UNIVERSITY
OF OSLO

Master thesis

Cost Effectiveness Analysis of Elective Inductions in low-risk Nulliparous Women in Norway

A model-based study

Lana Vidmar

Health Economics, Policy and Management - Economic Evaluation in Healthcare

30 ECTS

Institute of Health and Society

Faculty of Medicine

Cost Effectiveness Analysis of Elective Inductions in low-risk Nulliparous Women in Norway – A model-based study

Author: Lana Vidmar

Thesis supervisor: Professor Lumbwe Chola

Master Thesis

Department of Health Management and Health Economics

Faculty of Medicine

University of Oslo

November 2023

Abstract

Background: *Previous studies have indicated that elective induction of labor at 39 weeks of gestation for low-risk nulliparous women can be cost-effective. However, the health-related outcomes proved to be difficult to generalize across populations, and cost related outcomes depend on the healthcare system settings. Therefore, an update is necessary to assess the local context and draw valid conclusions.*

Objective: *The objective of this study was to assess the cost-effectiveness of elective induction of labor for low-risk nulliparous women in Norway in comparison to expectant management from the health payer perspective. Additionally, this study aimed to determine the optimal time to induce labor: at 39 weeks or at 40 weeks.*

Methods: *Two decision analytic models were developed in Microsoft Excel. One model compared elective induction of labor at 40 weeks of gestation for the hypothetical cohort of 15 000 low-risk nulliparous women versus expectant management until induction at week 41. The second model was informed by the best outcome decision in week 40 and compared induction of labor at 39 weeks of gestation versus continued expectant management. Observed effects were health outcomes as measured by QALY and cesarean sections avoided. The models relied on estimates of costs as provided by Norwegian Directorate of Health, and probabilities and health utilities obtained from the scientific literature.*

Results: *The study showed that elective induction of labor at 39 weeks of gestation was a potentially cost-saving strategy compared to expectant management with ICER of 73 904 NOK per QALY gained and a total of 346 cesarean sections avoided. The results held true for 92% of the cases of 10 000 Monte Carlo simulations at willingness to pay threshold of 275 000 NOK. Elective induction of labor at 40 weeks of gestation was shown to be a potentially cost-saving strategy compared to expectant management with ICER of 69 218 NOK per QALY gained and a total of 852 cesarean sections avoided. The results held true for 87% of the cases. The overall conclusion was robust to changes in model parameters, with adverse neonatal outcome probabilities and cesarean section rates mostly affecting the magnitude of cost savings. Week 39 induction was the cost-effective strategy when compared to expectant management ending in elective induction at week 40.*

Conclusion: *This study shows that elective induction is possibly cost-effective from the health payer perspective. However, an additional retrospective observational study is recommended together with the cost-effectiveness analysis from the hospital perspective to more accurately characterize the resulting health outcomes and capture the costs of this procedure.*

Acknowledgements

I would like to humbly give my words of gratitude to all that helped me with my studies and in the process of writing this thesis.

I built on the work of countless researchers that came before me. Without their dedication and hard work in the field of health economics, I would not have been able to continue. I am also thankful to all the professors at Health Economics, Policy, and Management Masters's program. It was incredible to learn from all of you. You equipped me with knowledge that will shape my professional life. Special thanks to Liv Solvår Nymark who taught me how to do literature research. It saved me so much time.

I would not have made it even through the first semester without the generous help of Mari Elisabeth Mjøen. Thank you, Mari, you are the best.

Throughout my thesis writing process, I had many conversations with Andrea Solnes Miltenburg. Thank you for your time and effort. Your input was valuable to me.

The greatest thanks go to my supervisor, Lumbwe Chola, whose kindness, patience, and knowledge helped me more than I can put into words. Thank you Lumbwe, I couldn't have gotten a better supervisor.

Many thanks to my daughter Greta, without whom I would have gotten myself a Netflix subscription instead of enrolment into master's program. Greta you are the light of my life, my everything. If only you would let me sleep more.

And to my wife, the best wife a wife can hope for. Nothing would have been possible without you. Nothing would matter without you. In the end, it is always just you. Also, I promise not to change Calibri to Arial. Because it is not the 90s anymore.

Contents

ABSTRACT I

ACKNOWLEDGEMENTS II

CONTENTS III

LIST OF FIGURES V

LIST OF TABLES VI

ABBREVIATIONS VII

1. INTRODUCTION 1

2. BACKGROUND 4

2.1 MEDICAL PERSPECTIVE 4
2.2 ECONOMIC PERSPECTIVE 8

3. THEORETICAL FRAMEWORK 12

3.1 ECONOMIC EVALUATION 12
3.2 DECISION-ANALYTIC MODELLING 15
3.3 DETERMINISTIC AND PROBABILISTIC SENSITIVITY ANALYSES 17

4. METHODOLOGY 19

4.1 LITERATURE REVIEW 19
4.2 DECISION ANALYTIC MODEL 21
4.3 MODEL INPUTS 24
4.3.1 PROBABILITIES 24
4.3.2 UTILITIES 25
4.3.3 COSTS 27
4.4 SENSITIVITY ANALYSIS 28

5. FINDINGS 30

5.1 DETERMINISTIC SENSITIVITY ANALYSIS 31
5.2 PROBABILISTIC SENSITIVITY ANALYSIS 34

6. DISCUSSION 38

6.1 SUMMARY OF THE FINDINGS 38
6.2 LIMITATIONS AND STRENGTHS 39
6.2.1 PERSPECTIVE 39
6.2.2 LONG TERM VS SHORT TERM OUTCOMES 40
6.2.3 MATERNAL VS NEONATAL HEALTH OUTCOMES 41
6.2.4 QALYS VS OTHERWISE DEFINED HEALTH EFFECTS 41
6.2.5 LOW RISK POPULATION 42
6.2.6 DECISION TREE MODEL 42
6.3 IMPLICATIONS FOR FURTHER RESEARCH 44

7. CONCLUSION 45

LIST OF REFERENCES 46

APPENDIX A: LITERATURE REVIEW – INCLUDED STUDIES I

APPENDIX B: CHEERS 2022 CHECKLIST VI

APPENDIX C: FULL PARAMETER NAMES IX

APPENDIX D: FULL TORNADO DIAGRAMS XII

List of Figures

Figure 1: Increase in percentage of inductions of laboor in Norway. 2
Figure 2: Cost-effectiveness plane. 14
Figure 3: Decision tree model. 16
Figure 4: Markov model. 16
Figure 5 Study selection process and corresponding results. 20
Figure 6: Tree schematic Model 1: Labor induction at 39 weeks of gestation versus expectant management including new decision. 23
Figure 7: Tree schematic Model 2: Labor induction at 40 weeks of gestation versus expectant management until labor induction at week 41. 23
Figure 8: Tornado Diagram - Week 39, Induction of labor vs Expectant management sensitivity analysis. 32
Figure 9: Tornado Diagram - Week 40, Induction of labor vs Expectant management sensitivity analysis. 32
Figure 10: One-way sensitivity analysis: ICER vs cost of induction for weeks 39 and 40. 33
Figure 11: Cost-effectiveness plane: Elective Induction at week 39 vs Expectant Management. 34
Figure 12: Cost-effectiveness acceptability curves: Elective Induction at week 39 vs Expectant Management. 35
Figure 13 Cost-effectiveness plane: Elective Induction at week 40 vs Expectant Management. 35
Figure 14 Cost-effectiveness acceptability curves: Elective Induction at week 40 vs Expectant Management. 36
Figure 15 Cost-effectiveness plane: Elective Induction at week 39 vs Expectant Management followed by Elective Induction at week 40. 36
Figure 16 Cost-effectiveness acceptability curves: Elective Induction at week 39 vs Expectant Management followed by Elective Induction at week 40. 37
Figure 17: Value of information analysis: population Expected Value of Perfect Information. 37

List of Tables

Table 1: Criteria for study selection. 19

Table 2: Literature search strategy and results. 20

Table 3: Decision Analytic Model Inputs - Probabilities. 26

Table 4: Decision Analytic Model Inputs - Utilities. 27

Table 5 Decision Analytic Model Inputs - Costs. 28

Table 6: Results per strategy. 31

Abbreviations

ARRIVE	A Randomized Trial of Induction Versus Expectant Management
BMI	Body mass index
CEA	Cost effectiveness analysis
CUA	Cost utility analysis
CEAC	Cost effectiveness acceptability curve
CEAF	Cost effectiveness acceptability frontier
CS	Cesarean section
DALY	Disability-adjusted life years
DRG	Diagnosis-Related Group
EVPI	Expected value of perfect information
EVPPI	Expected value of partial perfect information
GP	General practitioner
HYE	Healthy-Years Equivalent
ICER	Incremental cost effectiveness ratio
MBR	Medisinsk fødselsregister (Medical Birth Registry of Norway)
NB	Net benefit
NMB	Net monetary benefit
pEVPI	Population expected value of perfect information
pEVPPI	Population expected value of partial perfect information
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PSA	Probabilistic sensitivity analysis
QALY	Quality Adjusted Life Years
SLV	Statens Legemiddelverk (Norwegian Medicines Agency)
SSB	Statistisk sentralbyrå (Statistics Norway)
SWEPIS	Swedish Post-term Induction Study
VOI	Value of information
WHO	World Health Organization
WTP	Willingness to pay

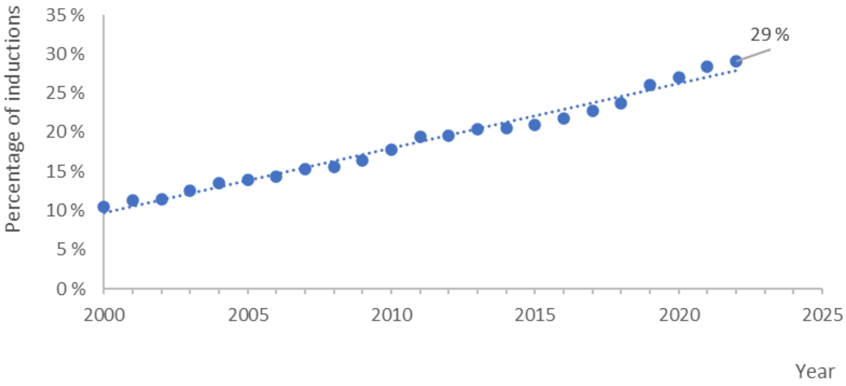
1. Introduction

The Norwegian Society of Gynecology and Obstetrics (2022) defines induction of labor as a medical procedure aimed at terminating a pregnancy due to maternal or fetal indication where vaginal birth is not contraindicated. Common medical indications for inducing labor include post-term pregnancy, preeclampsia, hypertension, pre-gestational hypertension, gestational diabetes, premature rupture of membranes after 37 weeks, twin pregnancy, intrahepatic cholestasis of pregnancy, and other medical reasons. Elective induction refers to the induction of labor without clear medical indications for delivery relative to continuing pregnancy (Dögl et al., 2018).

Vogel et al. (2014) highlight that women may have diverse motivations for opting for elective induction of labor. These motivations can range from practical concerns like residing far from the hospital, particularly in areas with limited access to specialized maternity services, where timely access to medical care becomes a priority. Some women may choose induction to relieve discomfort or fatigue experienced during pregnancy. Additionally, concerns about potential complications for both the mother and baby can influence the decision for elective induction. Factors contributing to this decision may include maternal anxiety, fear of adverse outcomes, recommendations from healthcare providers to manage specific conditions or potential risks, as well as financial or scheduling considerations (Vogel et al., 2014). It is important to recognize that the decision-making process surrounding elective induction is multifaceted and varies based on individual circumstances and preferences.

The Medical Birth Registry of Norway reports a consistent increase in the rate of inductions, which now accounts for 29% of all labor onsets (Medisinsk fødselsregister - statistikkbank, 2023), as visible in Figure 1. Although data on the prevalence of elective inductions in Norway is not readily available, Dögl et al. (2018) conducted a prospective observational study in which they found that elective inductions accounted for 10% of all inductions. The most common reasons cited for choosing elective induction were maternal request (35%), previous negative delivery experience or difficult obstetric history (19%), maternal fatigue/tiredness (17%), and anxiety (15%) (Dögl et al., 2018).

Figure 1: Increase in percentage of inductions of laboor in Norway.



Source: Medical Birth Registry of Norway, 2023.

The Norwegian Society of Gynecology and Obstetrics, along with the World Health Organization, advises against elective inductions due to inconclusive evidence on their benefits (WHO 2022). However, elective induction may still provide some advantages, such as reducing the number of cesarean deliveries, preventing stillbirths, and potentially mitigating hypertensive pregnancy disorders that occur in the later stages of pregnancy (Grobman et al., 2018; Stock et al., 2012).

It is important to differentiate between nulliparous and multiparous women in studies examining the association between induction and cesarean delivery. This is because these groups have different baseline risks of cesarean delivery and can be impacted differently by induction. Nulliparous women who elect to undergo induction of labor may experience a higher rate of cesarean delivery compared to those who begin labor spontaneously, as shown in studies by Grobman (2007) and Little (2017). It is therefore vital to stratify the study population based on parity when examining this association.

This was confirmed true in the Norwegian context when a study conducted by Sørbye et al. (2020) revealed significant variations in the practice and outcomes of induction of labor. The highest rate of cesarean delivery following induction was observed in the nulliparous term cephalic cohort, where almost one in five women underwent a cesarean delivery. The study noted a range of induction techniques used, but few units followed standardized induction protocols, thus highlighting the need for standardization, particularly for the nulliparous population. It is noteworthy that reducing the rate of cesarean deliveries is crucial, especially for nulliparous women, since the first cesarean delivery increases the likelihood of having cesarean deliveries in subsequent pregnancies. As a result, researchers have considered low-risk nulliparous women as a potentially suitable population for elective induction. However, it is important to recognize that inductions can be resource intensive. Simpson and Atterbury (2003) highlighted that inducing labor, regardless of medical necessity, is not a simple intervention. It involves multiple personnel, resources, and monitoring, in addition to the costs associated with medications and procedural materials.

With regards to the costs involved, it is essential to clearly define the benefits of elective induction to justify its use. Conducting cost-effectiveness analyses can help inform future recommendations. Although there are limited studies available, the existing evidence suggests that elective induction in the 39th week of gestation for low-risk nulliparous women may be cost-effective compared to expectant management until 41 weeks of gestation (Kaimal et al., 2011; Hersh et al., 2019; Fitzgerald, Kaimal and Little, 2023).

It is worth noting that there has been limited research exploring the cost-effectiveness of electively inducing labor at 39 weeks compared to 40 weeks. This gap creates an opportunity for further research, as evident in the research questions of this master's thesis:

Are elective inductions for low-risk nulliparous women cost-effective compared to expectant management? If so, what is the optimal time to induce labor from the cost-effectiveness perspective: at 39 weeks or at 40 weeks?

Investigating these research questions will not only provide valuable insights into whether elective induction should be offered to low-risk nulliparous women in Norway but could also assist hospitals in effectively planning and allocating resources during periods when elective induction rates are increasing. This research can have practical implications for healthcare providers, ultimately leading to informed decision-making and improved resource management.

2. Background

There is an agreement in the scientific community that induction of labor is a necessary and safe medical procedure that can prevent maternal and infant mortality, as well as the harmful effects of complicated births (Vogel et al., 2014). However, elective induction has been the subject of much debate, with varying opinions. Recently, the discussion has focused on identifying the specific subgroup of pregnant women who would benefit from elective induction. Most researchers suggest that low-risk nulliparous women would be ideal candidates for this procedure (Grobman, 2007). However, others argue that this group should be further stratified into women with favorable and unfavorable cervical statuses (Vogel et al., 2014; Fitzgerald, Kaimal and Little, 2023).

What researchers do agree on is that delivery before 39 weeks of gestation without medical indication is associated with worse perinatal outcomes than delivery at full term (Grobman, 2007; Grobman et al., 2018; Parikh et al., 2014). Optimum timing for the induction of labor remains a topic of contention as pregnancies extending beyond 41 weeks of gestation have been linked to undesirable outcomes for both mothers and infants (WHO, 2022).

While induction of labor has been recommended as a preventive measure against such outcomes, global consensus on the ideal timing of this strategy has yet to be established. It should be noted that elective induction not only poses a challenge for healthcare personnel but also for health economists, who must carefully consider both the costs and benefits of offering this intervention as a standard of care. This chapter aims to provide insight into the current views on elective induction from both medical and economic perspectives.

2.1 Medical perspective

Traditionally, there have been apprehensions that the elective induction of labor may lead to a surge in cesarean delivery rates. In 2013, a retrospective cohort study by Baud et al. (2013) demonstrated that elective induction in a low-risk patient population has outcomes that are equivalent to medically indicated induction. The study also found that it significantly increases the risk of obstetrical and neonatal complications when compared to spontaneous labor.

Conversely, Davey and King (2016) discovered that low-risk nulliparous women who underwent elective induction deliveries had almost double the number of cesarean deliveries in contrast to those who underwent spontaneous labor.

On the other hand, several observational studies offered contrasting findings. Darney et al. (2013) conducted a retrospective cohort study on all deliveries in California in 2006 that had no prior cesarean delivery. The study concluded that elective induction of labor is associated with reduced odds of cesarean delivery compared to expectant management regardless of parity (Darney et al., 2013). Likewise, a large retrospective cohort study of the Scottish population database by Stock et al. (2012) compared outcomes across different gestation weeks for singleton pregnancies with expectant management and indicated that elective induction of labor at term reduces perinatal mortality without increasing the risk of operative delivery (Stock et al., 2012).

These disparities have spurred Darney and Caughey (2014) to emphasize the significant limitations of existing studies. Specifically, these studies have different approaches in defining indications for induction without medical indication, comparison groups, and data sources, and have focused on various gestational ages or outcomes. One significant consideration when studying elective induction of labor is whether women being induced are compared with those delivering spontaneously at the same week or with the appropriate control group of women who are not induced but managed expectantly at that gestational age. This factor impacts the results of these studies significantly, causing a shift from being worse with induction of labor to being improved by induction of labor. The authors recommended addressing these limitations and employing consistent and rigorous study designs to provide a more comprehensive understanding of the risks and benefits of elective induction of labor, enabling healthcare providers and patients to make well-informed decisions (Darney and Caughey, 2014).

Little (2017) has also highlighted further limitations of retrospective cohort studies. One such issue is the challenge of presenting database information by week rather than day, resulting in potential ambiguity about whether women who delivered within the same week as the induction group should be included. This decision can induce varying findings, as demonstrated by multiple studies (Stock et al., 2012). Furthermore, retrospective data may risk residual confounding since induced women can differ from those who opt for expectant management in terms of preference, labor experience, lifestyle factors, and risk perception, all of which may influence their decision-making process (Little, 2017).

In 2018, the scientific community made significant strides in resolving the issue when a sizeable randomized controlled trial involving a population of 6 106 women was conducted. The 2018 A Randomized Trial of Induction Versus Expectant Management (ARRIVE) trial, conducted at 41 hospitals found that inducing labor at 39 weeks in low-risk nulliparous women did not result in a significant decrease in the incidence of perinatal death or severe neonatal complications, but it did lead to a significantly reduced rate of cesarean delivery (Grobman et al., 2018). Grobman and Caughey (2019) and Sotiriadis et al. (2019) supported these findings with subsequent meta-analyses.

However, other studies, such as individual patient meta-analysis conducted by Walker et al. (2016), systematic review and meta-analysis by Saccone et al. (2019), and systematic review and meta-analysis by Fonseca et al. (2020), have indicated no significant association between induction of labor and cesarean section rates, raising doubts about the results and methodology of the ARRIVE trial.

The limitations of the ARRIVE trial need to be addressed as well. Carlson (2018) highlights the potential lack of generalizability due to the fundamental differences between the trial participants and the broader population of US childbearing women. Additionally, many healthcare providers do not follow all of the intervention steps examined in the trial, leading to failed inductions and subsequent cesarean sections. Carlson also points out the lack of uniformity in considering women's preferences regarding induction across the country. Furthermore, Green (2018) raises concerns about the demographics of the trial participants and their applicability to more diverse populations. The study included a higher proportion of white, college-educated, and high-income women, with a relatively high BMI, potentially limiting the transferability of the findings. Pinto et al. (2018) echo the concerns regarding demographics and question whether the results would have differed if the expectant-management group had undergone induction at 41 weeks. While the trial observed a lower rate of cesarean delivery in the elective induction group, the potential risks may outweigh the benefits, particularly in more diverse and resource-limited populations.

