Maternal and iatrogenic factors influencing the duration of labour

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Scientific environment

The projects investigating the effect of induction on labour duration and effects of a judicious oxytocin protocol were performed in Stavanger University hospital in collaboration with clinicians and midwives.

The BMI and active second stage duration project comprising data from three different university hospitals in Norway came about through a collaboration between Haukeland University Hospital, St.Olavs Hospital and Stavanger University Hospital.

The project which entailed ultrasound measurements in the active second stage of labour came about through an international collaboration between Stavanger University Hospital, University Hospital of Bologna, Trondheim University Hospital (St.Olavs), Queen Charlotte's and Chelsea Hospital, Lund University Hospital, Hvidovre University Hospital and University Hospital of Parma.

From 2018 I have been a PhD candidate at the Medical Faculty at the University of Bergen, Department of Clinical Science 2 (KI2).

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Abstract in English

Background

Prolonged labour is the leading cause of caesarean section and operative vaginal delivery worldwide. However, the definition of normal labour progression and duration is part of an ongoing scientific discourse. Labour progression and duration can furthermore be influenced by maternal, foetal and iatrogenic factors, and thus, definitions of normality for large groups may not be applicable for the individual woman. Furthermore, perceptions of normal labour progression and duration have throughout the 20th century been influenced by other factors than purely medical ones, such as access to care, provider preference and financial purposes.

Prolonged labour is a potential risk factor for unfavourable outcome for mother and child. However, the tools to correct prolongation are limited. Augmentation of contractions with oxytocin, or performing operative delivery are common solutions, regardless of the underlying cause. They both present a potential risk to the mother and foetus in themselves.

Methods

All papers included are observational cohort studies. Paper 1-3 are retrospective cohort studies, and paper 4 is a prospective cohort study. Ten Group Classification System was used throughout in order to obtain comparable groups. As studies of duration of labour and labour phases in contemporary cohorts is complex due to interventions, survival methods were employed where appropriate.

Overall aim

The overall aim of this thesis was to investigate effects of maternal and iatrogenic factors on the duration of phases of labour.

Paper 1

The frequency of labour induction is increasing. In paper one we aimed to compare the duration of the active phase of labour in nulliparous and parous women with spontaneous and induced labour. The study was a retrospective observational study over four years at Stavanger University Hospital from 2010 - 2013. We included women with a singleton foetus in cephalic presentation at term and excluded women with a previous caesarean section. The women were stratified into a nulliparous and a multiparous group, and we compared spontaneously labouring with induced women in each group, respectively. A total of 16.125 women were available for analysis. The main outcome measure was the estimated duration of active phase of labour analysed with survival methods. We found that the estimated median duration was nearly one and a half hours longer in nulliparous women with induced labours compared with spontaneously labouring women. This should be considered when managing nulliparous women undergoing induction. The overall difference in parous women was small and probably without clinical importance.

Paper 2

Increasing BMI is associated with many complications during pregnancy and labour. However, clinical experience indicated that the active pushing is effective in obese women. In paper two we aimed to explore the duration of the active second stage of labour in nulliparous and parous women stratified by BMI groups. It was a retrospective study in three Norwegian University hospitals over eight years (2012-2019). Nulliparous and parous women without previous caesarean section with a live singleton foetus in cephalic presentation and spontaneous onset of labour were selected for analysis. The estimated median duration of the active phase of the second stage of labour was calculated using survival analyses. Caesarean sections and operative vaginal deliveries during the active phase were censored. A total of 47.942 women were included. We found that increasing BMI was associated with shorter estimated median duration of the active second stage in both nulliparous and parous women. The results were the same in analyses stratified by oxytocin augmentation

and epidural analgesia. These findings may be a positive counterweight to the negative stigma associated with obesity in pregnancy.

