for women that may be more likely with induction at 40-42 weeks (nulliparous women only)

Outcomes	Induction of labour at 39 weeks	Induction of labour at 40-42 weeks	Risk difference
Caesarean birth	About 1,860 per 10,000 women would be expected to have a caesarean birth (so 8,140 would not)	About 2,220 per 10,000 women would be expected to have a caesarean birth (so 7,780 would not)	About 360 more women per 10,000 whose labour was induced at 40-42 weeks would be expected to have a caesarean birth; so for 9,640 per 10,000 the outcome would be the same irrespective of the timing of induction
NICU admission	About 1,170 per 10,000 babies would be expected to be admitted to NICU (so 8,830 would not)	About 1,300 per 10,000 babies would be expected to be admitted to NICU (so 8,700 would not)	About 130 more babies per 10,000 whose mothers' birth was induced at 40-42 weeks would be expected to be admitted to NICU; so for 9,870 the outcome would be the same irrespective of the timing of induction

For sources of risk data, see evidence review C.

Comparison group at 40 to 42 weeks: as specified in the protocol, includes expectant

management to a specified timepoint at which induction then occurs.

Table 2: Outcomes for women that may be more likely with induction at 42 weeks (mixed parity)

Outcomes	Induction of labour at 41 weeks	Induction of labour at 42 weeks	Risk difference
Perinatal death	About 4 per 10,000 babies would be expected to die (so 9,996 would not)	About 35 per 10,000 babies would be expected to die (so 9,965 would not)	About 31 more babies per 10,000 whose mothers gave birth at 42 weeks would be expected to die; so for about 9,969 babies per 10,000 the outcome would be the same irrespective of the timing of induction
NICU admission	About 300 per 10,000 babies would be expected be admitted to NICU (so 9,700 would not)	About 440 per 10,000 babies would be expected to be admitted to NICU (so 9,560 would not)	About 140 more babies per 10,000 whose mothers gave birth at 42 weeks would be expected to be admitted to NICU; so for about 9,860 babies per 10,000 the outcome would be the same irrespective of the timing of induction

For sources of risk data, see evidence review C.

Comparison group at 42 weeks: as specified in the protocol, includes expectant management to a specified timepoint at which induction then occurs.

Table 3: Outcomes for women that may be more likely with induction at 43 weeks (mixed parity)

Outcomes	Induction of labour at 42 weeks	Induction of labour at 43 weeks	Risk difference
Caesarean birth	About 1,330 per 10,000 women would be expected to have a caesarean birth (so 8,670 would not)	About 2,040 per 10,000 women would be expected to have a caesarean birth (so 7,960 would not)	About 710 more women per 10,000 would be expected to have a caesarean birth; so for about 9,290 the outcome would be the same irrespective of the timing of induction

For sources of risk data, see evidence review C.

Comparison group at 43 weeks: as specified in the protocol, includes expectant management to a specified timepoint at which induction then occurs.

Table 4: Outcomes for women that are likely to be the same with induction at 39 weeks and 40-42 weeks (nulliparous women only)

Outcomes
• Maternal death • Perinatal death • Meconium aspiration syndrome (MAS) • Hypoxic-ischaemic encephalopathy (HIE) • Instrumental vaginal birth For sources of risk data, see evidence review C. Comparison group at 40 to 42 weeks: as specified in the protocol, includes expectant management to a specified timepoint at which induction then occurs.

Table 5: Outcomes for women that are likely to be the same with induction at 41 weeks and 42 weeks (mixed parity)

Outcomes

- Maternal death
- Caesarean birth
- Instrumental vaginal birth
- Unassisted vaginal birth
- Meconium aspiration syndrome (MAS)
- Hypoxic-ischaemic encephalopathy (HIE)

For sources of risk data, see evidence review C.

Comparison group at 42 weeks: as specified in the protocol, includes expectant management to a specified timepoint at which induction then occurs.

Table 6: Outcomes for women that are likely to be the same with induction at 42 weeks and 43 weeks (mixed parity)

Outcomes

- Perinatal death
- Instrumental vaginal birth
- Unassisted vaginal birth
- Neonatal intensive unit (NICU) admission
- Meconium aspiration syndrome (MAS)
- Hypoxic-ischaemic encephalopathy (HIE)

For sources of risk data, see evidence review C.

Comparison group at 43 weeks: as specified in the protocol, includes expectant management to a specified timepoint at which induction then occurs.

Appendix B: Risks and benefits of induction of labour compared to expectant management for suspected fetal macrosomia (in women without diabetes)

Table 7: Outcomes for babies and women

Outcome	Induction of labour	Expectant management	Risk difference
Shoulder dystocia	About 410 babies would per 10,000 would be expected to have a shoulder dystocia (so 9,590 would not)	About 680 babies per 10,000 would be expected to have a shoulder dystocia (so 9,320 would not)	About 270 more babies per 10,000 whose mother's birth was managed expectantly would be expected to have a shoulder dystocia; so for 9,730 the outcome would be the same irrespective of the management strategy
Third or fourth degree perineal tears	About 260 per 10,000 women would be expected to have third or fourth degree tears (so 9,740 would not)	About 69 per 10,000 women would be expected to have third or fourth degree tears (so 9,931 would not)	About 191 women whose labour was induced would be expected to have third or fourth degree tears; so for 9,809 the outcome would be the same irrespective of the management strategy

For sources of risk data, see evidence review A.

Table 8: Outcomes for babies and women that are likely to be the same with induction of labour and expectant management

Outcomes

- Perinatal death
- Brachial plexus injury
- Caesarean birth

For sources of risk data, see evidence review A.

Appendix C: Risks of hyperstimulation associated with different pharmacological methods of inducing labour

Table 9: Risks of hyperstimulation with dinoprostone and misoprostol

Preparation (dose or type)	Risk of hyperstimulation with fetal heart rate changes compared to placebo in women with a Bishop score of 6 or less (OR, 95% Credible Interval)
Oral misoprostol (under 50 micrograms)	1.54 (0.32 to 7.60)
Titrated oral (low dose) misoprostol	1.96 (0.65 to 8.12)
Vaginal dinoprostone tablet	2.22 (0.59 to 6.03)
Oral misoprostol (50 micrograms or more)	3.09 (1.10 to 9.19)
Vaginal dinoprostone gel	3.45 (1.24 to 10.53)
Vaginal misoprostol (under 50 micrograms)	4.12 (1.57 to 11.60)
Vaginal dinoprostone pessary (slow release)	4.98 (1.82, 15.01)
Vaginal misoprostol (50 micrograms or more)	5.92 (2.26, 16.81)

Preparation (dose or type)	Risk of hyperstimulation with fetal heart rate changes compared to placebo in women with a Bishop score of 6 or less (OR, 95% Credible Interval)
Buccal/sublingual misoprostol	7.07 (2.22, 24.45)

For sources of data and more complete information on risks of hyperstimulation, see evidence review B.

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