To verify the results of the ARRIVE trial in the domestic population, Wennerholm et al. (2019) carried out a multicenter, open-label, randomized controlled trial in Sweden from 2016 to 2018. They discovered that there was no variation in the proportion of cesarean delivery, instrumental vaginal delivery, or any significant maternal morbidity between the groups of women induced at 41 weeks and those assigned to the expectant management group in low-risk uncomplicated singleton pregnancies. The trial was discontinued due to a substantially higher rate of perinatal mortality in the expectant management group.

In a study conducted by Tita et al. (2021), the risks of various maternal and perinatal outcomes in low-risk nulliparous women undergoing expectant management were explored using data from the ARRIVE trial. The study examined the risks of cesarean delivery, perinatal composite outcomes, and other relevant outcomes based on the completed week of gestation after 39 weeks. The findings indicated that in low-risk nulliparous patients undergoing expectant management, the rates of medically indicated induction of labor increased significantly from 39 to 42 weeks of gestation, along with an increased risk of cesarean delivery. However, there was no significant increase in the perinatal composite outcome. These results suggest that caution should be exercised when continuing expectant management beyond 39 weeks of gestation in low-risk nulliparous women. Medically indicated induction of labor may be a suitable alternative to expectant management in such cases.

Zenzmaier and colleagues (2021) conducted a retrospective cohort study to investigate the association between elective induction and cesarean delivery in singleton term and post-term hospital births in Austria. The study utilized multivariate logistic regression to analyze this association for each week of gestation from week 37 to week 41. The study highlighted the significance of defining the expectant management group when evaluating the outcomes of elective induction in retrospective cohort studies. It emphasized that the choice between non-medically indicated labor is not limited to a binary decision between elective induction and indefinite expectant management. Pregnant women have the option to choose elective induction at any point after week 39, and expectant management does not necessarily have to lead to natural onset of labor. The authors presented a useful clinical decision-making approach by defining the control group as all births in the next week. This enables the estimation of the risks associated with expectant management until the next appointment, compared to the immediate induction of labor. This approach offers a more detailed view of the risks and benefits of different management strategies (Zenzmaier et al., 2021).

There is a recent trend in research to apply the findings of the ARRIVE trial to local settings. However, this has proven to be challenging, with some studies reporting conflicting results. Tassis and colleagues (2022) reported that expectant management in low-risk pregnancies achieved better maternal and perinatal outcomes, while Lewis, Zhao, and Schorn (2022) found no statistically significant differences between elective induction and expectant management in terms of the number of cesarean deliveries. Therefore, despite recent systematic reviews and meta-analyses confirming the ARRIVE findings for the general population, such as the Hong et al. (2023) study, caution is still needed when generalizing the recommendations for elective induction of labor.

2.2 Economic perspective

Fahy and colleagues (2013) conducted a review of all available studies on the economic costs of different methods of childbirth delivery. The study aimed to identify any deficiencies in existing research. The primary findings of the review suggested that there is no internationally recognized classification system for childbirth costs and clinical outcomes, which makes comparisons between different delivery methods challenging. The authors recommended the development of an improved classification system to comprehend the costs and related clinical outcomes of childbirth better. This would enable valid comparisons between maternity units, ultimately informing policy makers and hospital management (Fahy et al., 2013).

Research indicates that the policy of elective induction of labor results in additional costs and resource use compared to spontaneous labor (Hersh et al., 2020). However, when the costs are analyzed in the context of low-risk nulliparous women undergoing elective labor or expectant management, it seems that despite having different components, the costs are comparable (Einerson et al., 2020; Grobman et al., 2020).

Health economics research has frequently concentrated on the topic of induction of labor, with much of the research focusing on evaluating and comparing different methods of medically indicated induction. One of the most significant studies in this field has been a systematic review, network meta-analysis, and cost-effectiveness analysis conducted by Alfirevic and colleagues (2016). Their review revealed that all methods of induction were cost-saving compared to no treatment. The authors noted that there is significant uncertainty regarding their cost-effectiveness estimates, with the majority of the interventions having very similar utility values and varying primarily in total costs (Alfirevic et al., 2016).

However, there are relatively few studies that specifically focus on the economic evaluation of elective labor induction compared to expectant management.

One of the earliest economic evaluations of elective induction versus expectant management was conducted by Kaufman and colleagues (2002). The study developed a decision-tree model incorporating a Markov analysis to compare the decision to either electively induce labor at term or expectantly manage the pregnancy until 42 weeks' gestation. Main outcome measures, stratified by parity, cervical ripeness, and gestational age at induction, were the number of cesarean deliveries and costs to the healthcare system. The authors concluded that elective induction of labor at term is not cost-effective and results in a large excess of cesarean deliveries. Furthermore, the costs were significantly affected by the timing of induction, parity, and cervical ripeness (Kaufman, Bailit and Grobman, 2002).

As medical understanding of the outcomes of elective induction improved, the balance shifted towards elective induction intervention becoming more cost-effective. Kaimal and colleagues (2011) developed a decision analytic model comparing induction of labor at 41 weeks with expectant management with antenatal testing until 42 weeks in nulliparous women. They concluded that induction of labor at 41 weeks was cost-effective and resulted in a lower rate of adverse obstetric outcomes, including neonatal demise, shoulder dystocia, meconium aspiration syndrome, and severe perineal lacerations. This study provides evidence that elective induction of labor may be a more cost-effective option than expectant management in certain populations (Kaimal et al., 2011).

Alkmark and colleagues (2022) conducted a cost-effectiveness analysis to compare induction of labor at 41 weeks of gestation with expectant management until 42 weeks of gestation. The analysis was run alongside the Swedish Post-term Induction Study (SWEPIS), a multicentre, randomized controlled superiority trial. Health benefits were measured in life years and quality-adjusted life years for the mother and child. The study found that induction of labor at 41 weeks resulted in better health outcomes and no significant difference in costs between the two options. (Alkmark et al., 2022).

Hersh and colleagues (2019) investigated the cost-effectiveness and outcomes of induction of labor at 39 weeks compared to expectant management in low-risk nulliparous women in the United States. The authors developed a cost-effectiveness model that included outcomes such as mode of delivery, hypertensive disorders of pregnancy, macrosomia, stillbirth, permanent brachial plexus injury, and neonatal death, in addition to cost and quality-adjusted life years for both the woman and neonate. The study found that induction of labor resulted in fewer cesarean deliveries, fewer cases of hypertensive disorders of pregnancy, stillbirth, and neonatal deaths. Although the outcomes were improved for the mother and baby, the costs increased, and the results were sensitive to various inputs. Therefore, authors cautioned that offering routine induction of labor at 39 weeks requires further and broader research before implementation. The authors also pointed out that whether individual clinicians and healthcare systems offer routine induction of labor at 39 weeks will depend on local capacity, careful evaluation and allocation of healthcare resources, and patient preferences (Hersh et al., 2019).

Fitzgerald and colleagues (2023) conducted a recent study focused on the specific population of women with favorable or unfavorable cervical examinations to determine the cost-effectiveness of inducing labor at 39 weeks of gestation. They created two decision analysis models, one for nulliparous women with unfavorable cervical exams and another for those with favorable cervical exams. Cost, probability, and health state utility estimates were obtained from existing literature. The study's results indicated that inducing labor at 39 weeks may be cost-effective for patients with unfavorable cervical examinations but not for those with favorable cervical examinations. The findings support the authors' premise that women with favorable cervical examinations are likely to have a lower initial risk of cesarean delivery and higher rates of spontaneous labor (Fitzgerald, Kaimal, and Little, 2023). This study highlights the importance of considering cervical examination results when evaluating the cost-effectiveness of induction of labor.

Other than Alkmark et al. (2022) all the above studies were grounded in the American settings. Given that costs vary significantly based on the health systems, similar analysis would need to be conducted in a localized setting to confirm their findings.

3. Theoretical Framework

Economic evaluation in healthcare is a comparative method used to inform decisions regarding the allocation of health resources (Briggs, Claxton and Sculpher, 2011). It can be defined as the comparison of alternative options in terms of their costs and consequences. Alternative options refer to the range of ways in which healthcare resources can be used to increase population health. Healthcare costs refer to the value of tangible and intangible resources used within the healthcare system, while consequences represent all the effects of healthcare programs other than those on resources (Drummond et al., 2015; Briggs, Claxton and Sculpher, 2011). This chapter provides the theoretical background for this thesis.

3.1 Economic evaluation

Cost-effectiveness analysis (CEA) is a type of economic evaluation that compares the cost and effect outcomes of multiple decision options. It is used in situations where the decision maker operates within a given budget and needs to choose between a limited range of options. However, one of the most prominent limitations of this method is its inability to capture the opportunity cost of other programs covered by the same budget (Briggs, Claxton, and Sculpher, 2011).

Cost-utility analysis is a type of economic evaluation that enables the broad comparability of treatment options by incorporating generic measurement units that quantify the utility or health gains. DALYs (Disability-Adjusted Life Years), HYEs (Healthy-Years Equivalent), and QALYs (Quality-Adjusted Life Years) are the common outcomes used in cost-utility analyses (Drummond et al., 2015; Briggs, Claxton and Sculpher, 2011).

DALYs measure the overall burden of disease in a population, taking into account both years lived with disability and premature death. This measure combines the years of healthy life lost due to disability with the years of life lost due to premature death. DALYs are used for comparing the relative impact of different diseases or conditions, and are generally used in prioritizing health interventions. HYEs represent the number of years lived without diet-related diseases or conditions. HYEs are used specifically in the context of evaluating the health impact and effectiveness of interventions promoting healthy eating habits. QALYs are a measure of health output that expresses both quality (reduced morbidity) and quantity (reduced mortality) gains through a single measure. The number of QALYs is calculated by multiplying the time spent in each health state with a quality-adjustment weight for each state, and the values are then summed. QALYs are the most widely used generic measurement unit of health output in economic analysis. By considering the impact of interventions on quality of life, QALYs provide a way to compare and prioritize different treatments or interventions (Drummond et al., 2015; Briggs, Claxton, and Sculpher, 2011; WHO, 2022). Although these measures serve different objectives, they are all necessary in understanding health outcomes.

The incremental cost-effectiveness ratio (ICER) and net benefits (NB) are different ways to represent the outcomes of cost-effectiveness analysis (CEA). The ICER is a measure used to compare the cost-effectiveness of two or more interventions or treatments. It is calculated by dividing the difference in costs (incremental cost ΔC) between the interventions by the difference in their health outcomes (incremental effect ΔE).

$$ICER = \frac{\Delta C}{\Delta E}$$

The ICER represents the additional cost required to achieve an additional unit of health benefit. It informs decision makers how much more a single unit increase in effects would cost (Briggs, Claxton, and Sculpher, 2011). Decision makers often have an upper limit, called the willingness-to-pay threshold (WTP or λ), which represents the maximum amount they are willing to spend for that single unit increase.

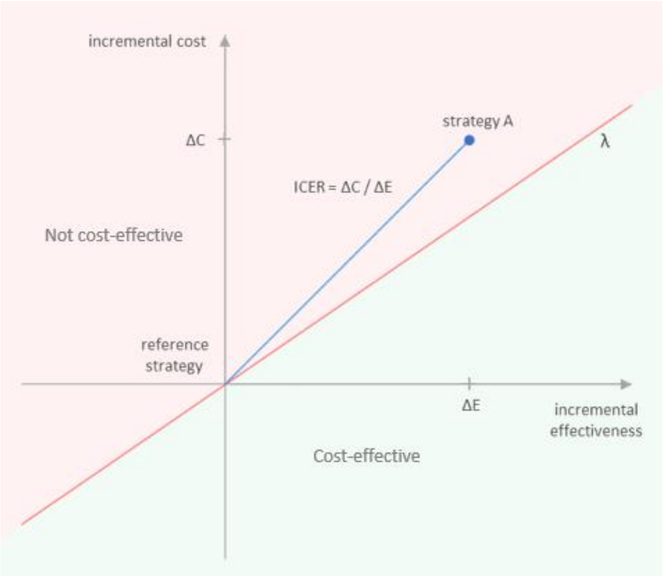
Net benefits refer to the overall economic value or utility gained from a particular policy, intervention, or decision. It takes into account both the benefits and costs associated with an option. Net benefits are calculated by subtracting the total costs of an option from the total benefits. A positive net benefit indicates that the benefits outweigh the costs, while a negative net benefit means that the costs outweigh the benefits. Net benefit analysis is frequently used in cost-benefit analysis to determine the desirability or feasibility of different choices or projects (Drummond et al., 2015; Briggs, Claxton, and Sculpher, 2011). Net monetary benefit (NMB) is a measure used to assess the monetary value gained from an intervention or treatment compared to an alternative or standard care. It represents the difference between the monetary benefits and the monetary costs of the observed intervention. NMB is calculated by subtracting the monetary cost of the intervention from the monetary value of the benefits.

$$NMB = \lambda \times \Delta E - \Delta C$$

A positive NMB indicates that the intervention is economically favorable, as the benefits outweigh the costs (Briggs, Claxton, and Sculpher, 2011).

The cost-effectiveness plane is a graphical representation used in cost-effectiveness analysis (CEA) to display the results of comparing different interventions or treatments in terms of their costs and outcomes per patient. It is a two-dimensional graph where the y-axis represents the incremental costs, and the x-axis represents the incremental effectiveness or health outcomes. Each point on the cost-effectiveness plane represents a different intervention or treatment strategy, and its position is determined by its incremental costs and incremental effectiveness compared to a reference strategy or standard care (Briggs, Claxton, and Sculpher, 2011). In the cost-effectiveness plane, the incremental cost-effectiveness ratios (ICERs) are presented as the slope of the line that joins any point on the plane to the origin.

Figure 2: Cost-effectiveness plane.



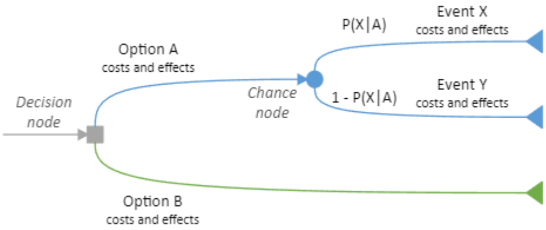
3.2 Decision-analytic modelling

Modeling is one of the approaches used in CEA to simplify the calculations by simulating complex systems. Decision-analytic modeling has its theoretical foundations in statistical decision theory, expected utility theory, and Bayesian statistics. A decision analysis has two key elements: the use of probabilities and expected values. Probabilities in decision-analytic modeling reflect the likelihood of events (changes in health), and expected values inform the decisions (Drummond et al., 2015). Decision analytic modeling is a tool that enables decision-makers to evaluate mutually exclusive alternatives, such as induced labor and expectant management. Health-economic models, which represent simplifications of reality, combine available evidence regarding a particular decision by synthesizing various parameters such as costs, treatment effects, and utilities. (Briggs, Claxton, and Sculpher, 2011; Drummond et al., 2015).

Decision analytic models can be categorized according to two dimensions (Briggs, Claxton, and Sculpher, 2011; Drummond et al., 2015): (1) whether they're based on data representing the average patient in a group (cohort model) or data that considers individual patient characteristics (individual sampling model); and (2) whether they use state transition models, which are either static, or dynamic transition models that can adapt more flexibly (Briggs, Claxton, and Sculpher, 2011; Drummond et al., 2015). Markov and Decision Tree models are commonly used in decision-making under uncertainty. Markov cohort models track a cohort as it moves through predetermined health states. Decision tree models, simplified versions of Markov Models, represent treatment options and potential outcomes through different branches. Decision tree models can become complex, especially when modeling long-term outcomes, but they are suitable for interventions with short-term costs and consequences.

A decision tree consists of a square decision node that represents a decision point and a circular chance node that signifies points where alternative events are possible. Pathways in a decision tree represent mutually exclusive sequences of events, and probabilities indicate the likelihood of each event occurring. The sum of all probabilities in the branches is 1. The first probability in the tree shows the probability of an event, while subsequent probabilities are conditional on that initial event (Drummond et al., 2015). To calculate the expected cost of the two therapies, the cost of each pathway is weighted by its corresponding probability, and the results are summed across all the pathways.

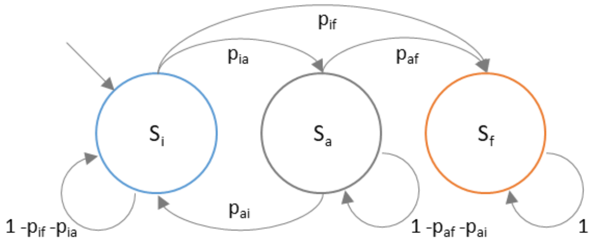
Figure 3: Decision tree model.



The decision tree has significant limitations (Drummond et al., 2015). First, events are typically assumed to occur instantaneously over a discrete period, and time is not explicitly defined. This makes it difficult to apply time-dependent elements of an economic evaluation, such as discounting, where the timing of costs and outcomes is crucial. The second limitation is the complexity that arises when using decision trees to model long-term and complicated prognoses, especially in cases of chronic diseases. For such long-term diseases, with patients at risk of events over many years, the decision tree may become complex and difficult to program and analyze, making it a time-consuming process.

The Markov model is a model structure developed to address the limitations of the decision tree. It is based on a series of "states" that a patient occupies at any given point in time. In a Markov model, time is taken into account, and a patient can occupy a given state over a series of discrete time periods known as cycles. The model typically ends when the patient enters the death state. Each state in the model has an associated cost. Since the Markov model is not relevant to this thesis, it is left to other literature to explore its structure and purpose in greater detail (Drummond et al., 2015).

Figure 4: Markov model.



3.3 Deterministic and probabilistic sensitivity analyses

The modeling approach in health care has its challenges, and one of the most prominent is the inherent uncertainty of the models. There is no perfect model, and errors can be introduced via model parameters, model structure, or calculations. Input parameter uncertainty can propagate through the model and manifest as outcome uncertainty, raising questions about the validity of the decision. One way to deal with uncertainty in a model is to adopt a probabilistic approach to analyze outcome uncertainties.

Sensitivity analysis is a technique used to study how changes in input variables or parameters affect the output of a model or system. It is necessary to understand the uncertainty of the results. In economic evaluation, deterministic and probabilistic sensitivity analyses are used (Drummond et al., 2015). One-way sensitivity analysis involves varying one input parameter at a time while keeping others constant to observe the impact on the output. This method is used when the goal is to identify the most influential parameters in the model. Multi-way sensitivity analysis is a method in which multiple input parameters are varied simultaneously to assess their combined effects on the output. The results of this analysis provide a more comprehensive understanding of the system's behavior.

Deterministic analyses have their place in economic evaluation, but they do not capture the true nature of uncertainty surrounding the decision. For that purpose, a probabilistic sensitivity analysis is used. This analysis considers uncertainty in input parameters by looking at probability distributions instead of fixed values. The results of this analysis provide a range of possible outcomes and their likelihoods (Drummond et al., 2015). Probabilistic sensitivity analysis (PSA) is required with all cost-effectiveness models.

The simplest way to perform probabilistic sensitivity analysis (PSA) in practice is through Monte Carlo simulations, where the input parameters are modeled as random variables. Each simulation involves random sampling from the input distributions and generating corresponding model outcomes. Repeating this process multiple times constructs outcome distributions, which can then be used to reason about uncertainty (Briggs, Claxton and Sculpher, 2011). In PSA, the optimal strategy is the one with the highest expected net benefit.

As a result of considerable debate regarding the best way to deal with uncertainty surrounding the estimate of cost-effectiveness, the cost-effectiveness acceptability curve (CEAC) was developed (van Hout et al., 1994; Briggs and Fenn, 1998; Briggs and Gray, 1999; O'Brien and Briggs, 2002). The CEAC shows the probability that an intervention is cost-effective compared to the alternative, given the observed data, for a range of maximum monetary values that a decision-maker is willing to pay for a particular unit change in outcome (Fenwick and Byford, 2005). The CEAC is calculated as the percentage of simulations in which a strategy had the highest net monetary benefit (NMB) compared to other strategies across all willingness-to-pay (WTP) values. It represents the probability that the strategy will be cost-effective at a certain WTP. The CEAC graph is often overlaid by the cost-effectiveness acceptability frontier (CEAF), which represents the optimal strategy over all WTP values.

After constructing the decision analytic model to represent the decision problem and conducting probabilistic analysis of the model, the question arises regarding how the results of probabilistic modeling should be interpreted. To answer this question, it is important to establish the value of additional information. Value of information (VOI) analysis addresses the question of whether the decision maker should proceed with the available information or finance a study that could help resolve parameter uncertainty, thereby increasing confidence in the decision (Briggs, Claxton and Sculpher, 2011).