Paper 3

The use of oxytocin has been found to be haphazard and unstructured in previous studies. In paper three we aimed to investigate whether judicious use of oxytocin augmentation would change how it was used, and possible influences on labour and foetal outcomes. Structured use of oxytocin augmentation was introduced at Stavanger University Hospital in 2010. Before this time augmentation was started if progression of labour was perceived as slow by the birth attendant. After implementation, oxytocin could only be started when the cervical dilation had crossed the four hour action line in the WHO partograph. We did an observational cohort study at Stavanger University Hospital and compared labour outcomes in 2010-2013 with a historical control (2009). In all, 20.227 women delivered with singleton term pregnancies, cephalic presentation, spontaneous or induced onset of labour, without previous caesarean section were included. The linear-by-linear association trend test was used for categorical analyses, and continuous variables were compared using one-way analysis of variance with Bonferroni correction.

The use of oxytocin augmentation was significantly lower after implementation of new routines. The rate of caesarean sections performed due to foetal distress and the frequency of children born with pH <7.1 in the umbilical artery fell. However, the rate of women with duration of active labour >12 hours increased and more women experienced postpartum haemorrhage. The findings may point to advantages and disadvantages of different protocols for augmentation of labour.

Paper 4

Long duration of operative deliveries is associated with maternal and foetal complications. In paper four, we aimed to assess whether ultrasound measurements of foetal position and station could predict duration of vacuum extractions, mode of delivery, and foetal outcome in nulliparous women with a prolonged second stage of labour. We performed a prospective, international, multi-center cohort study in seven

European labour wards. Foetal head position and foetal head station were determined using transabdominal and transperineal ultrasound, respectively. The main outcome was the duration of vacuum extraction in relation to ultrasound findings. Secondary outcomes were mode of delivery, and umbilical artery cord blood gas values after birth. A total of 222 women were included in the analyses. The duration of vacuum extraction was shorter in women with head-perineum distance ≤25 mm, and a high station and occiput posterior position were associated with increased risk of failure. A high station was also associated with low pH in the umbilical cord. These findings imply that ultrasound has the potential to predict labour outcome and duration of vacuum delivery. The obtained information could serve as a guide for decision making: Whether to attempt vacuum extraction in the labour ward or the operating theatre, or to perform a caesarean section in the setting of a prolonged second stage.

Discussion

A multitude of factors have the potential to influence labour duration in women, and this thesis has only scratched the surface. The awareness of the effects of factors such as induction of labour and BMI on the duration of labour phases could make our interventions more precise. In the case of oxytocin augmentation, its use may benefit from clear guidelines of indication and dosage to minimise the risk of iatrogenic injury. And, if operative delivery is considered for prolonged labour, knowing the precise position and station of the foetus is paramount, and prognostic tools may serve as an adjunct to clinical examination and in decision making.

Hopefully the results have provided some insight into the maternal and iatrogenic factors which are at play. As the discourse on labour duration and management evolves, the results may provide pieces to the puzzle of labour management, and how to adapt it to the individual woman.

Norsk sammendrag

Bakgrunn

Forlengede fødselsforløp er den fremste grunnen til keisersnitt og operative vaginale forløsninger på verdensbasis. Imidlertid er definisjonen av normal fødselsprogresjon og varighet gjenstand for en pågående vitenskapelig diskurs. Fødselsprogresjon og varighet kan videre påvirkes av maternelle, føtale og iatrogene faktorer. Derfor kan ikke nødvendigvis definisjoner av normalitet for en gruppe appliseres på den enkelte fødende kvinne. Enn videre har oppfatninger om normalitet innenfor fødselsprogresjon og varighet gjennom det tyvende århundre blitt påvirket av andre faktorer enn de rent medisinske, så som tilgang til helsehjelp, fødselshjelperens preferanser og økonomi.

Forlenget fødsel er en potensiell risikofaktor for negative utfall for mor og barn. Imidlertid er verktøyene for å avhjelpe tilstanden begrenset. Stimulering med oxytocin, eller en operativ forløsning er vanlige løsninger, uavhengig av underliggende årsak. Begge utgjør en risiko for skade på mor eller barn.

Undersøkelser av fødselsvarighet i en nåtidig populasjon er komplisert fordi intervensjoner kan fortkorte eller avslutte fødselen. Sammenlikninger av gjennomsnitt eller median kan derfor gi kunstig forkortelse av varigheten. Derfor har overlevelsesanalyser blitt brukt i flere av artiklene i denne avhandlingen. De utbedrer de statistiske feilene, men korrigerer dem ikke fullstendig.

Metoder

Alle artiklene i avhandlingen er observasjonsstudier. Artikkel 1-3 er retrospektive kohortstudier, og artikkel 4 er en prospektiv kohort studie. Ten Group Classification System er brukt gjennomgående. Ettersom studier på varighet av fødsel og faser av fødsel er komplisert en i en nåtidig kohort på grunn av intervensjoner som kan forkorte eller avslutte fødsel, ble overlevelsesanalyser benyttet der det var hensiktsmessig.

Hensikt med avhandlingen

Den overordnede målsetningen for avhandlingen var å undersøke effekten av maternelle og iatrogene faktorer på varigheten av fødselens faser.

Artikkel 1

Forekomsten av igangsatt fødsel er stigende. I artikkel 1 var hensikten å sammenlikne varighet av aktiv fødsel hos første- og flergangsfødende kvinner med spontan og igangsatt fødsel. Studien var en retrospektiv kohortstudie over fire år ved Stavanger Universitetssykehus, fra 2010-2013. Vi inkluderte kvinner med ett foster i hodeleie til termin, og ekskluderte kvinner med tidligere keisersnitt. Kvinnene ble stratifisert i en gruppe med førstegangsfødende og en gruppe med flergangsfødende, og vi sammenliknet kvinner med henholdsvis spontan fødselsstart og igangsatt fødsel. Det var totalt 16.125 kvinner med i analysene. Primærutfallet var estimert varighet av aktiv varighet av fødsel analysert med overlevelsesanalyse. Vi fant at median estimert varighet av fødsel hos førstegangsfødende med igangsatt fødsel var nesten en og en halv time lenger enn hos kvinner med spontan fødselsstart. Dette bør tas i betraktning når en håndterer fødselsforløp hos førstegangsfødende kvinner med igangssatt fødsel. Forskjellene hos flergangsfødende var små, og sannsynligvis uten klinisk betydning.

Artikkel 2

Økt BMI er forbundet med økt risiko for en rekke komplikasjoner under svangerskap og fødsel. Imidlertid var inntrykket fra klinikken at trykketiden kunne være kort og effektiv hos kvinner med fedme. I artikkel 2 var hensikten å utforske varigheten av trykketiden hos første- og flergangsfødende kvinner stratifisert på BMI-gruppe. Studien var en retrospektiv studie i tre norske universitetssykehus over en periode på åtte år (2012-2019). Første- og flergangsfødende kvinner uten tidligere keisersnitt med ett levende foster i hodeleie til termin og spontan fødselsstart ble valgt til analysene. Den estimerte varigheten av trykketiden ble undersøkt med overlevelsesanalyser. Keisersnitt og operative vaginalforløsninger i trykketiden ble sensurert. Totalt ble data fra 47.942 kvinner analysert. Vi fant at økt BMI var assosiert med kortere estimert trykketid hos både første- og flergangsfødende kvinner. Resultatene besto i analyse stratifisert på stimulering med oxytocin og

epiduralbedøvelse. Disse funnene kan fungere som en positiv motvekt til det negative stigma og tankesett rundt graviditet og fødsel hos overvektige.