The expected value of perfect information (EVPI) quantifies the value of acquiring perfect information about all aspects of the decision. The expected value of partial perfect information (EVPPI) quantifies the value of perfect information for a specific parameter in the decision. EVPI eliminates all uncertainty and is equivalent to the expected costs of uncertainty associated with making the decision based on the current evidence. EVPPI is the difference in the expected value of a decision made with perfect information for specific parameters and the expected value of the decision based on the current evidence (Fenwick et al., 2020). Population EVPI and EVPPI (pEVPI and pEVPPI) are values adjusted for the number of patients affected, the years the technology is in use, and discounted to present value. They illustrate the full impact of VOI and are used for comparison to the cost of research.

4. Methodology

This chapter outlines the methods and materials employed to conduct the cost-effectiveness analysis of elective induction of labor. The evaluation was done using a decision analytic model informed by a comprehensive literature review.

4.1 Literature review

A systematic literature search was performed with the aim of identifying studies conducted between 2010 and September 2023 that analyzed the cost effectiveness of elective induction versus expectant management in the general low-risk nulliparous population. The preferred methodological approach for the studies was decision analytical modeling. The outcomes of interest included the mode of delivery, delivery interventions, hospital stay, and maternal and neonatal complications. Table 1 shows detailed criteria for study selection summarized using the PICOTS framework (Page et al., 2021).

Table 1: Criteria for study selection.

P	Population	General population of low-risk nulliparous women
I	Intervention	Elective induction at gestation week 39 to 41
C	Comparator	Expectant management, spontaneous onset of labor (at term or late term) or the subsequent induction (late term or post term)
O	Outcome	Delivery mode, delivery interventions, hospital stay, maternal and neonatal complications
T	Timing	Published between 2010 and September 2023
S	Study type	Cost effectiveness analysis utilizing decision analytical model

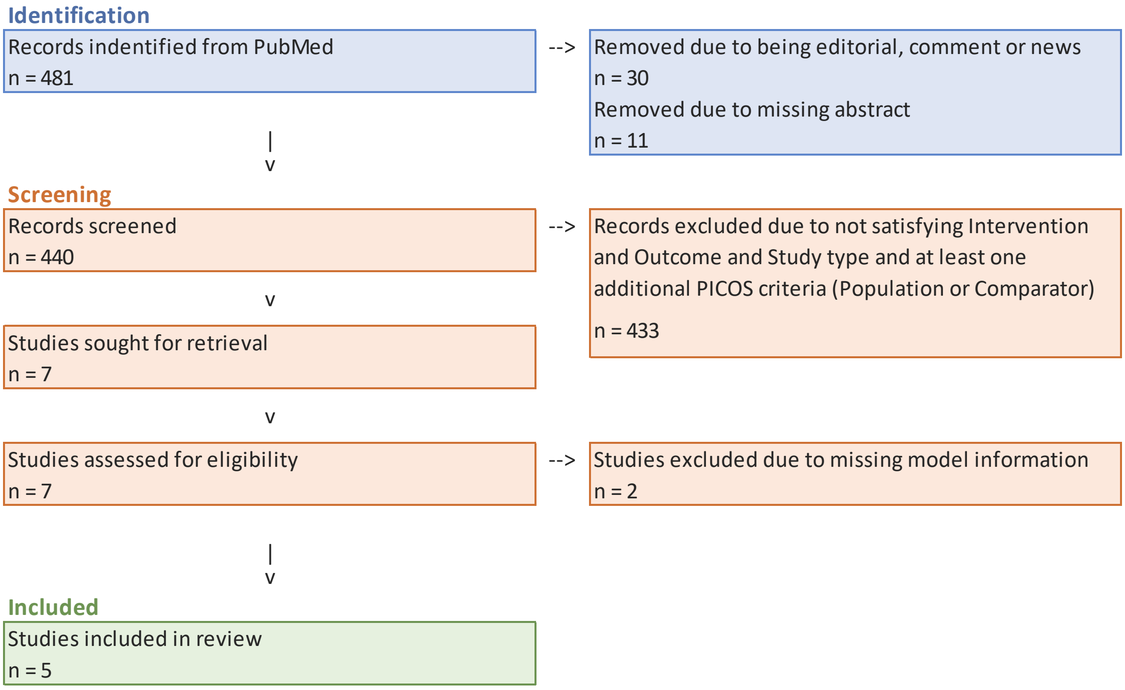
Based on the criteria outlined above, the search string was defined as any study related to induced labor (indexed by MeSH term heading) with either "elective" or "cost" in the title or abstract, or any study related to economics of delivery (indexed by MeSH term subheading) that had the word "model" in the title or abstract. This search string was applied to the PubMed database, which was used to search for English language articles published between 2010 and September 2023. Table 2 presents the search strategy and results.

Table 2: Literature search strategy and results.

Source	PubMed
Search string	(("Labor, Induced"[Mesh]) AND ((elective[Title/Abstract]) OR (cost[Title/Abstract]))) OR (("Delivery, Obstetric/economics"[Mesh]) AND (model[Title/Abstract]))
Timeline	2010 - September 2023
Limits	Language: English
Results	481

The screening process reviewed the titles and abstracts of the retrieved search results. Selection depended on the inclusion criteria outlined in Table 1. Additionally, the following exclusion criteria were applied: studies categorized as editorial, comment, or news articles; studies with missing abstracts; studies that did not satisfy the criteria for intervention, outcome, and study type, as well as at least one of the population or comparator criteria; and studies without a decision analytical model. The screening process followed the steps outlined in the PRISMA flow diagram (Page et al., 2021)

Figure 5 Study selection process and corresponding results.



From the initial literature search in PubMed, 481 articles were identified. Following screening of titles and abstracts, 7 papers were selected for full-text review. Out of these, 5 studies met the inclusion criteria, while the remaining 2 were excluded, one due to the incorrect study type and the other due to insufficient information on the model used. The PRISMA flow chart, presented in Figure 5 illustrates the study selection process and corresponding results. The relevant studies included are presented in the background chapter, and the complete comparison table is provided in Appendix A: Literature review – included studies.

4.2 Decision analytic model

The cost-effectiveness analysis was undertaken from the health payer perspective, using two decision analytic models created in Microsoft Excel. At the decision node of both models, women were stratified into 2 strategies, (1) universal elective induction of labor for a hypothetical cohort of 15 000 low-risk nulliparous women and (2) expectant management. Elective induction of labor was defined as induction without a clear medical indication (Dögl et al., 2018). Expectant management was defined as routine pregnancy care until women go into spontaneous labor or require induction of labor for an indication such as hypertensive disorders of pregnancy or late-term or post-term pregnancy or due to personal reasons (Zenzmaier et al., 2021; Fitzgerald, Kaimal, and Little, 2023).

The first model (Figure 6) compared elective induction of labor at 39+0 days of gestation versus expectant management in the week 39 proceeding to one of the two sub-scenarios: (1) elective induction of labor at 40+0 days of gestation or (2) continued expectant management. Given that the choice of sub-scenario is not possible beforehand, the decision which path to take was modeled by the “best decision” probability defined as the probability of choosing the path that maximizes the health-related outcomes. The second model was used to derive the outcomes of the sub-scenarios by comparing (1) elective induction of labor at 40+0 days of gestation versus (2) expectant management until late term pregnancy indicated induction at week 41. To investigate the optimal timing for the elective induction with respect to cost-effectiveness the first model was simulated considering only elective induction at week 40 sub-strategy.

The decision tree model used in this study was adapted from Hersh et al. (2019). The primary focus of the analysis was on cost-effectiveness, while the secondary outcome considered was the reduction in the number of cesarean sections performed. The decision tree represented a hypothetical group of 15 000 nulliparous women with low-risk, singleton, cephalic gestations. This cohort size was based on the population of nulliparous women in Norway without pregnancy complications, as reported by Sima et al. (2022). The cohort undergoing induction of labor at 39 weeks of gestation had the option between vaginal delivery or cesarean section. Both delivery methods carried a risk of neonatal demise. Vaginal delivery also posed a potential risk of complications, such as shoulder dystocia, which could result in permanent brachial plexus injury. Additionally, both the induction of labor and expectant management branches included the risk of hypertensive disorders of pregnancy, which was factored into the evaluation of cost outcomes for each branch.

The group of women undergoing expectant management during week 39 of gestation had several possible outcomes. They could either go into spontaneous labor, undergo induction due to a medical indication, experience fetal demise, or remain pregnant until week 40. The probability of medical induction was taken into consideration when assessing the cost outcomes. Similar to the induction group, delivery for expectant management could be either vaginal or cesarean.

Women who had not delivered by day 40+0 had the option of either choosing elective induction at day 40+0 or continue with the expectant management route. The model assumed that the option chosen would be the one that maximized health outcomes. This decision served as the entry point into the second model, as depicted in Figure 7. In this case, elective induction at day 40+0 was modeled in a similar manner to elective induction at day 39+0, but with adjusted probabilities to reflect the later gestational age. In the second model, expectant management was defined as the continuation of pregnancy follow-up until fetal demise, delivery, or induction of labor in week 41.

The models were simulated and the results were presented in the form of an incremental cost-effectiveness ratio (ICER). To determine the cost-effectiveness decision relating to health outcomes, a willingness-to-pay threshold of 275 000 Norwegian Crowns per QALY was utilized, as specified by Norwegian Medicines Agency (SLV, 2023). For the cost-effectiveness analysis of cesareans averted, the cost of cesarean section per cesarean averted was used as the basis for the decision-making process.

Figure 6: Tree schematic Model 1: Labor induction at 39 weeks of gestation versus expectant management including new decision.

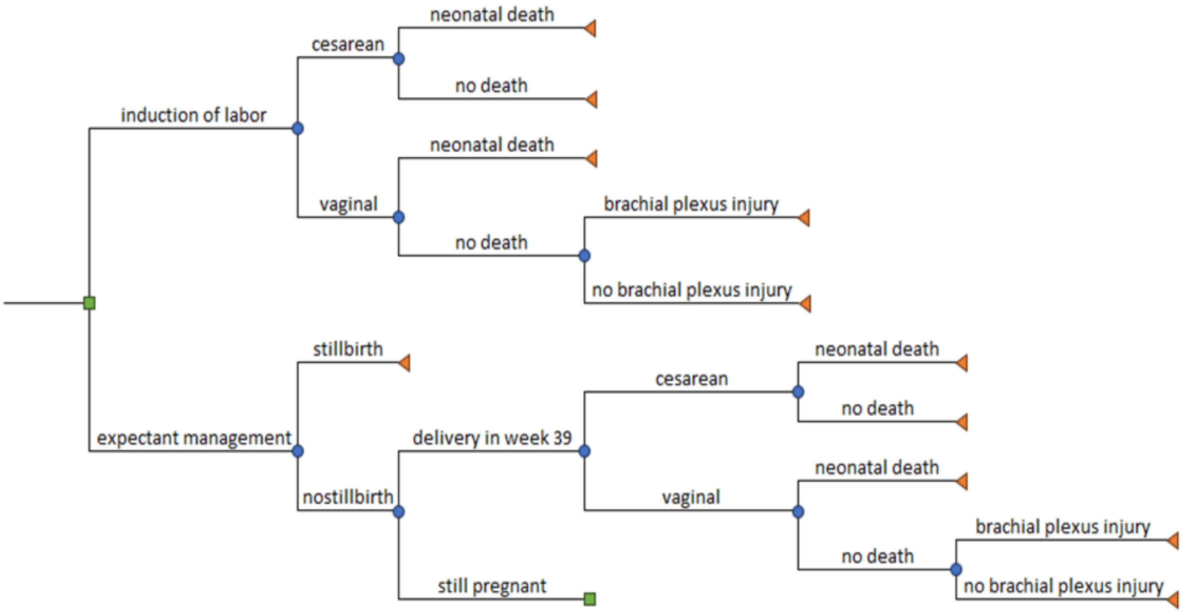
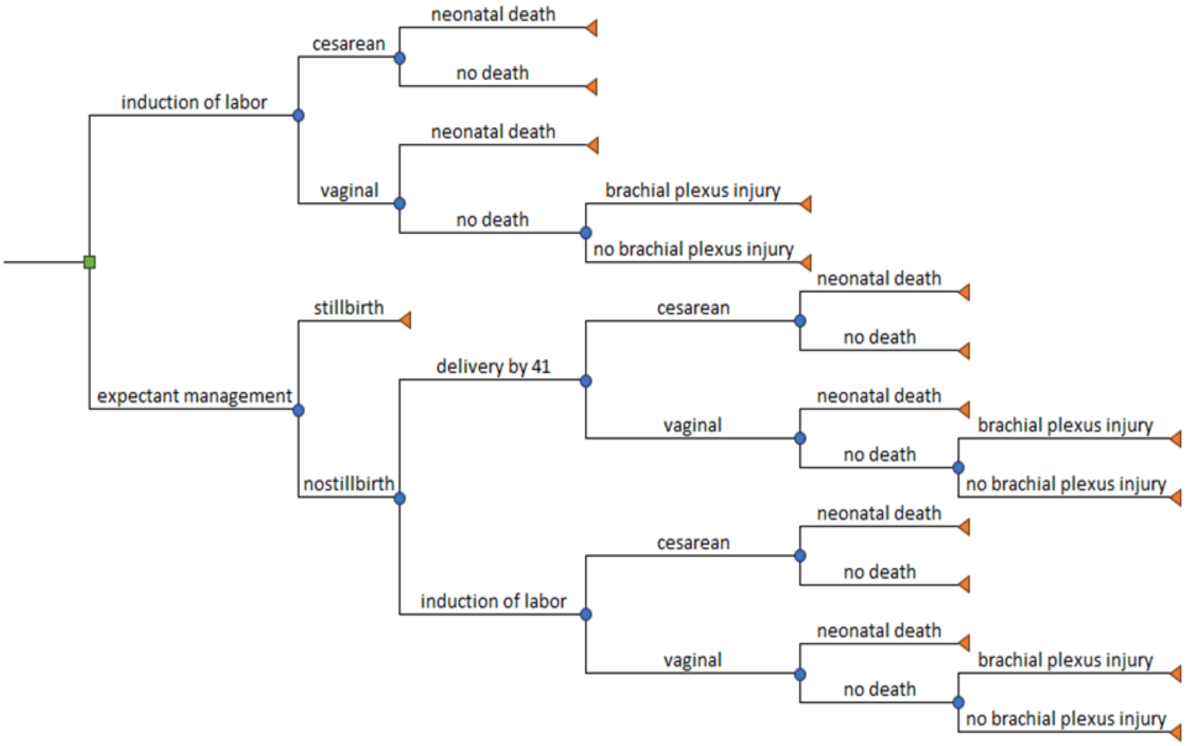


Figure 7: Tree schematic Model 2: Labor induction at 40 weeks of gestation versus expectant management until labor induction at week 41.



4.3 Model inputs

Both models utilized estimates of costs, probabilities, and health utilities obtained from relevant literature, including Norway specific data where possible.

4.3.1 Probabilities

The estimates of event probabilities utilized in the models were obtained from published literature (Table 3). The probabilities employed in the scenario for induced labor at 39 weeks were sourced from Grobman et al. (2018), whereas the probabilities for induced labor at weeks 40 and 41 were obtained from Tita et al. (2021). This study reported the probabilities of a cesarean section following expectant management, the numbers of spontaneous and medically indicated deliveries, the incidence of shoulder dystocia and hypertensive disorders of pregnancy in weeks 39, 40, and 41 for the expectant management population. The probability of developing hypertensive disorders of pregnancy for the induced population was taken from Grobman et al. (2018).

Both Tita et al. (2021) and Grobman et al. (2018) reported on the outcomes of the ARRIVE trial and their results match the ARRIVE population. Special care was taken when selecting the ranges for the probabilities that were the main drivers of outcome differences, to detail the model and account for the Norwegian population. Lower range for the probability of cesarean section was estimated from a number of cesareans following the spontaneous onset of labor in the subsequent week, while the upper limit was twice that number (Miller et al., 2015). For the delivery probabilities, lower range was taken from the Medical Birth Registry of Norway for the general population (under the assumption that nulliparous women who make up approximately 40 percent of the population are known to have longer gestations). The upper limit was derived by considering the deliveries in the previous week as well (Medisinsk fødselsregister - statistikkbank, 2023).

Limits for the probabilities of the medically indicated deliveries were taken from Haavaldsen et al. (2023) and percentage of total inductions in Norway respectively. For shoulder dystocia the lower limit was taken from Øverland, Vatten and Eskild (2014) while the upper was assumed as 20% increase.

The probability of brachial plexus injury was obtained from numbers reported by Christoffersson and Rydhstroem (2002). The probabilities of neonatal death for both vaginal and cesarean deliveries were sourced from Centers for Disease Control and Prevention delivery data, as reported by Hersh et al. (2019). The probabilities of fetal demise at weeks 39, 40, and 41 were obtained from a study by Yao et al. (2014). Due to the low incidence of fatal neonatal outcomes in the Norwegian population, it was difficult to determine precise probabilities and their limits. In this case, the limits by Hersh et al. (2019) were utilized.

4.3.2 Utilities

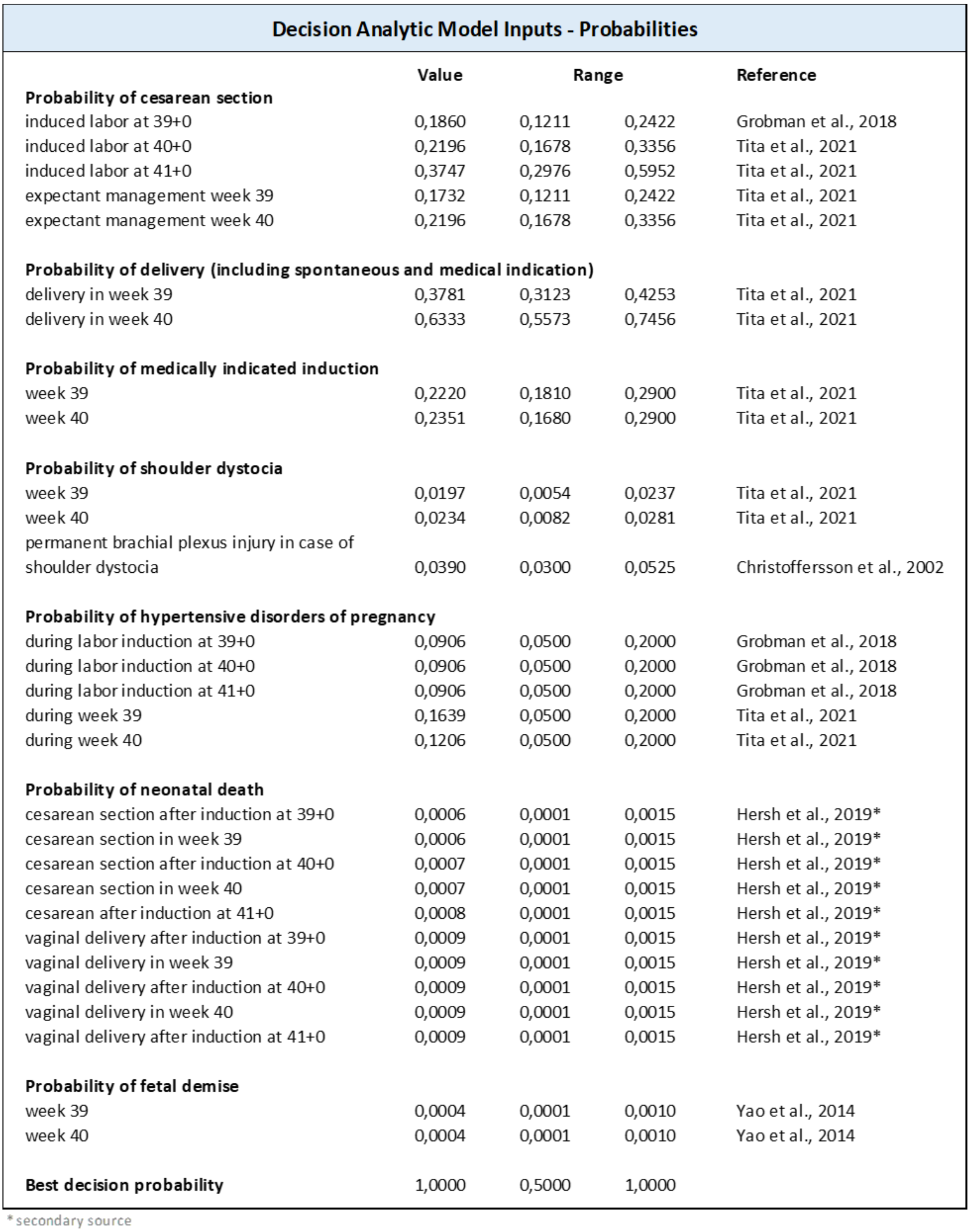
The study considered both maternal and neonatal perspectives, and utilities were assigned to determine the quality of life associated with each outcome. These utilities were applied to life expectancy or the duration of the condition to calculate the QALYs. The utility values were discounted at a rate of 3%, as recommended by the Panel on Cost-Effectiveness in Health Medicine, as reported by Sanders et al. (2016). In the sensitivity analysis, the health utility discount rate varied from 0% to 5%. The focus of this study was on long-term outcomes, and as such, all utilities represented long-term or permanent decreases in health outcomes.