Artikkel 3

Bruk av oxytocin for å påskynde fødselen har i flere studier blitt funnet å være tilfeldig og ustrukturert. I Artikkel 3 var hensikten å undersøke om en indikasjonsbasert og strukturert bruk av oxytocinstimulering kunne endre bruken av medikamentet, og hvorvidt det kunne ha effekt på utfall av fødsel, og effekter på mor og barn. Strukturert bruk av oxytocin for stimulering av fødsel ble innført ved Stavanger Universitetssykehus i 2010. Før dette kunne stimulering med oxytocin begynne dersom fødselshjelperen oppfattet fødselsforløpet som tregt. Etter implementering av strukturert bruk kunne oxytocinstimulering kun startes dersom fødselsforløpet hadde krysset tiltakslinjen i WHO-partogrammet. Vi gjorde en observasjonell kohortstudie ved Stavanger Universitetssykehus og sammenliknet fødselsutfall etter implementering (2010-2013) med en historisk kontroll (2009). Totalt fødte 20.227 kvinner med ett barn i hodeleie og uten tidligere keisersnitt til termin i denne perioden. Utfallene ble analysert med lineær-lineær assosiasjonstest for kategoriske variabler og kontinuerlige variabler ble sammenliknet med ANOVA med Bonferronikorreksjon. Bruken av oxytocin falt signifikant etter innføringen av strukturert bruk. Keisersnittfrekvensen på grunn av unormal fosterlyd og barn født med pH <7.1 i navlesnorsarterien fakt. Imidlertid økte forekomsten av varighet av aktiv fødsel over 12 timer, og flere kvinner fikk postpartumblødning. Studien illustrerer fordeler og ulemper med ulike metoder for bruk av oxytocin som ristimulerende middel.

Artikkel 4

Langvarig forsøk på operativ vaginal forløsning er forbundet med komplikasjoner for mor og barn. I artikkel fire var hensikten å finne ut om ultralydmålinger av fosterhodets posisjon og nivå i bekkenet kunne forutsi varighet av vakuumforløsninger, forløsningsmetode, og utfall for barnet hos førstegangsfødende kvinner med forlenget trykketid. Vi gjorde en prospektiv, internasjonal, multisenter kohortstudie i sju europeiske fødeavdelinger. Fosterhodets posisjon og nivå ble

undersøkt med abdominal og transperineal ultralyd. Primærutfallet var varighet av vakuumforløsning i relasjon til ultralydfunn. Sekundære utfall var forløsningsmetode og blodgassverdier i navlesnorsarterien etter fødsel. Totalt ble 222 kvinner inkludert i analysene. Varigheten av vakuumforløsning var kortere blant kvinner med kort avstand ≤25mm mellom fosterhodet og perineum, og stor avstand til fosterhodet og occiput posterior («stjernekikker») var forbundet med økt risiko for mislykket operativ vaginal forløsning. Stor avstand til fosterhodet var også forbundet med lav pH i navlesnorsarterien. Informasjon fra studien kan bidra i beslutningstakning i trykketiden: Hvorvidt fødselshjelperen skal forsøke å legge en sugekopp på fødestuen, på operasjonsstuen, eller heller gjøre et keisersnitt.

Diskusjon

En mengde faktorer kan påvirke varighet av fødsel og av fødselens faser, og denne avhandlingen har bare skrapt i overflaten. Kunnskap om effekten av faktorer som igangsettelse av fødsel og mors BMI på varigheten av fødselen og dens faser er viktig for å gjøre intervensjonene våre mer målrettet. Når det gjelder stimulering med oxytocin kan det være hensiktsmessig med klare retningslinjer for bruk for å minimere risiko for skade. Dersom det er nødvendig med operativ forløsning, er korrekt og presis informasjon om barnets posisjon og nivå i bekkenet avgjørende, og ultralyd kan bidra som tilskudd til klinisk undersøkelse for å fatte riktig avgjørelse om håndtering.

Det er et håp at resultatene vi har funnet har gitt innsikt i noen av faktorene ved den fødende kvinnen og ved fødselshjelpen som virker inn i prosessen. Ettersom diskusjonen rundt fødselsvarighet og håndtering av forlengede fødselsforløp skrider frem kan disse resultatene være noen av puslebitene i hvordan håndtering av fødselsforløp kan bli mindre sjablongpreget, og bedre kan tilpasses den enkelte kvinnen og hennes barn.

Table of Contents

List of Publications

1: Østborg TB, Romundstad PR, Eggebø TM. Duration of the active phase of labor in spontaneous and induced labors. Acta Obstet Gynecol Scand. 2017 Jan;96(1):120-127. doi: 10.1111/aogs.13039. Epub 2016 Nov 9. PMID: 27731890.

2: Østborg TB, Sande RK, Kessler J, Tappert C, Brandis P, Eggebø TM. Put your weight behind it – effect of BMI on the active second stage of labour: A retrospective cohort study. BJOG. 2022 Apr 11. doi: 10.1111/1471-0528.17186. Epub ahead of print. PMID: 35404537.

3: Rossen J, Østborg TB, Lindtjørn E, Schulz J, Eggebø TM. Judicious use of oxytocin augmentation for the management of prolonged labor. Acta Obstet Gynecol Scand. 2016 Mar;95(3):355-61. doi: 10.1111/aogs.12821. Epub 2015 Dec 8. PMID: 26576009.

4: Kahrs BH, Usman S, Ghi T, Youssef A, Torkildsen EA, Lindtjørn E, Østborg TB, Benediktsdottir S, Brooks L, Harmsen L, Romundstad PR, Salvesen KÅ, Lees CC, Eggebø TM. Sonographic prediction of outcome of vacuum deliveries: a multicenter, prospective cohort study. Am J Obstet Gynecol. 2017 Jul;217(1):69.e1-69.e10. doi: 10.1016/j.ajog.2017.03.009. Epub 2017 Mar 19. PMID: 28327433.

Abbreviations

ACOG	The American College of Obstetricians and Gynecologists
BMI	Body Mass Index
CI	Confidence interval
CS	Caesarean section
CTG	Cardiotocography
HPD	Head-perineum distance
HR	Hazard Ratio
IU	International Units
OA	Occiput anterior
OP	Occiput posterior
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised Controlled Trial
REK	Regional committees for Medical and Health Research Ethics
TGCS	Ten Group Classification System
UK	United Kingdom
USA	United States of America
WHO	World Health Organization

1. Introduction

1.1 Preamble

Upon starting as a junior doctor on the labour ward, obstetrics seemed almost esoteric. Its practices, from the perspective of a novice, seemed to be governed by a set of rules which seemed implicit or at least not fully elucidated. After a month or so, the wisdom of such a rule was bestowed upon me from a junior consultant: "Active labour should not last more than 12 hours." I was insubordinate enough to ask: "Why?" She scanned my face, somewhat puzzled and exclaimed: "That is how it is!" I later realised it was her representation of my supervisor's extrapolation of the world health organization (WHO) partograph, - and decided to dub it "Eggebø's rule".

This thesis is not in any way meant as criticism to neither the rule, the consultant nor my supervisor, - there is simply no way for us in our clinical life to get to the bottom of every empirical rule or expert opinion. However, I do believe that scratching the surface of some of them gives more nuance and perhaps moments of clarity. Or confusion. Or both.

The papers comprising this thesis, revolve around a common theme: Prolonged labour. From exploring the duration of labour in spontaneous and induced labours (Paper 1), investigating how fast or slow women push depending on their body mass index (BMI) (Paper 2), treating prolonged labour with oxytocin (Paper 3), to ultrasound before performing operative delivery for prolonged second stage of labour (Paper 4).

Whether these research questions are clinically or even scientifically important depend on whether what seems to have become an obstetric axiom holds true:

Time is important.

And in contemporary practice time is not just important, it is essential. Prolonged labour is the indication for most caesarean sections (CS) worldwide[1]. Oxytocin is used in a more than a 40% of first-time mothers with spontaneous onset of labour in Norway regardless of whether a Zhang or WHO partograph was used[2].

All the while, there is no unified or universal definition of normal duration or progression of labour. It is an ongoing discourse, and definitions of normal duration and progression of labour seem everchanging. And how can we diagnose the abnormal without truly knowing the normal?

The papers comprising this thesis were inspired by variations of the following questions:

> What is the normal duration of labour and its stages?
> Do definitions of normal duration transcend place and time, or do they depend on birthing population, induction, BMI, and other factors?
> Which tools may aid us in the diagnosis and in predicting outcome; - are our clinical observations or hands sufficient, or does ultrasound have a role to play?

The thesis itself will attempt to explore some of the historical and current background and context for the papers included.