The utilities used in the study were estimated from published literature (Table 4). For cesarean delivery, the utility values were sourced from Angeja et al. (2006). The utility values for stillbirth and brachial plexus injury were obtained from Carroll and Downs (2006).

The life expectancies of women following childbirth and healthy neonates were drawn from Statistic Norway (SSB-05375, 2023). Furthermore, the utilities associated with the maternal perspectives on neonatal death were taken from Grobman et al. (2002).

The study utilized a utility score of 1 for women who experienced an uncomplicated vaginal delivery, with no adverse events occurring for either the mother or the child (Hersh et al., 2019). For women who underwent a cesarean delivery, a utility score of 0.996 was applied to account for the potential effect on the woman's future fertility during her estimated remaining reproductive years, as reported by Angeja et al. (2006).

Table 3: Decision Analytic Model Inputs - Probabilities.

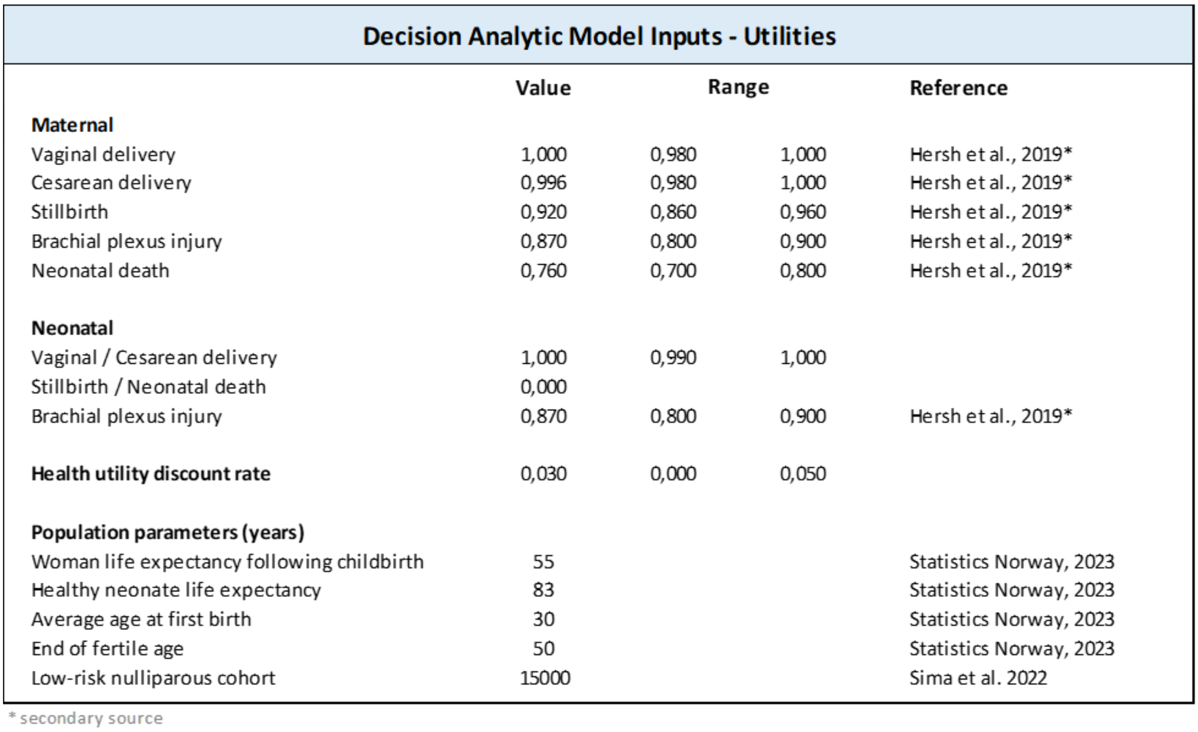


Decision Analytic Model Inputs - Probabilities	Value	Range		Reference
Probability of cesarean section				
induced labor at 39+0	0,1860	0,1211	0,2422	Grobman et al., 2018
induced labor at 40+0	0,2196	0,1678	0,3356	Tita et al., 2021
induced labor at 41+0	0,3747	0,2976	0,5952	Tita et al., 2021
expectant management week 39	0,1732	0,1211	0,2422	Tita et al., 2021
expectant management week 40	0,2196	0,1678	0,3356	Tita et al., 2021
Probability of delivery (including spontaneous and medical indication)				
delivery in week 39	0,3781	0,3123	0,4253	Tita et al., 2021
delivery in week 40	0,6333	0,5573	0,7456	Tita et al., 2021
Probability of medically indicated induction				
week 39	0,2220	0,1810	0,2900	Tita et al., 2021
week 40	0,2351	0,1680	0,2900	Tita et al., 2021
Probability of shoulder dystocia				
week 39	0,0197	0,0054	0,0237	Tita et al., 2021
week 40	0,0234	0,0082	0,0281	Tita et al., 2021
permanent brachial plexus injury in case of shoulder dystocia	0,0390	0,0300	0,0525	Christoffersson et al., 2002
Probability of hypertensive disorders of pregnancy				
during labor induction at 39+0	0,0906	0,0500	0,2000	Grobman et al., 2018
during labor induction at 40+0	0,0906	0,0500	0,2000	Grobman et al., 2018
during labor induction at 41+0	0,0906	0,0500	0,2000	Grobman et al., 2018
during week 39	0,1639	0,0500	0,2000	Tita et al., 2021
during week 40	0,1206	0,0500	0,2000	Tita et al., 2021
Probability of neonatal death				
cesarean section after induction at 39+0	0,0006	0,0001	0,0015	Hersh et al., 2019*
cesarean section in week 39	0,0006	0,0001	0,0015	Hersh et al., 2019*
cesarean section after induction at 40+0	0,0007	0,0001	0,0015	Hersh et al., 2019*
cesarean section in week 40	0,0007	0,0001	0,0015	Hersh et al., 2019*
cesarean after induction at 41+0	0,0008	0,0001	0,0015	Hersh et al., 2019*
vaginal delivery after induction at 39+0	0,0009	0,0001	0,0015	Hersh et al., 2019*
vaginal delivery in week 39	0,0009	0,0001	0,0015	Hersh et al., 2019*
vaginal delivery after induction at 40+0	0,0009	0,0001	0,0015	Hersh et al., 2019*
vaginal delivery in week 40	0,0009	0,0001	0,0015	Hersh et al., 2019*
vaginal delivery after induction at 41+0	0,0009	0,0001	0,0015	Hersh et al., 2019*
Probability of fetal demise				
week 39	0,0004	0,0001	0,0010	Yao et al., 2014
week 40	0,0004	0,0001	0,0010	Yao et al., 2014
Best decision probability	1,0000	0,5000	1,0000	

* secondary source

With an average age of 30.2 years at first delivery, the estimated life expectancy for women was 54.76 years. The fertile age limit for women was assumed to be 50 years. The life expectancy for an infant delivered without any medical complications was estimated to be 82.63 years, utilizing data from Statistic Norway (SSB-05375, 2023).

Table 4: Decision Analytic Model Inputs - Utilities.



Decision Analytic Model Inputs - Utilities				
	Value	**Range**		**Reference**
Maternal				
Vaginal delivery	1,000	0,980	1,000	Hersh et al., 2019*
Cesarean delivery	0,996	0,980	1,000	Hersh et al., 2019*
Stillbirth	0,920	0,860	0,960	Hersh et al., 2019*
Brachial plexus injury	0,870	0,800	0,900	Hersh et al., 2019*
Neonatal death	0,760	0,700	0,800	Hersh et al., 2019*
Neonatal				
Vaginal / Cesarean delivery	1,000	0,990	1,000	
Stillbirth / Neonatal death	0,000			
Brachial plexus injury	0,870	0,800	0,900	Hersh et al., 2019*
Health utility discount rate	0,030	0,000	0,050	
Population parameters (years)				
Woman life expectancy following childbirth	55			Statistics Norway, 2023
Healthy neonate life expectancy	83			Statistics Norway, 2023
Average age at first birth	30			Statistics Norway, 2023
End of fertile age	50			Statistics Norway, 2023
Low-risk nulliparous cohort	15000			Sima et al. 2022

* secondary source

4.3.3 Costs

The costs associated with brachial plexus injury, cesarean section, induction of labor, neonatal death, stillbirth, vaginal delivery, visits for pregnancy screening, and hypertensive disorders of pregnancy were derived from the Norwegian Diagnosis-Related Group (DRG). The DRG system is utilized for hospital reimbursements, with hospitals receiving a set rate based on the DRG assigned to each case.

For this study, the cost calculations were solely based on the DRG scheme. All costs were expressed in NOK 2022, with 2022 being the base year for reference DRG calculation, as reported by the Norwegian Directorate of Health (2023).

A 100% DRG value was assumed for all costs (since the percentage of lump sum each hospital awards its maternity ward was not possible to obtain). The range was assumed to be within a 5% decrease and 25% increase of the base value. A detailed breakdown of the costs and associated DRGs is provided in the Table 5.

Table 5 Decision Analytic Model Inputs - Costs.

Decision Analytic Model Inputs - Costs

	Value	Range		Reference
brachial plexus injury	46 787,16	44 447,80	58 483,95	DRG 390*
cesarean section	65 167,83	61 909,44	81 459,79	DRG 371*
induction	3 676,13	3 492,33	4 595,17	DRG 814R*
neonatal death	64 929,12	61 682,66	81 161,40	DRG 385A*
stillbirth	64 929,12	61 682,66	81 161,40	DRG 385A*
vaginal delivery	27 403,91	26 033,71	34 254,89	DRG 373*
visit with pregnancy screening	1 193,55	1 133,87	1 491,94	DRG 914P*
hypertensive disorders of pregnancy	20 720,03	19 684,03	25 900,04	DRG 384*
cesarean with complications	90 566,57	86 038,25	113 208,22	DRG 370*
vaginal delivery with complications	41 965,22	39 866,96	52 456,52	DRG 372*
healthy newborn	25 064,55	23 811,32	31 330,69	DRG 391*
Willingness to pay threshold	275 000,00			Norwegian Medicines Agency, 2023

* 100% value with reference of 47742 NOK (2022) obtained from the Norwegian Directorate of Health

4.4 Sensitivity analysis

To assess the robustness of the results, one-way sensitivity analyses were conducted on probabilities, costs, and utilities. This involved varying individual model inputs within a defined range while holding the others constant and evaluating the effect of input variations on the model outcomes, as described in Chapter 3. A Tornado chart was utilized to identify the variables with the highest impact on the Incremental Cost-Effectiveness Ratio (ICER) of the model. Subsequently, more targeted one-way sensitivity analyses were performed specifically on these influential model inputs to determine their impact on the model's outcomes.

In addition to the one-way sensitivity analyses, a probabilistic sensitivity analysis was performed using 10 000 Monte Carlo simulations. This analysis aimed to evaluate the robustness of the results when multiple inputs, such as probabilities, costs, and utilities, were simultaneously varied. For each relevant model input, a distribution was assigned, and random sampling was conducted to select new parameter values. The model was then run with these new parameters. This methodology enabled a better understanding of the uncertainty associated with the deterministic results obtained from the base case analysis.

For probability and utility parameters, the beta distribution was used instead of the standard normal distribution. This choice was made because the standard normal distribution extends beyond the range of 0 to 1, violating assumptions about probability. The beta distribution, on the other hand, can approximate the normal distribution while ensuring that all values remain between 0 and 1. The deterministic value of parameters was assumed to be the mean. The largest interval between the mean and the range limit was used to approximate 3 standard deviations. The alpha and beta parameters were derived using the method of moments, as described by Briggs, Claxton and Sculpher (2011):

$$\alpha = \bar{\mu}\left(\frac{\bar{\mu}\,(1-\bar{\mu}\,)}{s^2} - 1\right), \qquad \beta = \alpha\,\frac{(1-\bar{\mu}\,)}{\bar{\mu}}$$

For cost parameters, the gamma distribution was utilized to account for any outliers in the upper cost ranges, due to its right-skewed nature. Despite the costs being direct expenses of the health payer, it was still important to evaluate their impact on the model. For the cost distribution, the standard deviation was assumed to be 10% of the mean. The alpha and beta parameters were derived using the method of moments (Briggs, Claxton, and Sculpher, 2011):

$$\alpha = \frac{\bar{\mu}^2}{s^2}, \qquad \beta = \frac{s^2}{\bar{\mu}}$$

The results were plotted in the cost-effectiveness plane, and CEAC (cost-effectiveness acceptability curve) and CEAF (cost-effectiveness acceptability frontier) charts were produced for varying values of willingness-to-pay threshold. Assuming a bivariate normal distribution, the probabilistic results in the cost effectiveness plane were fitted with 95% confidence ellipses using the chi-square method with 2 degrees of freedom (Confidence Ellipse, 2023). VOI (value of information) analysis was also performed, following the methods outlined in literature (Briggs et al., 2011; Drummond et al., 2015).

5. Findings

This chapter presents the results of the decision-analytic model, encompassing both deterministic and probabilistic outcomes. The key measures included are the Incremental Cost-Effectiveness Ratio (ICER) for both total health outcomes and number of cesarean sections avoided. Additionally, the chapter outlines the results of the deterministic and probabilistic sensitivity analyses. The findings of the value of information analyses are presented, providing insights into the potential value of acquiring additional information for decision-making purposes.

The results of the analysis indicate that compared to expectant management, elective induction of labor at week 39 is a potentially cost-effective option. The ICER for all willingness to pay thresholds shows that the intervention is cost-saving with an estimated 73 904 NOK/QALY gained (i.e. 73 904 NOK is saved for each additional QALY gained). In the total population of 15 000 women, elective induction of labor at 39 weeks gestation results in 346 fewer cesarean sections, compared to expectant management. The incremental cost per cesarean section avoided (ICER) indicates a cost-saving of 49 193 NOK per cesarean section avoided. Overall, the analysis demonstrates that this strategy is potentially highly cost-effective for all values of the willingness to pay.

Similar outcomes were observed for the elective induction of labor at week 40 compared to expectant management following the induction of labor at week 41. The strategy is cost-effective for all values of willingness to pay threshold, with savings of 69 218 NOK/QALY gained. In the population of 15 000 women, the elective induction strategy decreases the number of cesarean sections by 852 compared to expectant management and is cost-effective with a cost-saving of 18 179 NOK per cesarean section avoided.

Elective induction of labor at week 39 is potentially cost-saving when compared to expectant management following elective induction at week 40, with cost-savings of 74 547 NOK per QALY gained and 62 873 NOK per cesarean section avoided.

Table 6 provides a summary of the cost and health-related outcomes, incremental outcomes, and ICER results per strategy.

Table 6: Results per strategy.

Cost effectiveness

Population = 15000	cost [NOK 2022]	effect [QALY]	cesareans
Elective induction at 39+0	988 663 330	883 650	2 790
Expectant management until 40+0, following a new decision	1 005 682 141	883 419	3 136
Elective induction at 40+0	1 008 234 054	883 602	3 294
Expectant management until 41+0	1 023 716 141	883 378	4 146
Incremental results	ΔC [NOK 2022]	ΔE [QALY]	ΔE (cesareans avoided)
Week 39: Elective induction vs Expectant management	-17 018 811	230	346
Week 40: Elective induction vs Expectant management	-15 482 087	224	852

Per delivery	cost [NOK 2022]	effect [QALY]	cesareans
Elective induction at 39+0	65 910,89	58,91	0,19
Expectant management until 40+0, following a new decision	67 045,48	58,89	0,21
Elective induction at 40+0	67 215,60	58,91	0,22
Expectant management until 41+0	68 247,74	58,89	0,28
Incremental results	ΔC [NOK 2022]	ΔE [QALY]	ΔE (cesareans avoided)
Week 39: Elective induction vs Expectant management	-1 134,59	0,02	0,02
Week 40: Elective induction vs Expectant management	-1 032,14	0,01	0,06

Result	Quadrant	ICER [NOK/QALY]	ICER [NOK/CA]
Week 39: Elective induction vs Expectant management	4: cost-effective	-73 904,01	-49 193,67
Week 40: Elective induction vs Expectant management	4: cost-effective	-69 218,25	-18 179,61

5.1 Deterministic sensitivity analysis

Deterministic sensitivity analysis was performed to ensure the robustness of the results. Each model parameter was varied within its respective range, while keeping the other parameters constant. The resulting differences in NMB of the incremental outcomes for the most relevant parameters are displayed in Figure 8 and Figure 9.

The analysis revealed that the results were sensitive to several parameters, most notably the probabilities of neonatal death, likelihoods of cesarean sections (especially in the induction branches), probabilities of hypertensive disorders of pregnancy, and stillbirths. However, the induction strategies remained cost-effective at a willingness to pay threshold of 275 000 NOK/QALY in all cases except one. If the probability of cesarean section resulting from elective induction at week 40 exceeds 32%, the strategy is no longer cost-effective compared to expectant management.

Figure 8: Tornado Diagram - Week 39, Induction of labor vs Expectant management sensitivity analysis.

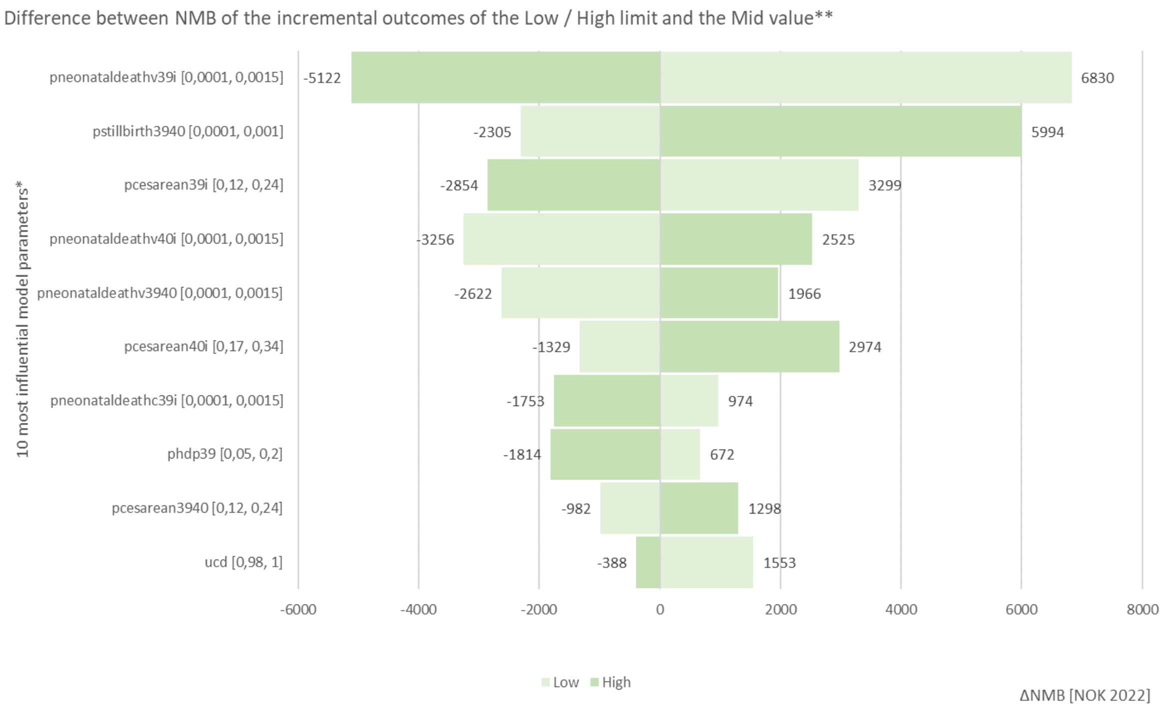
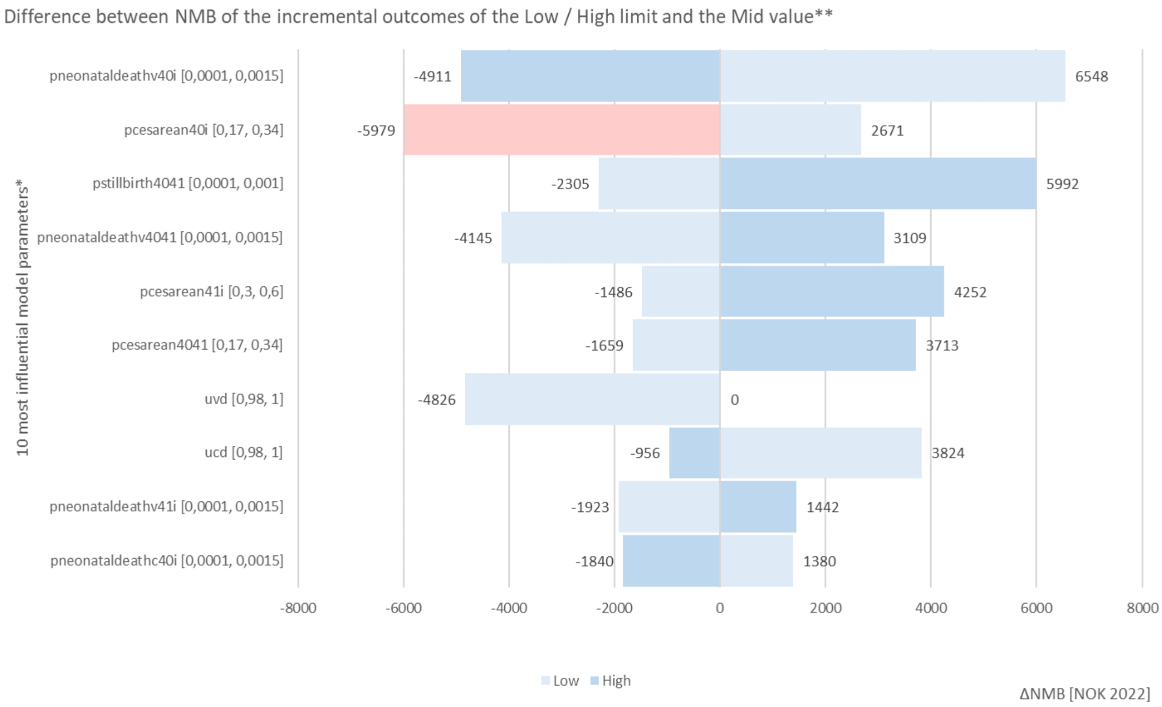


Figure 9: Tornado Diagram - Week 40, Induction of labor vs Expectant management sensitivity analysis.



The highlighted bar represents the case where Expectant Management was the dominant strategy.

*Full parameter names in Appendix C: full parameter names, full tornado diagrams available in Appendix D: Full Tornado Diagrams

**At willingness to pay threshold of 275 000 NOK/QALY

Varying the health utility discount rate did not alter the cost-effectiveness conclusion. The ICER results for parameter values of 0% and 5% indicated cost-savings of 29 844 NOK/QALY and 110 315 NOK/QALY, respectively for elective induction in week 39. For elective induction in week 40, the results were cost-savings of 30 011 NOK/QALY and 98 124 NOK/QALY, respectively. The probability of making the "best decision" also did not significantly influence the results. Even if all decisions captured maximum health outcomes in the expectant management branch, elective induction at week 39 remained cost-effective.

Figure 10: One-way sensitivity analysis: ICER vs cost of induction for weeks 39 and 40.

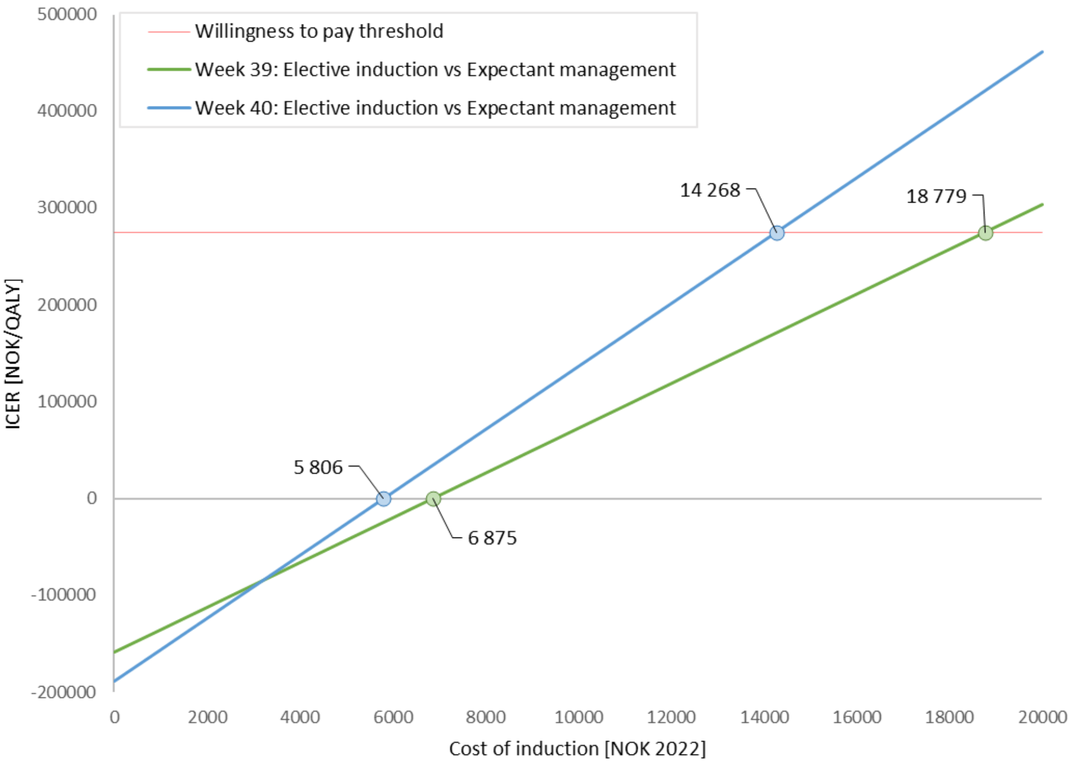


Figure 10 provides insights into the influence of the induction costs on the cost-effectiveness outcome. For the week 39 induction strategy, if the cost is below 6 875 NOK, the strategy is considered cost-effective for any value of the willingness to pay threshold. In the range between 6 875 NOK and 18 779 NOK, the induction strategy is more expensive than expectant management but still cost-effective under the willingness to pay threshold of 275 000 NOK/QALY. However, if the cost of induction exceeds 18 779 NOK for week 39, the elective induction strategy is no longer considered cost-effective. For the week 40 induction strategy, if the cost is below 5 806 NOK, the strategy is cost-effective regardless of the willingness to pay threshold. In the range between 5 806 NOK and 14 268 NOK the strategy is cost-effective under the willingness to pay threshold of 275 000 NOK/QALY. Above the cost of 14 268 NOK per induction, elective induction at week 40 is no longer cost-effective.

5.2 Probabilistic sensitivity analysis

At a willingness to pay threshold of 275 000 NOK/QALY, the elective induction of labor in week 39 is cost-effective compared to expectant management in 92% of the cases (Figure 11 shows the simulation results in the cost-effectiveness plane), while the elective induction of labor in week 40 is cost-effective compared to expectant management in 87% of the cases (Figure 13). For the secondary outcome, 80% of the cases confirm that the induction of labor at week 39 is cost-effective with respect to the cost of a cesarean section, and 81% of the cases confirm the same for elective induction at week 40.

Figure 11: Cost-effectiveness plane: Elective Induction at week 39 vs Expectant Management.

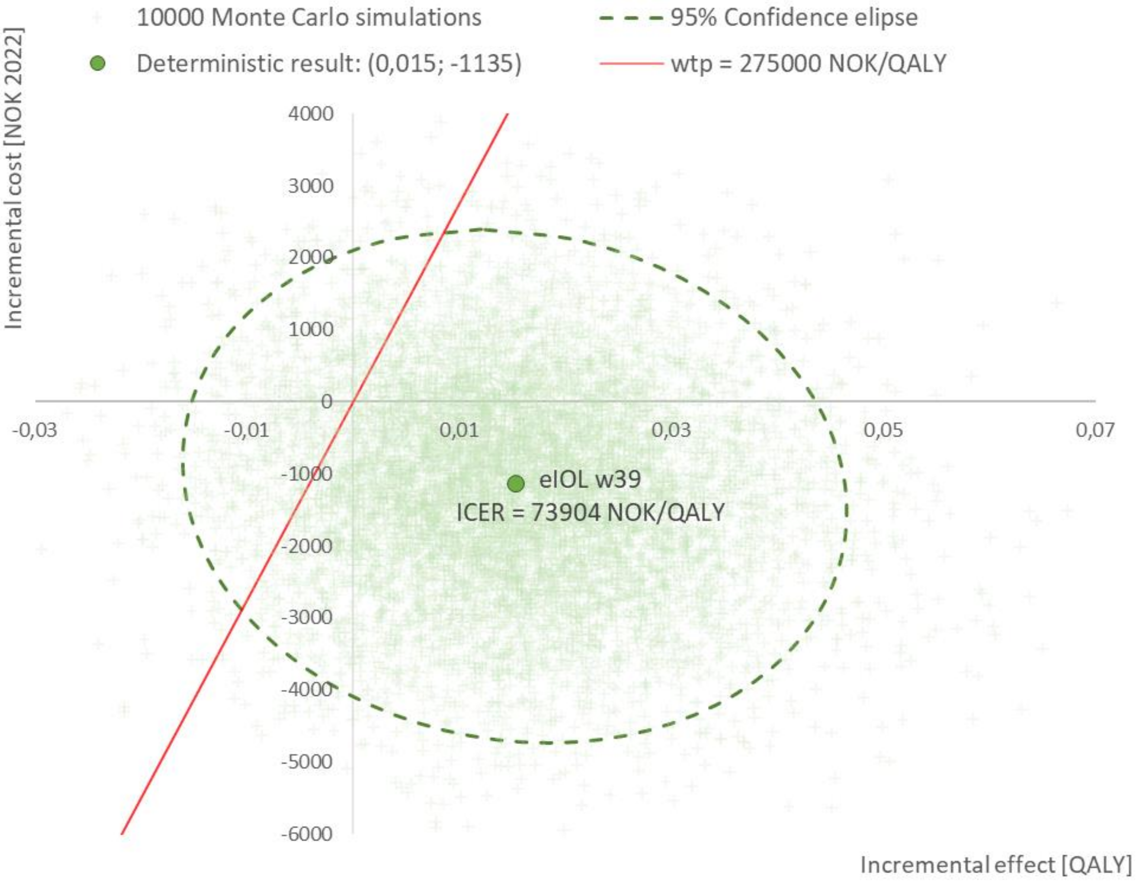
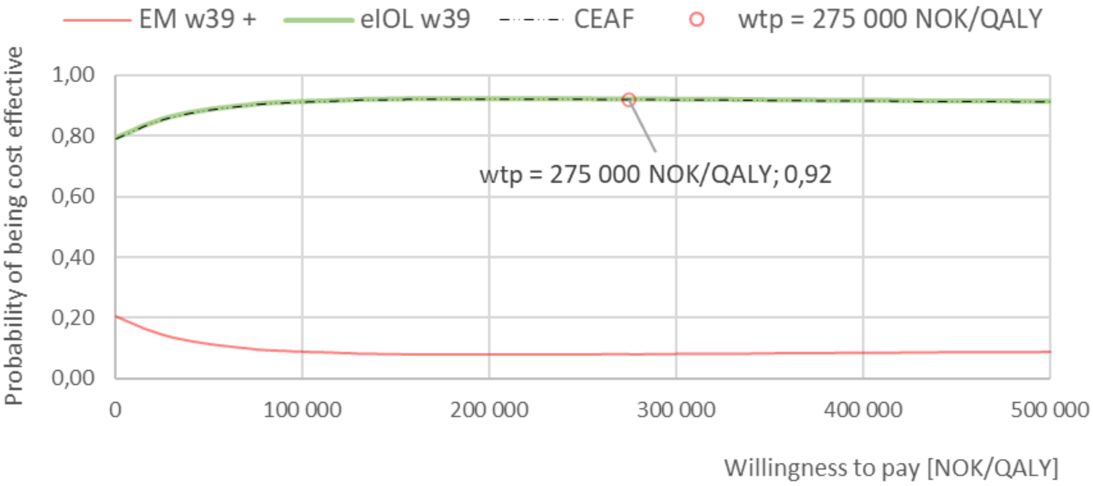


Figure 12: Cost-effectiveness acceptability curves: Elective Induction at week 39 vs Expectant Management.



Both strategies appear to remain cost-effective over a wide range of willingness to pay thresholds, as depicted in Figure 12 and Figure 14. This suggests that the elective induction of labor in both week 39 and week 40 is likely to be a cost-effective option for improving health outcomes in the population studied.

Figure 13 Cost-effectiveness plane: Elective Induction at week 40 vs Expectant Management.

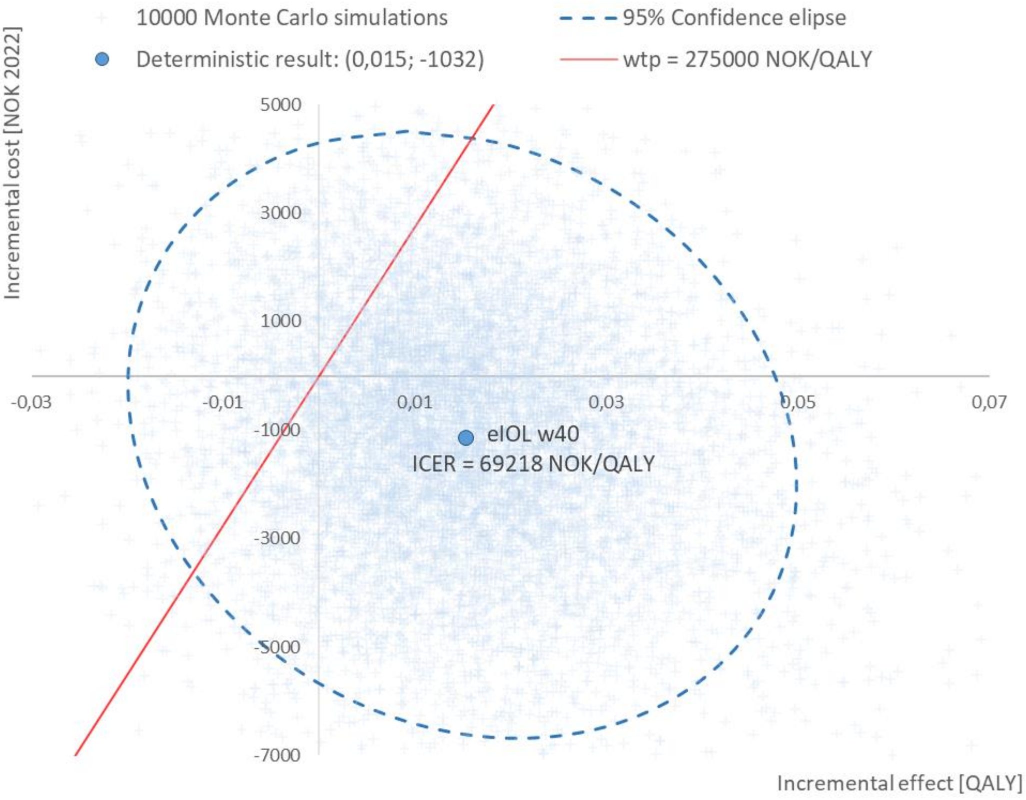
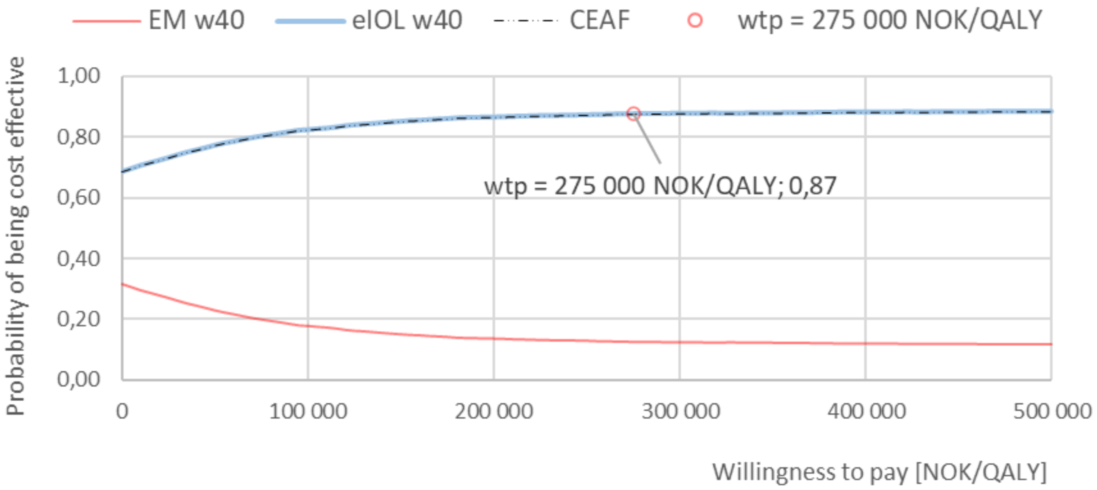


Figure 14 Cost-effectiveness acceptability curves: Elective Induction at week 40 vs Expectant Management.



Elective induction in week 39 is the dominant strategy compared to expectant management followed by elective induction in week 40 in 88% of the cases as depicted in Figure 15 and Figure 16. This implies that week 39 is the optimal timing for the elective induction at term.

Figure 15 Cost-effectiveness plane: Elective Induction at week 39 vs Expectant Management followed by Elective Induction at week 40.

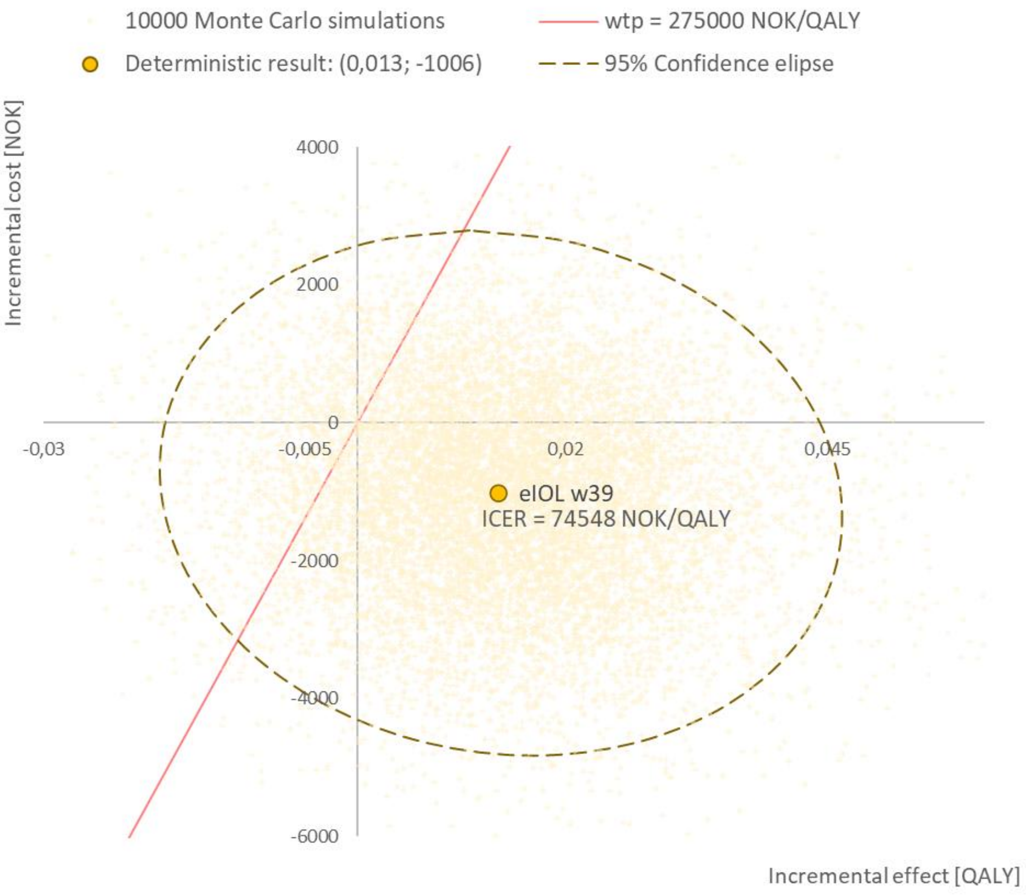
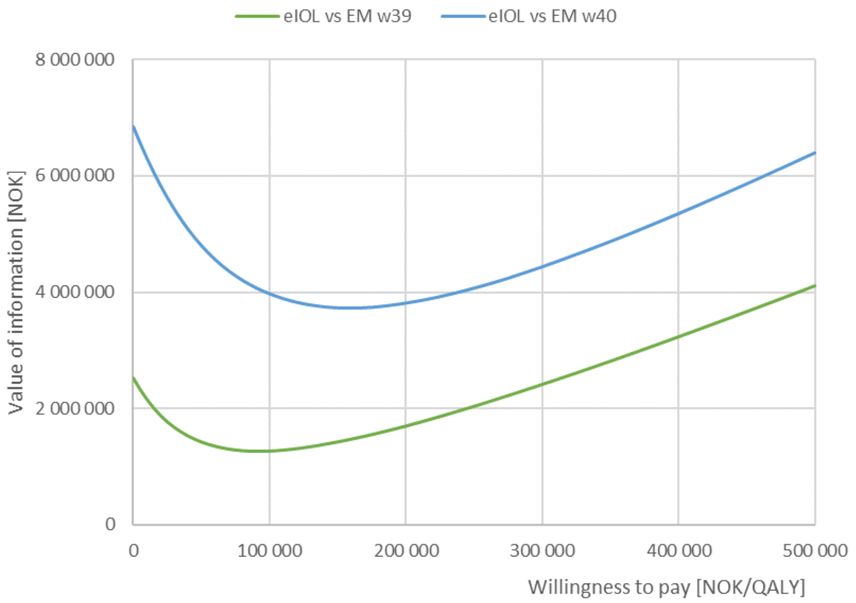


Figure 16 Cost-effectiveness acceptability curves: Elective Induction at week 39 vs Expectant Management followed by Elective Induction at week 40.

The population Expected Value of Perfect Information (pEVPI) is displayed in Figure 17. Considering the low level of uncertainty in the results, any potential study aimed at investigating the combined model parameters would need to have a budget of no more than 6 million NOK at a willingness to pay threshold of 275 000 NOK/QALY in order to provide value for the money. This budget may not be sufficient to conduct a randomized controlled trial. Therefore, an alternative approach could be a retrospective observational study set in the Norwegian context, which may offer valuable insights at a lower cost.

Figure 17: Value of information analysis: population Expected Value of Perfect Information.



6. Discussion

This chapter will provide a brief overview of the findings from the decision-analytic model. It will highlight the most noteworthy results and consider their implications for policy and practice. Furthermore, it will compare the results from this study to those from similar studies in literature, exploring potential areas of agreement and disagreement.

In addition, it will discuss the limitations and strengths of this research, examining potential areas for improvement and avenues for future inquiry. Lastly, it will consider the implications of presented findings for further research in the field, offering recommendations for scholars and practitioners alike.

6.1 Summary of the Findings

The findings indicate that elective induction at 39 weeks of gestation is potentially cost-effective compared to expectant management, with a probability of 92% at a willingness to pay threshold of 275 000 NOK/QALY. Notably, this strategy resulted in decreased rates of cesarean sections and overall improvement in maternal and neonatal health outcomes without increasing costs. Similar cost-effective results were observed for elective induction at 40 weeks of gestation, with a probability of 87%. These findings suggest that elective induction is not only cost-effective but also a cost-saving strategy for managing low-risk pregnancies.

Previous studies have reported similar findings, with elective induction being a dominant strategy compared to expectant management, as reported by Kaimal et al. (2011), Hersh et al. (2019) and Fitzgerald, Kaimal and Little (2023). However, while Kaimal et al. (2011) reported robust results, uncertainty played a greater role in Hersh et al. (2019) and Fitzgerald, Kaimal and Little (2023) conclusions, with Hersh reporting marginal cost-effectiveness and Fitzgerald, Kaimal and Little (2023) reporting different results for each subgroup based on cervix examination.

One key difference in this thesis approach is the inclusion of an alternative definition of expectant management. This recognizes that choices and preferences can change from week to week, accounting for the choice of elective induction later in pregnancy in the developed model. Another notable difference is the sourcing of model parameters. This thesis was based in the Norwegian context, with selected parameters reflecting that context. As a result, the cost parameters based on the diagnoses-related group system were less uncertain compared to studies that focused on privately financed healthcare systems.

6.2 Limitations and Strengths

There are three important factors to address when discussing the modeling approach, model context, model structure and model parameters. Each of these factors shape the modeling decision and influence the results, each with its own characteristic limitations.

6.2.1 Perspective

It is important to note that the model developed in this study considered the health payer perspective, with costs obtained from the Norwegian Directorate of Health (2023) and reflecting what the health system pays hospitals for listed diagnoses and procedures. Although the costs appear accurate, this can be misleading. Issues with DRG-related financing for maternity wards have been previously raised in the literature, with the report on changes in birthing population (Norwegian Directorate of Health, 2020) pointing specifically to the additional costs that induction of labor incurs due to the subsequent duration of hospital stay that is not covered by the DRG group.

Another issue is the composition of the refund, with the current system being financed by 50% DRG and a lump sum intended to cover the rest of the hospital's running expenses. However, this lump sum is left to the discretion of the hospital to distribute, leading to difficulties in allocating resources between different hospital wards, as pointed out by Mathisen et al. (2002). They have shown that this financing scheme was not sufficient to cover the actual expenses of deliveries, and any complications led to cost overruns. Therefore, although costs were sourced from the Norwegian DRG system, they do not precisely reflect the actual expenses. The implication of this is that while the induction of labor appears to be cost effective from the health payer perspective, future analyses should attempt to capture the true costs based on a hospital perspective.

6.2.2 Long term vs short term outcomes

Another important choice in modeling is the time frame. This study focused solely on long-term effects, informed by the sensitivity analysis by Hersh et al. (2019) that highlighted the dominance of permanent outcomes over short-term ones. However, this approach has limitations, particularly in disregarding medical conditions that may arise during and shortly after labor. It is incorrect to assume that all complications at birth have lifelong impacts on the mother and baby. Despite many of these conditions resolving within the lifetime perspective, they still pose significant challenges in terms of health and resources. Conditions such as postpartum anxiety and depression, physical injuries such as perineal rift, pelvic floor injuries, neonatal bone fractures and complications such as infection, or postpartum hemorrhage all require medical attention spanning weeks or possibly months and affect the health of an already vulnerable population.

Furthermore, it may have been beneficial to include specific outcomes such as meconium aspiration syndrome or macrosomia in the analysis as these conditions have been noted in multiple studies in relation to expectant management (Osmundson, Ou-Yang and Grobman, 2011; Hussain et al., 2011; Grobman and Caughey, 2019; Ren et al., 2023). Although these conditions were not directly measured, their most severe outcomes were represented in the analysis through neonatal demise and brachial plexus injury. To expand future research, it is suggested to broaden the range of potential complications and outcomes observed.

Another aspect that the model did not account for is any subsequent delivery. The mode of first delivery often influences decision-making for subsequent births, which is why the nulliparous population is of particular interest. However, this model did not consider the effect of mode of delivery on subsequent births, except for a maternal utility reduction following cesarean section during the fertile age.

While sensitivity analysis showed the largest impact comes from long-term outcomes following neonatal or fetal demise, the assumed permanence of maternal impacts may not hold true. Research has shown that women may recover from the psychological effects of stillbirth (Gravensteen et al. 2018). However, a successful vaginal birth does not guarantee perfect health for the neonate for the next 80 years. Long-term impacts of a single event introduce a high level of uncertainty into the analysis. Discounting health-related outcomes can somewhat offset this issue, but uncertainty arising from the assumption of long-term outcomes should be considered when interpreting the results.

Considering all of these factors, it is recommended to conduct a similar study with a more restricted time frame, such as six months to five years after birth. This would allow for a more comprehensive assessment of both short-term and long-term outcomes and their associated costs and benefits.

6.2.3 Maternal vs neonatal health outcomes

Neonatal outcomes are an important consideration in any model evaluating the costs and benefits of induction of labor. While including them in the model structure adds complexity and introduces a degree of uncertainty, omitting them fails to capture an essential part of the reality. This is a challenge recognized in literature, with Fitzgerald et al. (2023) notably avoiding neonatal outcomes in their study. The main concern is that neonatal outcomes may dominate the model and skew the analysis results. This study's findings were also notably influenced by neonatal outcomes, leading to challenges in intuitively interpreting the net monetary benefit results (NMB of the week 39 elective induction strategy at willingness to pay of 275 000 NOK/QALY was 16.1 MNOK). One way to address this concern is to categorize the reported results into maternal and neonatal outcomes, or maternal and overall outcomes to increase transparency.

6.2.4 QALYs vs otherwise defined health effects

The use of QALYs as a measure of health outcomes in the context of birth has its limitations as noted in this study. The challenges with presenting intuitive results and the limited suitability of current health utilities raise questions about the appropriateness of this measure in this context. As such, future studies could explore alternative indicators of effect that address the limitations of QALYs and provide a more grounded analysis. For example, one potential alternative to QALYs is the use of cesareans avoided as a simpler and more precise outcome measure, particularly in settings of high uncertainty. This measure better reflects the tangible benefits associated with induction of labor and provides a more intuitive and accessible output for policymakers and healthcare providers. However, it does not capture the full range of health outcomes associated with different delivery methods.

6.2.5 Low risk population

The population chosen for this study was low risk nulliparous women. However, a challenge in providing policy recommendations based on the study results is the limited number of this population in Norway. In addition, low-risk nulliparous women represent a heterogeneous group, meaning that there may be further subgroups within this population that could exhibit different outcomes and results based on individual characteristics, such as age, BMI, or health status such as cervix ripeness. Additionally, defining what qualifies as a "low-risk" woman can be challenging, as it requires comprehensive individual medical assessments considering various factors such as medical history, pre-existing conditions, age, and overall health. All these considerations underscore the importance of personalized medical assessments to ensure optimal care and outcomes for each individual woman. This reinforces the need for healthcare providers to engage in shared decision-making with pregnant women, taking into account their specific circumstances and preferences. In that context, rather than providing clear policy guidelines, this study needs to be taken as an informative element.

6.2.6 Decision tree model

Labor induction and delivery represent relatively short-term events in women's overall reproductive health, typically lasting only a few hours to a few days. In comparison to chronic medical conditions, such as cancer or heart disease, the decision-making process for induction of labor and delivery benefits more from a decision tree model rather than Markov state transition model.

Of all the decision tree models found in literature, the one by Hersh et al. (2018) proved to be the most appropriate for adaption to the study goals. Only minor changes were necessary to adjust the model, with the most work dedicated to finding updated, Norwegian specific parameter values. However, it was not clear from Hersh et al. (2018) if this model was validated and how. Subsequent use of the similar model in Fitzgerald et al. (2023) points to this model being recognized in literature. Of course, the best way to settle the question of cost effectiveness of elective induction would be an appropriately sized RCT comparable to the ARRIVE trial. However, the size of the population affected, and outcomes documented, as shown in the VOI analysis would not justify the costs of such a study. Nevertheless, a retrospective cohort study in the Norwegian context could support the validation, highlight specificities of the population, and serve as a starting point for more detailed modeling.

The limitations of this study include its reliance on model inputs derived from the literature. The primary reference, the ARRIVE Trial, may not adequately represent the Norwegian population, impacting the quality of the analysis. Additionally, wider confidence intervals associated with some of the data used introduce uncertainty and potential bias. These limitations should be considered when interpreting the results and further research is needed to enhance the quality and generalizability of the analysis.

The utilities used in this model were derived from three studies: Carroll and Downs (2006), Angeja et al. (2006), and Grobman et al. (2002). It is important to note that these studies are not recent and were conducted on populations that may not precisely reflect the Norwegian healthcare context. However, these studies were chosen under the assumption of generalizability of the health outcomes.

This study did not examine the socio-economic factors within the Norwegian healthcare system, such as the availability of healthcare personnel in birthing clinics, the geographic distribution of hospitals, and the preferences of women giving birth. Both labor and the induction of labor require significant amounts of time and resources. An increase in elective inductions could add additional pressure on the entire system, potentially calling into question the sustainability of maternity-led units.

Despite its limitations, this study has several noteworthy strengths. While previous studies, including Hersh (2019) and Fitzgerald (2023), assumed induction in week 41, they based their models on data from the ARRIVE Trial, which continued expectant management until week 42. In contrast, the model in this study relied on a different research study, namely Tita (2021), which prevented the same methodological issue from arising.

Additionally, this study adopts an active approach to expectant management, acknowledging that the initial decision made by the woman at week 39 of gestation may be subject to change at the next pregnancy follow-up appointment. The study cleverly resolves this methodological challenge by embedding the second model into the expectant management branch of the first and using probability to select between the two constructed sub-scenarios. This accounts for the possibility of choosing elective induction at 40 weeks and provides an accurate comparator for investigating the optimal timing of elective induction.

6.3 Implications for Further Research

Initially, this study was intended to include a retrospective observational study that would have collected data from the Norwegian Birth Registry. The registry contains comprehensive information about all births in Norway per patient, per year, enabling the calculation of probabilities that are more representative of the Norwegian context. This would have improved the accuracy and reliability of the analysis. However, the restricted accessibility of the Norwegian Birth Registry due to privacy policies and associated costs limited access to registry data, necessitating the use of data obtained from the literature to inform the model.

Despite this limitation, it is widely acknowledged that optimal research into the cost-effectiveness of elective induction must take into account the unique characteristics of each setting, with populations, birthing practices, preferences of pregnant women, and healthcare systems differing from one setting to another.

Therefore, further research should focus on closely examining individual countries' specific circumstances using real-life data. Conducting hospital-level research would also provide valuable insights that could enhance our overall comprehension of the intricate issue of elective induction of labor.

7. Conclusion

An economic evaluation was conducted from the health payer perspective to determine the cost-effectiveness of elective induction in weeks 39 and 40 of gestation in the context of Norwegian low-risk nulliparous women. The results showed that elective induction of labor at 39 weeks of gestation is potentially a cost-saving strategy compared to expectant management with ICER of 73 904 NOK per QALY gained with 92% probability at willingness to pay of 275 000 NOK/QALY, and the total of 346 cesarean sections avoided with 80% probability of 49 193 NOK saved per cesarean avoided at the cost of 65 000 NOK per cesarean avoided. Similar results were shown for the elective induction at week 40 with potential cost-savings of 69 218 NOK per QALY gained with 87% probability, and the total of 852 cesarean sections avoided with 80% probability of 18 179 NOK saved per cesarean avoided. The sensitivity analysis mostly affected the magnitude of cost savings, but the overall conclusion was robust. Week 39 elective induction is potentially cost-saving compared to expectant management followed by elective induction in week 40 with ICER of 74 547 per QALY gained with 88% probability at willingness to pay threshold of 275 000 NOK/QALY.

Answering the research questions, elective inductions of labor at term appear to be cost-effective when compared to expectant management. Based on the findings, week 39 was determined to be the optimal timing for elective induction.

In conclusion, the increasing rates of induction in Norway necessitate further research on the cost-effectiveness and health outcomes for different population groups. This study provides a foundation for future research on the cost-effectiveness of elective induction for low-risk nulliparous women; however, more investigation is necessary before practical recommendations can be made. To address the uncertainty in the model structure and parameters, a retrospective observational study utilizing Norwegian Birth Registry data is proposed. Additionally, the hospital perspective is necessary to accurately assess the costs of this procedure, which may be obscured by the DRG financing system.

List Of References

05375: Life expectancy, by sex and age 1986 - 2022. Statbank Norway (no date). Available at: https://www.ssb.no/en/statbank/table/05375 (Accessed: 12 November 2023).

Alfirevic, Z. *et al.* (2016) ‘Which method is best for the induction of labour? A systematic review, network meta-analysis and cost-effectiveness analysis’, *Health Technology Assessment (Winchester, England)*, 20(65), pp. 1–584. Available at: https://doi.org/10.3310/hta20650.

Alkmark, M. *et al.* (2022) ‘Induction of labour at 41 weeks of gestation versus expectant management and induction of labour at 42 weeks of gestation: A cost-effectiveness analysis’, *BJOG: an international journal of obstetrics and gynaecology*, 129(13), pp. 2157–2165. Available at: https://doi.org/10.1111/1471-0528.16929.

Allen, R. and O’Brien, B.M. (2009) ‘Uses of misoprostol in obstetrics and gynecology’, *Reviews in Obstetrics & Gynecology*, 2(3), pp. 159–168.

Angeja, A.C.E. *et al.* (2006) ‘Chilean women’s preferences regarding mode of delivery: which do they prefer and why?’, *BJOG: an international journal of obstetrics and gynaecology*, 113(11), pp. 1253–1258. Available at: https://doi.org/10.1111/j.1471-0528.2006.01069.x.

Baud, D. *et al.* (2013) ‘Adverse obstetrical and neonatal outcomes in elective and medically indicated inductions of labor at term’, *The Journal of Maternal-Fetal & Neonatal Medicine: The Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, 26(16), pp. 1595–1601. Available at: https://doi.org/10.3109/14767058.2013.795533.

Bergholt, T. *et al.* (2004) ‘Danish obstetricians’ personal preference and general attitude to elective cesarean section on maternal request: a nation-wide postal survey’, *Acta Obstetricia Et Gynecologica Scandinavica*, 83(3), pp. 262–266. Available at: https://doi.org/10.1111/j.0001-6349.2004.0312.x.

Bernitz, S., Aas, E. and Øian, P. (2012) ‘Economic evaluation of birth care in low-risk women. A comparison between a midwife-led birth unit and a standard obstetric unit within the same hospital in Norway. A randomised controlled trial', *Midwifery*, 28(5), pp. 591–599. Available at: https://doi.org/10.1016/j.midw.2012.06.001.

Bettes, B.A. *et al.* (2007) 'Cesarean delivery on maternal request: obstetrician-gynecologists' knowledge, perception, and practice patterns', *Obstetrics and Gynecology*, 109(1), pp. 57–66. Available at: https://doi.org/10.1097/01.AOG.0000249608.11864.b6.

Briggs, A. and Fenn, P. (1998) 'Confidence intervals or surfaces? Uncertainty on the cost-effectiveness plane', *Health Economics*, 7(8), pp. 723–740. Available at: https://doi.org/10.1002/(sici)1099-1050(199812)7:8<723::aid-hec392>3.0.co;2-o.

Briggs, A.H., Claxton, K. and Sculpher, M. (2011) *Decision modelling for health economic evaluation*. Repr. [d. korr. Ausg. von 2007]. Oxford: Oxford Univ. Press (Handbooks in health economic evaluation series).

Briggs, A.H. and Gray, A.M. (1999) 'Handling uncertainty when performing economic evaluation of healthcare interventions', *Health Technology Assessment (Winchester, England)*, 3(2), pp. 1–134.

Burger, R.J. *et al.* (2023) 'Gestational age and socio-demographic factors associated with school performance at the age of 12 years, a population-based study', *Paediatric and Perinatal Epidemiology*, 37(7), pp. 643–651. Available at: https://doi.org/10.1111/ppe.12990.

Carlson, N.S. (2018) 'Current Resources for Evidence-Based Practice, November/December 2018', *Journal of Midwifery & Women's Health*, 63(6), pp. 735–741. Available at: https://doi.org/10.1111/jmwh.12926.

Carroll, A.E. and Downs, S.M. (2006) 'Comprehensive cost-utility analysis of newborn screening strategies', *Pediatrics*, 117(5 Pt 2), pp. S287-295. Available at: https://doi.org/10.1542/peds.2005-2633H.

Caughey, A.B. *et al.* (2009) 'Systematic review: elective induction of labor versus expectant management of pregnancy', *Annals of Internal Medicine*, 151(4), pp. 252–263, W53-63. Available at: https://doi.org/10.7326/0003-4819-151-4-200908180-00007.

Christoffersson, M. and Rydhstroem, H. (2002) 'Shoulder dystocia and brachial plexus injury: a population-based study', *Gynecologic and Obstetric Investigation*, 53(1), pp. 42–47. Available at: https://doi.org/10.1159/000049410.

Confidence Ellipse | Real Statistics Using Excel (no date). Available at: https://real-statistics.com/multivariate-statistics/multivariate-normal-distribution/confidence-ellipse/ (Accessed: 12 November 2023).

Darney, B.G. *et al.* (2013) 'Elective induction of labor at term compared with expectant management: maternal and neonatal outcomes', *Obstetrics and Gynecology*, 122(4), pp. 761–769. Available at: https://doi.org/10.1097/AOG.0b013e3182a6a4d0.

Darney, B.G. and Caughey, A.B. (2014) 'Elective induction of labor symposium: nomenclature, research methodological issues, and outcomes', *Clinical Obstetrics and Gynecology*, 57(2), pp. 343–362. Available at: https://doi.org/10.1097/GRF.0000000000000029.

Davey, M.-A. and King, J. (2016) 'Caesarean section following induction of labour in uncomplicated first births- a population-based cross-sectional analysis of 42,950 births', *BMC pregnancy and childbirth*, 16, p. 92. Available at: https://doi.org/10.1186/s12884-016-0869-0.

Dögl, M. *et al.* (2018) 'Elective induction of labor: A prospective observational study', *PloS One*, 13(11), p. e0208098. Available at: https://doi.org/10.1371/journal.pone.0208098.

Dögl, M., Vanky, E. and Heimstad, R. (2016) 'Changes in induction methods have not influenced cesarean section rates among women with induced labor', *Acta Obstetricia Et Gynecologica Scandinavica*, 95(1), pp. 112–115. Available at: https://doi.org/10.1111/aogs.12809.

Drummond, M.F. *et al.* (2015) *Methods for the economic evaluation of health care programmes*. Fourth edition. Oxford New York: Oxford University Press.

Einerson, B.D. *et al.* (2020) 'Cost of Elective Labor Induction Compared With Expectant Management in Nulliparous Women', *Obstetrics and Gynecology*, 136(1), pp. 19–25. Available at: https://doi.org/10.1097/AOG.0000000000003930.

Fahy, M. *et al.* (2013) 'Economics of childbirth', *Acta Obstetricia Et Gynecologica Scandinavica*, 92(5), pp. 508–516. Available at: https://doi.org/10.1111/aogs.12117.

Fenwick, E. *et al.* (2020) 'Value of Information Analysis for Research Decisions-An Introduction: Report 1 of the ISPOR Value of Information Analysis Emerging Good Practices Task Force', *Value in Health: The Journal of the International Society for*

Pharmacoeconomics and Outcomes Research, 23(2), pp. 139–150. Available at: https://doi.org/10.1016/j.jval.2020.01.001.

Fenwick, E. and Byford, S. (2005) 'A guide to cost-effectiveness acceptability curves', *The British Journal of Psychiatry: The Journal of Mental Science*, 187, pp. 106–108. Available at: https://doi.org/10.1192/bjp.187.2.106.

Fitzgerald, A.C., Kaimal, A.J. and Little, S.E. (2023) 'Cost-effectiveness of induction of labor at 39 weeks vs expectant management by cervical examination', *American Journal of Obstetrics and Gynecology*, 229(2), p. 162.e1-162.e9. Available at: https://doi.org/10.1016/j.ajog.2023.01.010.

Fonseca, M.J. *et al.* (2020) 'Does induction of labor at term increase the risk of cesarean section in advanced maternal age? A systematic review and meta-analysis', *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, 253, pp. 213–219. Available at: https://doi.org/10.1016/j.ejogrb.2020.08.022.

Gravensteen, I.K. *et al.* (2018) 'Anxiety, depression and relationship satisfaction in the pregnancy following stillbirth and after the birth of a live-born baby: a prospective study', *BMC pregnancy and childbirth*, 18(1), p. 41. Available at: https://doi.org/10.1186/s12884-018-1666-8.

Greene, M.F. (2018) 'Choices in Managing Full-Term Pregnancy', *The New England Journal of Medicine*, 379(6), pp. 580–581. Available at: https://doi.org/10.1056/NEJMe1807747.

Grobman, W.A. *et al.* (2002) 'Preference assessment of prenatal diagnosis for Down syndrome: is 35 years a rational cutoff?', *Prenatal Diagnosis*, 22(13), pp. 1195–1200. Available at: https://doi.org/10.1002/pd.494.

Grobman, W.A. (2007) 'Elective induction: When? Ever?', *Clinical Obstetrics and Gynecology*, 50(2), pp. 537–546. Available at: https://doi.org/10.1097/GRF.0b013e31804bdec4.

Grobman, W.A. *et al.* (2018) 'Labor Induction versus Expectant Management in Low-Risk Nulliparous Women', *The New England Journal of Medicine*, 379(6), pp. 513–523. Available at: https://doi.org/10.1056/NEJMoa1800566.

Grobman, W.A. *et al.* (2020) 'Health resource utilization of labor induction versus expectant management', *American Journal of Obstetrics and Gynecology*, 222(4), p. 369.e1-369.e11. Available at: https://doi.org/10.1016/j.ajog.2020.01.002.

Grobman, W.A. and Caughey, A.B. (2019) ‘Elective induction of labor at 39 weeks compared with expectant management: a meta-analysis of cohort studies’, *American Journal of Obstetrics and Gynecology*, 221(4), pp. 304–310. Available at: https://doi.org/10.1016/j.ajog.2019.02.046.

Grytten, J. *et al.* (2011) ‘The impact of hospital revenue on the increase in Caesarean sections in Norway. A panel data analysis of hospitals 1976-2005’, *BMC health services research*, 11, p. 267. Available at: https://doi.org/10.1186/1472-6963-11-267.

Haavaldsen, C. *et al.* (2023) ‘Is the increasing prevalence of labor induction accompanied by changes in pregnancy outcomes? An observational study of all singleton births at gestational weeks 37-42 in Norway during 1999-2019’, *Acta Obstetricia Et Gynecologica Scandinavica*, 102(2), pp. 158–173. Available at: https://doi.org/10.1111/aogs.14489.

Hersh, A.R. *et al.* (2019) ‘Induction of labor at 39 weeks of gestation versus expectant management for low-risk nulliparous women: a cost-effectiveness analysis’, *American Journal of Obstetrics and Gynecology*, 220(6), p. 590.e1-590.e10. Available at: https://doi.org/10.1016/j.ajog.2019.02.017.

Hersh, A.R. *et al.* (2020) ‘Maternal and Neonatal Hospitalization Costs Associated With Elective Induction of Labor at Term in California, 2007-2011’, *Obstetrics and Gynecology*, 136(1), pp. 8–18. Available at: https://doi.org/10.1097/AOG.0000000000003865.

Hong, J. *et al.* (2023) ‘Comparison of Maternal Labor-Related Complications and Neonatal Outcomes Following Elective Induction of Labor at 39 Weeks of Gestation vs Expectant Management: A Systematic Review and Meta-analysis’, *JAMA network open*, 6(5), p. e2313162. Available at: https://doi.org/10.1001/jamanetworkopen.2023.13162.

van Hout, B.A. *et al.* (1994) ‘Costs, effects and C/E-ratios alongside a clinical trial’, *Health Economics*, 3(5), pp. 309–319. Available at: https://doi.org/10.1002/hec.4730030505.

Husereau, D. *et al.* (2022) ‘Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Statement: Updated Reporting Guidance for Health Economic Evaluations’, *Value in Health: The Journal of the International Society for*

Pharmacoeconomics and Outcomes Research, 25(1), pp. 3–9. Available at: https://doi.org/10.1016/j.jval.2021.11.1351.

Hussain, A.A. *et al.* (2011) ‘Elective induction for pregnancies at or beyond 41 weeks of gestation and its impact on stillbirths: a systematic review with meta-analysis’, *BMC public health*, 11 Suppl 3(Suppl 3), p. S5. Available at: https://doi.org/10.1186/1471-2458-11-S3-S5.

Induksjon/igangsettelse av fødsel - Modning av cervix/livmorhalsen før fødsel (no date). Available at: https://www.legeforeningen.no/foreningsledd/fagmed/norsk-gynekologisk-forening/veiledere/veileder-i-fodselshjelp/induksjonigangsettelse-av-fodsel-modning-av-cervixlivmorhalsen-for-fodsel/ (Accessed: 13 November 2023).

Innsatsstyrt finansiering (ISF) – regelverk - Helsedirektoratet (no date). Available at: https://www.helsedirektoratet.no/tema/finansiering/innsatsstyrt-finansiering-og-drg-systemet/innsatsstyrt-finansiering-isf (Accessed: 12 November 2023).

Kaimal, A.J. *et al.* (2011) ‘Cost-effectiveness of elective induction of labor at 41 weeks in nulliparous women’, *American Journal of Obstetrics and Gynecology*, 204(2), p. 137.e1–9. Available at: https://doi.org/10.1016/j.ajog.2010.08.012.

Kaufman, K.E., Bailit, J.L. and Grobman, W. (2002) ‘Elective induction: an analysis of economic and health consequences’, *American Journal of Obstetrics and Gynecology*, 187(4), pp. 858–863. Available at: https://doi.org/10.1067/mob.2002.127147.

Keirse, M.J.N.C. (2010) ‘Elective induction, selective deduction, and cesarean section’, *Birth (Berkeley, Calif.)*, 37(3), pp. 252–256. Available at: https://doi.org/10.1111/j.1523-536X.2010.00413.x.

Lewis, S., Zhao, Z. and Schorn, M. (2022) ‘Elective Induction of Labor or Expectant Management: Outcomes Among Nulliparous Women with Uncomplicated Pregnancies’, *Journal of Midwifery & Women’s Health*, 67(2), pp. 170–177. Available at: https://doi.org/10.1111/jmwh.13313.

Lindquist, A. *et al.* (2022) ‘Developmental Outcomes for Children After Elective Birth at 39 Weeks’ Gestation’, *JAMA pediatrics*, 176(7), pp. 654–663. Available at: https://doi.org/10.1001/jamapediatrics.2022.1165.

Little, S.E. (2017) ‘Elective Induction of Labor: What is the Impact?’, *Obstetrics and Gynecology Clinics of North America*, 44(4), pp. 601–614. Available at: https://doi.org/10.1016/j.ogc.2017.08.005.

Medisinsk fødselsregister - statistikkbank (no date). Available at: https://statistikkbank.fhi.no/mfr/ (Accessed: 12 November 2023).

Middleton, P. *et al.* (2020) ‘Induction of labour at or beyond 37 weeks’ gestation’, *The Cochrane Database of Systematic Reviews*, 7(7), p. CD004945. Available at: https://doi.org/10.1002/14651858.CD004945.pub5.

Middleton, P., Shepherd, E. and Crowther, C.A. (2018) ‘Induction of labour for improving birth outcomes for women at or beyond term’, *The Cochrane Database of Systematic Reviews*, 5(5), p. CD004945. Available at: https://doi.org/10.1002/14651858.CD004945.pub4.

Miller, N.R. *et al.* (2015) ‘Elective Induction of Labor Compared With Expectant Management of Nulliparous Women at 39 Weeks of Gestation: A Randomized Controlled Trial’, *Obstetrics and Gynecology*, 126(6), pp. 1258–1264. Available at: https://doi.org/10.1097/AOG.0000000000001154.

Minkoff, H. *et al.* (2004) ‘Ethical dimensions of elective primary cesarean delivery’, *Obstetrics and Gynecology*, 103(2), pp. 387–392. Available at: https://doi.org/10.1097/01.AOG.0000107288.44622.2a.

O’Brien, B.J. and Briggs, A.H. (2002) ‘Analysis of uncertainty in health care cost-effectiveness studies: an introduction to statistical issues and methods’, *Statistical Methods in Medical Research*, 11(6), pp. 455–468. Available at: https://doi.org/10.1191/0962280202sm304ra.

Osmundson, S., Ou-Yang, R.J. and Grobman, W.A. (2011) ‘Elective induction compared with expectant management in nulliparous women with an unfavorable cervix’, *Obstetrics and Gynecology*, 117(3), pp. 583–587. Available at: https://doi.org/10.1097/AOG.0b013e31820caf12.

Øverland, E.A., Vatten, L.J. and Eskild, A. (2014) ‘Pregnancy week at delivery and the risk of shoulder dystocia: a population study of 2,014,956 deliveries’, *BJOG: an international journal of obstetrics and gynaecology*, 121(1), pp. 34–41. Available at: https://doi.org/10.1111/1471-0528.12427.

Page, M.J. *et al.* (2021) 'The PRISMA 2020 statement: an updated guideline for reporting systematic reviews', *BMJ (Clinical research ed.)*, 372, p. n71. Available at: https://doi.org/10.1136/bmj.n71.

Parikh, L.I. *et al.* (2014) 'Neonatal outcomes in early term birth', *American Journal of Obstetrics and Gynecology*, 211(3), p. 265.e1-265.e11. Available at: https://doi.org/10.1016/j.ajog.2014.03.021.

Pinto, P.V., Rodrigues, T. and Montenegro, N. (2018) 'Labor Induction vs. Expectant Management of Low-Risk Pregnancy', *The New England Journal of Medicine*, 379(23), p. 2277. Available at: https://doi.org/10.1056/NEJMc1812323.

Prioriteringskriteriene ved offentlig finansiering av legemidler (no date). Available at: https://www.legemiddelverket.no/offentlig-finansiering/slik-far-legemidler-offentlig-finansiering/hva-inneberer-prioriteringskriteriene-ressursbruk-nytte-og-alvorlighet (Accessed: 12 November 2023).

Ren, H. *et al.* (2023) 'Whether induction of labor ahead in low-risk women improves pregnancy outcomes?: A retrospective cohort, observational study', *Medicine*, 102(14), p. e33426. Available at: https://doi.org/10.1097/MD.0000000000033426.

Saccone, G. *et al.* (2019) 'Induction of labor at full-term in pregnant women with uncomplicated singleton pregnancy: A systematic review and meta-analysis of randomized trials', *Acta Obstetricia Et Gynecologica Scandinavica*, 98(8), pp. 958–966. Available at: https://doi.org/10.1111/aogs.13561.

Sanders, G.D. *et al.* (2016) 'Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine', *JAMA*, 316(10), pp. 1093–1103. Available at: https://doi.org/10.1001/jama.2016.12195.

Selvaratnam, R.J. *et al.* (2023) 'Elective induction of labour at full-term gestations and childhood school outcomes', *Journal of Paediatrics and Child Health*, 59(9), pp. 1028–1034. Available at: https://doi.org/10.1111/jpc.16449.

Sima, Y.T. *et al.* (2022) 'Cesarean delivery in Norwegian nulliparous women with singleton cephalic term births, 1967-2020: a population-based study', *BMC pregnancy and childbirth*, 22(1), p. 419. Available at: https://doi.org/10.1186/s12884-022-04755-3.

Simpson, K.R. and Atterbury, J. (2003) ‘Trends and issues in labor induction in the United States: implications for clinical practice’, *Journal of obstetric, gynecologic, and neonatal nursing: JOGNN*, 32(6), pp. 767–779. Available at: https://doi.org/10.1177/0884217503258528.

Skrondal, T.F., Bache-Gabrielsen, T. and Aune, I. (2020) ‘All that I need exists within me: A qualitative study of nulliparous Norwegian women’s experiences with planned home birth’, *Midwifery*, 86, p. 102705. Available at: https://doi.org/10.1016/j.midw.2020.102705.

Sørbye, I.K. *et al.* (2020) ‘Induction of labor and nulliparity: A nationwide clinical practice pilot evaluation’, *Acta Obstetricia Et Gynecologica Scandinavica*, 99(12), pp. 1700–1709. Available at: https://doi.org/10.1111/aogs.13948.

Sotiriadis, A. *et al.* (2019) ‘Maternal and perinatal outcomes after elective induction of labor at 39 weeks in uncomplicated singleton pregnancy: a meta-analysis’, *Ultrasound in Obstetrics & Gynecology: The Official Journal of the International Society of Ultrasound in Obstetrics and Gynecology*, 53(1), pp. 26–35. Available at: https://doi.org/10.1002/uog.20140.

Stock, S.J. *et al.* (2012) ‘Outcomes of elective induction of labour compared with expectant management: population based study’, *BMJ (Clinical research ed.)*, 344, p. e2838. Available at: https://doi.org/10.1136/bmj.e2838.

Tassis, B.M.G. *et al.* (2022) ‘An hypothetical external validation of the ARRIVE trial in a European academic hospital’, *The Journal of Maternal-Fetal & Neonatal Medicine: The Official Journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstetricians*, 35(22), pp. 4291–4298. Available at: https://doi.org/10.1080/14767058.2020.1849108.

Tita, A.T.N. *et al.* (2021) ‘Maternal and Perinatal Outcomes of Expectant Management of Full-Term, Low-Risk, Nulliparous Patients’, *Obstetrics and Gynecology*, 137(2), pp. 250–257. Available at: https://doi.org/10.1097/AOG.0000000000004230.

Vogel, J.P. *et al.* (2014) ‘Global perspectives on elective induction of labor’, *Clinical Obstetrics and Gynecology*, 57(2), pp. 331–342. Available at: https://doi.org/10.1097/GRF.0000000000000031.

Walker, K.F. *et al.* (2016) ‘Induction of labour versus expectant management at term by subgroups of maternal age: an individual patient data meta-analysis’, *European Journal of Obstetrics, Gynecology, and Reproductive Biology*, 197, pp. 1–5. Available at: https://doi.org/10.1016/j.ejogrb.2015.11.004.

Wennerholm, U.-B. *et al.* (2019) ‘Induction of labour at 41 weeks versus expectant management and induction of labour at 42 weeks (SWEdish Post-term Induction Study, SWEPIS): multicentre, open label, randomised, superiority trial’, *BMJ (Clinical research ed.)*, 367, p. l6131. Available at: https://doi.org/10.1136/bmj.l6131.

WHO recommendations: Induction of labour at or beyond term (2018). Geneva: World Health Organization (WHO Guidelines Approved by the Guidelines Review Committee). Available at: http://www.ncbi.nlm.nih.gov/books/NBK535795/ (Accessed: 30 October 2023).

WHO recommendations on induction of labour, at or beyond term (2022). Geneva: World Health Organization (WHO Guidelines Approved by the Guidelines Review Committee). Available at: http://www.ncbi.nlm.nih.gov/books/NBK585296/ (Accessed: 21 October 2023).

Yao, R. *et al.* (2014) ‘Obesity and the risk of stillbirth: a population-based cohort study’, *American Journal of Obstetrics and Gynecology*, 210(5), p. 457.e1–9. Available at: https://doi.org/10.1016/j.ajog.2014.01.044.

Zenzmaier, C. *et al.* (2021) ‘Cesarean delivery after non-medically indicated induction of labor: A population-based study using different definitions of expectant management’, *Acta Obstetricia Et Gynecologica Scandinavica*, 100(2), pp. 220–228. Available at: https://doi.org/10.1111/aogs.13989.

Appendix A: Literature review – included studies

Author (Year): Title	**Kaimal et al (2011):** Cost-effectiveness of elective induction of labor at 41 weeks in nulliparous women	**Lakic et al (2014):** Cost-Effectiveness Analysis of Different Types of Labor for Singleton Pregnancy: Real Life Data	**Hersh et al (2019):** Induction of labor at 39 weeks of gestation versus expectant management for low-risk nulliparous women: a cost-effectiveness analysis	**Callander et al (2020):** Reducing caesarean delivery: An economic evaluation of routine induction of labour at 39 weeks in low-risk nulliparous women	**Fitzgerald et al (2023):** Cost-effectiveness of induction of labor at 39 weeks vs expectant management by cervical examination
Population	hypothetical cohort of 200,000 nulliparous women with low risk, singleton, cephalic gestations, beginning at 41 weeks of pregnancy	low-risk obstetric population (i.e. no major fetal anomalies, no pregnancy complication), singleton pregnancies retrospective observational cohort: 667 pregnancies 54.8% nulliparous, no significant difference in the delivery type 94.8% vertex presentation gestation week (mean ± sd) 38.73 ± 2.24	theoretical cohort of 1.6 million low-risk nulliparous women	low-risk, nulliparous women with singleton pregnancies, vertex presentations and no medical conditions who had completed 38 weeks of pregnancy for budget analysis, estimated 63,649 women were considered as theoretical cohort	theoretical cohort of low-risk nulliparous patients at 39 weeks of gestation (results presented for cohort size: 100,000 - favorable cervix, 100,000 - unfavorable cervix, total 200,000 people)

Intervention	induction of labor at 41 weeks	elective induction	induction of labor at 39 weeks	routine induction of labor at 39 weeks	planned induction of labor at 39 weeks of gestation (divided into two groups, favorable and unfavorable cervix)
Comparator	expectant management until 42 weeks	vaginal labor elective cesarean section	expectant management: routine pregnancy care until woman goes into spontaneous labor or require induction of labor for an indication such as hypertensive disorders of pregnancy or late-term or post-term pregnancy model assumed induction at 41 weeks unless birth already occurred	Standard care: Current public hospital standard care within Australia (model assumed induction before 43+0 weeks unless birth already occurred), caseload midwifery, chart audit	expectant management, patients who reached 41 weeks of gestation would undergo IOL at that time (divided into two groups, favorable and unfavorable cervix)

Health Related Outcomes	Mode of delivery Maternal: Mortality Severe perineal laceration Neonatal: Macrosomia Shoulder dystocia Permanent neonatal injury Meconium-stained fluid Meconium aspiration Neonatal demise	Maternal: occurrence of hemorrhage, perineal lacerations (cervix and/or perineum) cesarean delivery in cases of vaginal labor Newborn: Apgar score >= 7 in the fifth minute of life	Mode of delivery Maternal: hypertensive disorders of pregnancy Neonatal: macrosomia stillbirth permanent brachial plexus injury neonatal death	Mode of delivery Special care nursery admission NICU admission stillbirth, neonatal or infant death	Mode of delivery hypertensive disorders of pregnancy stillbirths
Costs	Cost of antenatal testing Cost of cesarean delivery Cost of epidural Additional cost of induction Cost of vaginal delivery Cost of uncomplicated newborn stay Cost of complicated newborn stay Cost of neonatal demise	direct medical costs: hospital days prenatal and postnatal care of the newborn all labor interventions health technologies applied during and after birth costs of healthcare workers	Induction of labor Office visit Triage visit Vaginal delivery Cesarean delivery Hypertensive disorders of pregnancy Stillbirth Neonatal death Brachial plexus injury	Assigned per model state, taken from Maternity1000 study (services covered under the Medicare Benefits Schedule, plus prescription pharmaceuticals) Mode of birth cost, SCN admission and NICU admission were costed based upon the National Efficient Cost	Vaginal delivery Cesarean delivery Additional cost for induction of labor Hypertensive disorder of pregnancy Fetal demise Cost for outpatient care per week remaining pregnant

Effectiveness / Utilities	Considered both maternal and neonatal perspective: Maternal and neonatal mortality Utility of cesarean delivery Utility of intrauterine fetal demise Utility of vaginal delivery	% of successful deliveries: labors that began up to 42 gestation weeks, without maternal mortality Apgar >= 7 in the fifth minute of life	Considered both maternal and neonatal perspective: Cesarean delivery Induction of labor Stillbirth Neonatal death Brachial plexus injury	taken from literature for each state	Only maternal perspective: Vaginal delivery Cesarean delivery Hypertensive disorder of pregnancy Stillbirth
Study type	Cost utility analysis (QALY) Decision analytic model Decision Tree	Cost effectiveness analysis Decision analytic model Decision Tree	Cost utility analysis (QALY) Decision analytic model Decision Tree	Cost utility analysis (QALY) Decision analytic model Markov microsimulation model start: 39 + 0 weeks 105 cycles of one week in length six states	Cost utility analysis (QALY) Decision analytic model Decision Tree
Perspective	societal	societal (national insurance)	societal	health system perspective	payer perspective
WTP	100,000 USD per QALY	20,000 EUR per successful delivery	100,000 USD per QALY	50,000 AUD per QALY	100,000 USD per QALY

Results	induction of labor is cost-effective with ICER of 10,945 USD per QALY	induction of labor is cost-effective with CE ratio of 469.86 EUR per successful delivery induction of labor is the dominant strategy	induction of labor is marginally cost effective with ICER of 87,692 USD per QALY	ICER not reported all interventions, plus standard care, produced similar health outcomes induction of labor had lower cost than standard care caseload midwifery had lower cost than induction of labor	favorable cervix: induction of labor is not cost-effective with ICER 115,100 USD per QALY, unfavorable cervix: induction of labor is cost-effective with ICER 2152 USD per QALY
Sensitivity	deterministic: result robust to changes to vaginal and cesarean delivery rates probabilistic: cost effective for more than 98% of scenarios	probabilistic: cost effective for more than 95% of scenarios	deterministic: result sensitive to small changes of most variables probabilistic: cost effective for 65% of scenarios (1000 Monte Carlo simulations)	deterministic: results robust to additional costs probabilistic: cost effective for 99.99% of scenarios (1000 Monte Carlo simulations with 10,000 microsimulation trials)	deterministic: sensitive to costs, likelihood of cesarean delivery and weekly probabilities of spontaneous labor probabilistic: favorable cervix: not cost effective for 55.4% of scenarios, unfavorable cervix: cost effective for 64.1% of scenarios (100,000 Monte Carlo simulations)

Appendix B: CHEERS 2022 Checklist

Topic	No.	Item	Location where item is reported
Title			
	1	Identify the study as an economic evaluation and specify the interventions being compared.	Title
Abstract			
	2	Provide a structured summary that highlights context, key methods, results, and alternative analyses.	Abstract
Introduction			
Background and objectives	3	Give the context for the study, the study question, and its practical relevance for decision making in policy or practice.	Introduction, Chapter 1
Methods			
Health economic analysis plan	4	Indicate whether a health economic analysis plan was developed and where available.	N/A
Study population	5	Describe characteristics of the study population (such as age range, demographics, socioeconomic, or clinical characteristics).	Methodology, Chapter 4
Setting and location	6	Provide relevant contextual information that may influence findings.	Methodology, Chapter 4
Comparators	7	Describe the interventions or strategies being compared and why chosen.	Methodology, Chapter 4
Perspective	8	State the perspective(s) adopted by the study and why chosen.	Methodology, Chapter 4
Time horizon	9	State the time horizon for the study and why appropriate.	Methodology, Chapter 4
Discount rate	10	Report the discount rate(s) and reason chosen.	Methodology, Chapter 4
Selection of outcomes	11	Describe what outcomes were used as the measure(s) of benefit(s) and harm(s).	Methodology, Chapter 4

Topic	No.	Item	Location where item is reported
Measurement of outcomes	12	Describe how outcomes used to capture benefit(s) and harm(s) were measured.	Methodology, Chapter 4
Valuation of outcomes	13	Describe the population and methods used to measure and value outcomes.	Methodology, Chapter 4
Measurement and valuation of resources and costs	14	Describe how costs were valued.	Methodology, Chapter 4
Currency, price date, and conversion	15	Report the dates of the estimated resource quantities and unit costs, plus the currency and year of conversion.	Methodology, Chapter 4
Rationale and description of model	16	If modelling is used, describe in detail and why used. Report if the model is publicly available and where it can be accessed.	Methodology, Chapter 4
Analytics and assumptions	17	Describe any methods for analysing or statistically transforming data, any extrapolation methods, and approaches for validating any model used.	Methodology, Chapter 4
Characterising heterogeneity	18	Describe any methods used for estimating how the results of the study vary for subgroups.	N/A
Characterising distributional effects	19	Describe how impacts are distributed across different individuals or adjustments made to reflect priority populations.	N/A
Characterising uncertainty	20	Describe methods to characterise any sources of uncertainty in the analysis.	Methodology, Chapter 4
Approach to engagement with patients and others affected by the study	21	Describe any approaches to engage patients or service recipients, the general public, communities, or stakeholders (such as clinicians or payers) in the design of the study.	N/A
Results			
Study parameters	22	Report all analytic inputs (such as values, ranges, references) including uncertainty or distributional assumptions.	Methodology, Chapter 4

Topic	No.	Item	Location where item is reported
Summary of main results	23	Report the mean values for the main categories of costs and outcomes of interest and summarise them in the most appropriate overall measure.	Methodology, Chapter 4
Effect of uncertainty	24	Describe how uncertainty about analytic judgments, inputs, or projections affect findings. Report the effect of choice of discount rate and time horizon, if applicable.	Discussion, Chapter 5
Effect of engagement with patients and others affected by the study	25	Report on any difference patient/service recipient, general public, community, or stakeholder involvement made to the approach or findings of the study	N/A
Discussion			
Study findings, limitations, generalisability, and current knowledge	26	Report key findings, limitations, ethical or equity considerations not captured, and how these could affect patients, policy, or practice.	Discussion, Chapter 5
Other relevant information			
Source of funding	27	Describe how the study was funded and any role of the funder in the identification, design, conduct, and reporting of the analysis	N/A
Conflicts of interest	28	Report authors conflicts of interest according to journal or International Committee of Medical Journal Editors requirements.	N/A

From: Husereau D, Drummond M, Augustovski F, et al. Consolidated Health Economic Evaluation Reporting Standards 2022 (CHEERS 2022) Explanation and Elaboration: A Report of the ISPOR CHEERS II Good Practices Task Force. Value Health 2022;25. doi:10.1016/j.jval.2021.10.008

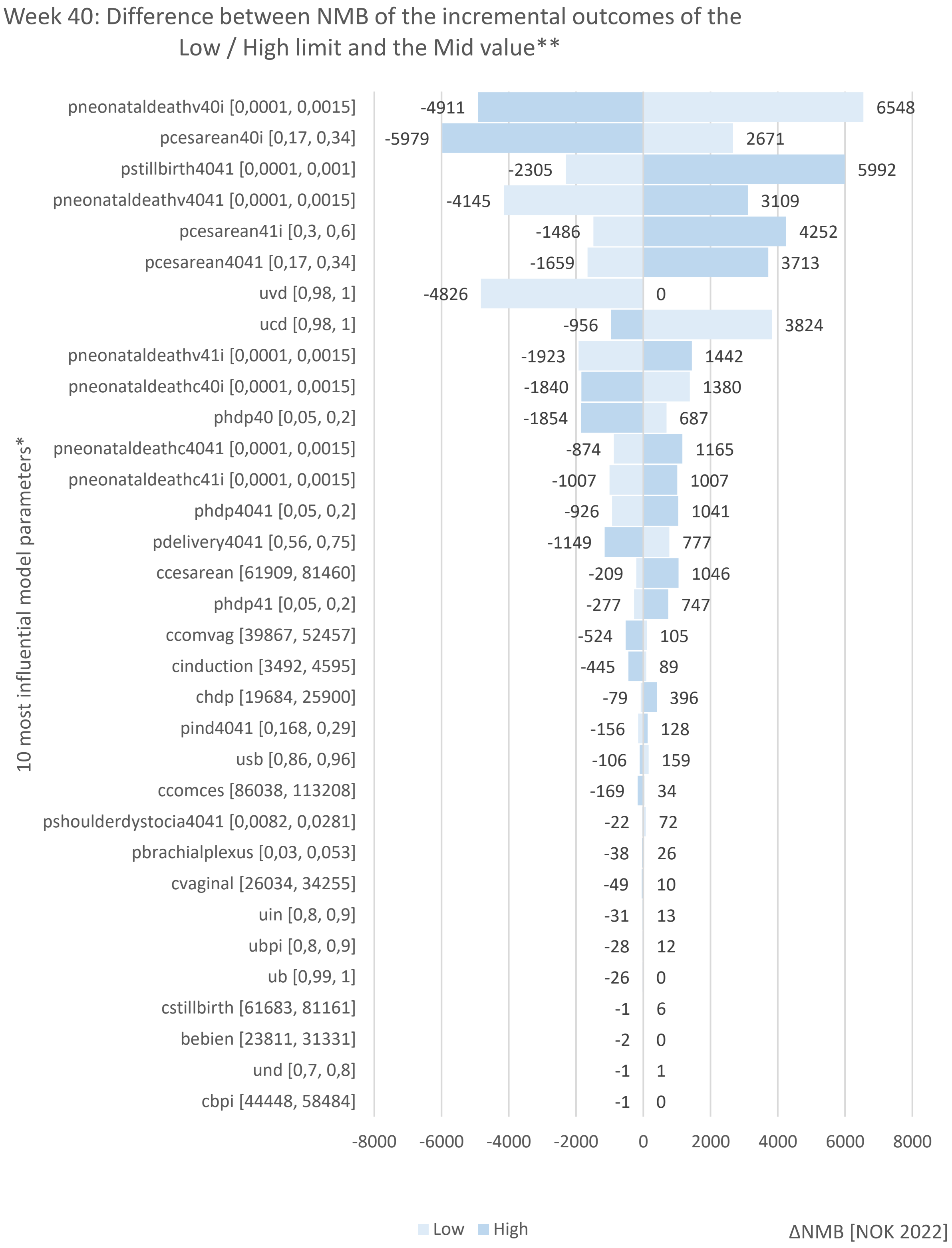
Appendix C: full parameter names

		value	deterministic		probabilistic			
Utilities	variable name	deterministic	lower limit	upper limit	distribution	alpha	beta	source
Maternal								
Vaginal delivery	uvd	1,000	0,980	1,000				Hersh et al., 2019
Cesarean delivery	ucd	0,996	0,980	1,000	beta	138,51	0,56	Hersh et al., 2019
Stillbirth	usb	0,920	0,860	0,960	beta	168,36	14,64	Hersh et al., 2019
Brachial plexus injury	ubpi	0,870	0,800	0,900	beta	179,86	26,88	Hersh et al., 2019
Neonatal death	und	0,760	0,700	0,800	beta	345,80	109,20	Hersh et al., 2019
Neonatal								
Vaginal / Cesarean delivery	ub	1,000	0,990	1,000				
Stillbirth / Neonatal death	ud	0,000						
Brachial plexus injury	uin	0,870	0,800	0,900	beta	179,86	26,88	Hersh et al., 2019
Health utility discount rate	dr	0,030	0,000	0,050				
Population parameters (years)								
Woman life expectancy following childbirth	wle	55						SSB, 2023
Healthy neonate life expectancy	nle	83						SSB, 2023
Average age at first birth	ana	30						SSB, 2023
End of fertile age	efa	50						SSB, 2023
Low-risk nulliparous cohort	pop	15 000,00						Sima et al. 2022

		value	deterministic		probabilistic			
Probabilities	variable name	deterministic	lower limit	upper limit	distribution	alpha	beta	source
Probability of cesarean section								
induced labor at 39+0	pcesarean39i	0,1860	0,1211	0,2422	beta	59,9549	262,3686	Grobman et al., 2018
induced labor at 40+0	pcesarean40i	0,2196	0,1678	0,3356	beta	24,9626	88,6992	Tita et al., 2021
induced labor at 41+0	pcesarean41i	0,3747	0,2976	0,5952	beta	15,8722	26,4868	Tita et al., 2021
expectant management week 39	pcesarean3940	0,1732	0,1211	0,2422	beta	46,8114	223,4052	Tita et al., 2021
expectant management week 40	pcesarean4041	0,2196	0,1678	0,3356	beta	24,9626	88,6992	Tita et al., 2021
Probability of delivery (including spontaneous and medical indication)								
delivery in week 39	pdelivery3940	0,3781	0,3123	0,4253	beta	184,5925	303,6214	Tita et al., 2021
delivery in week 40	pdelivery4041	0,6333	0,5573	0,7456	beta	104,3432	60,4205	Tita et al., 2021
Probability of neonatal death								
cesarean section after induction at 39+0	pneonataldeathc39i	0,0006	0,0001	0,0015	beta	3,9970	6657,6697	Hersh et al., 2019
cesarean section in week 39	pneonataldeathc3940	0,0006	0,0001	0,0015	beta	3,9970	6657,6697	Hersh et al., 2019
cesarean section after induction at 40+0	pneonataldeathc40i	0,0007	0,0001	0,0015	beta	6,8851	9828,9743	Hersh et al., 2019
cesarean section in week 40	pneonataldeathc4041	0,0007	0,0001	0,0015	beta	6,8851	9828,9743	Hersh et al., 2019
cesarean after induction at 41+0	pneonataldeathc41i	0,0008	0,0001	0,0015	beta	11,7449	14669,3776	Hersh et al., 2019
vaginal delivery after induction at 39+0	pneonataldeathv39i	0,0009	0,0001	0,0015	beta	11,3795	12632,4799	Hersh et al., 2019
vaginal delivery in week 39	pneonataldeathv3940	0,0009	0,0001	0,0015	beta	11,3795	12632,4799	Hersh et al., 2019
vaginal delivery after induction at 40+0	pneonataldeathv40i	0,0009	0,0001	0,0015	beta	11,3795	12632,4799	Hersh et al., 2019
vaginal delivery in week 40	pneonataldeathv4041	0,0009	0,0001	0,0015	beta	11,3795	12632,4799	Hersh et al., 2019
vaginal delivery after induction at 41+0	pneonataldeathv41i	0,0009	0,0001	0,0015	beta	11,3795	12632,4799	Hersh et al., 2019
Probability of fetal demise								
week 39	pstillbirth3940	0,0004	0,0001	0,0010	beta	2,6082	7449,4036	Yao et al., 2014
week 40	pstillbirth4041	0,0004	0,0001	0,0010	beta	2,6082	7449,4036	Yao et al., 2014
Probability of shoulder dystocia								
week 39	pshoulderdystocia3940	0,0197	0,0054	0,0237	beta	16,7606	833,6210	Tita et al., 2021
week 40	pshoulderdystocia4041	0,0234	0,0082	0,0281	beta	20,8330	869,3762	Tita et al., 2021
permanent brachial plexus injury in case of shoulder dystocia	pbrachialplexus	0,0390	0,0300	0,0525	beta	72,1428	1777,6720	Christoffersson et al., 2002
Probability of hypertensive pregnancy disorder								
during labor induction at 39+0	phdp39	0,0906	0,0500	0,2000	beta	5,5123	55,3617	Grobman et al., 2018
during labor induction at 40+0	phdp40	0,0906	0,0500	0,2000	beta	5,5123	55,3617	Grobman et al., 2018
during labor induction at 41+0	phdp41	0,0906	0,0500	0,2000	beta	5,5123	55,3617	Grobman et al., 2018
during week 39	phdp3940	0,1639	0,0500	0,2000	beta	15,4176	78,6494	Tita et al., 2021
during week 40	phdp4041	0,1206	0,0500	0,2000	beta	18,1476	132,3148	Tita et al., 2021
Probability of medically indicated induction								
week 39	pind3940	0,2220	0,1810	0,2900	beta	74,3845	260,6932	Tita et al., 2021
week 40	pind4041	0,2351	0,1680	0,2900	beta	84,2500	274,0886	Tita et al., 2021
Best decision probability	pbestcase	0,8000	0,5000	1,0000	beta	12,0000	3,0000	

		value	deterministic		probabilistic			
Costs (NOK 2022)	**variable name**	**deterministic**	**lower limit**	**upper limit**	**distribution**	**alpha**	**beta**	**source**
brachial plexus injury	cbpi	46 787,16	44 447,80	58 483,95	gamma	100,00	467,87	DRG 390
cesarean section	ccesarean	65 167,83	61 909,44	81 459,79	gamma	100,0000	651,6783	DRG 371
induction	cinduction	3 676,13	3 492,33	4 595,17	gamma	100,0000	36,7613	DRG 814R
neonatal death	cneonataldeath	64 929,12	61 682,66	81 161,40	gamma	100,0000	649,2912	DRG 385A
stillbirth	cstillbirth	64 929,12	61 682,66	81 161,40	gamma	100,0000	649,2912	DRG 385A
vaginal delivery	cvaginal	27 403,91	26 033,71	34 254,89	gamma	100,0000	274,0391	DRG 373
visit with pregnancy screening	cvisit	1 193,55	1 133,87	1 491,94	gamma	100,0000	11,9355	DRG 914P
hypertensive disorders of pregnancy	chdp	20 720,03	19 684,03	25 900,04	gamma	100,0000	207,2003	DRG 384
cesarean with complications	ccomces	90 566,57	86 038,25	113 208,22	gamma	100,0000	905,6657	DRG 370
vaginal delivery with complications	ccomvag	41 965,22	39 866,96	52 456,52	gamma	100,0000	419,6522	DRG 372
healthy newborn	bebien	25 064,55	23 811,32	31 330,69	gamma	100,0000	250,6455	DRG 391
Willingness to pay threshold	wtp	270 000,00						SLV, 2023

Appendix D: Full Tornado Diagrams


Week 40: Difference between NMB of the incremental outcomes of the Low / High limit and the Mid value**

Week 39: Difference between NMB of the incremental outcomes of the Low / High limit and the Mid value**