1.2 Birth in humans – safe with care, precarious without it

All humans are born, and birth is an inevitable part of human life. Contrary to popular belief, humans are not the only species experiencing troublesome deliveries. Cephalopelvic disproportion with neonatal death as an outcome is also observed in small bodied primates, (squirrel monkeys and macaques) but to a lesser extent in large bodied apes[3]. However, there is no denying that human birth is more complicated than in other higher primates due to bipedalism, pelvic shape and the

cephalopelvic disproportion resulting from the particular evolutionary branch on which humanity is situated. In parts of the world with limited access to obstetric assistance, obstructed labour carries significant risk of foetal and maternal morbidity and mortality[4]. Although we are accustomed to low risk of detrimental outcomes in Norway and the developed world, this is historically a relatively recent development. According to WHO, the maternal mortality rate in Sub-Saharan Africa was more than 40 times higher than in Europe and Central Asia, nevertheless a clear downward trend in all world regions is observed from 2000 – 2017[5].

1.3 Transitions, observable and invisible – and attempts to describe them

Birth is a process of transition. Some points in time of this transition are easily and objectively observable without intervention: The moment of birth, in which the woman becomes a mother and the foetus becomes a newborn child, and the subsequent delivery of the placenta. Yet, the process may take place in merely minutes in the case of a truly emergent CS. At the other end of the spectrum, painful irregular contractions or latent labour may undulate for days or even weeks until the onset of what birth attendants classify as active labour.

Attempting to define phases and stages of labour requires us to define the onset of labour and point of transition between phases and stages. It enables us to perform research and communicate uniformly between birth attendants, but our definition of duration may fail to describe the woman's perceived duration of her labour. Furthermore, definitions of the start of the active phase, though relatively stable from the 1950s throughout the late 20th century are now under scientific debate, and the onset of latent or early labour are insufficiently elucidated.

2. Normal and prolonged labour

2.1 What is normal labour?

> "*The judges of normality are present everywhere. We are in the society of the teacher-judge, the doctor-judge, the educator-judge, the 'social-worker'-judge; it is on them that the universal reign of the normative is based; and each individual, wherever he may find himself, subjects to it his body, his gestures, his behaviour, his aptitudes, his achievements*.[6]"

Normality is a fickle concept. What is normal? Is it the mean, the median, the upper 95th percentile? Is it merely what is common? Is it that which does not cause morbidity or mortality? Applying descriptive observation to establish norm should be justified beyond observed statistical standard error or 95 confidence intervals.

In the case of labour, progression and duration: Normative definitions are only justified where there are real-life consequences or increased risk when labour duration does not adhere to certain temporal limits. Even then, absolute versus relative risk need to be considered.

There is, as of now, no universal consensus of normal duration of human labour. Nevertheless, prolonged labour is a common diagnosis, known under many names: inertia, dystocia, arrest and protraction or just plain slow.

2.2 Descriptive analysis and pitfalls

Attempting a descriptive analysis of the duration of labour still has merit. It provides insight into the phenomenon of labour. But in contemporary cohorts across most of the globe, interventions take place to shorten or terminate labour. In other words, describing the "natural" duration of labour would be unethical, or lead us to exclude all labours with interventions. The latter introduces inclusion bias.

Furthermore, labour progression and duration are neither universal nor timeless. Birthing populations differ around the globe, and over time. Parity, maternal age, gestational age, obesity, may all affect progression and duration.

Before the 1930s, there was to my knowledge little scientific inquiry through systematic study of the duration and progression of labour. There is, however, expert opinion expressed through textbooks of Obstetrics or midwifery, such as in the textbook for Midwives by Faye, published in 1848[7]:

> *"A slow birth is that, which lasts beyond the ordinary time (12 to 18 hours) or even a couple of days. In some cases, only some of labours stages may be longer, whereas in other cases the entire process may be slow. In primiparous women the entirety of labour, and in particular the second stage are long, as the soft parts are slower to dilate. This must be considered in fine order, as long as the woman is otherwise healthy and the membranes are intact, as the pressure on the foetal head is not of the same significance as after the breach of the membranes and the presenting part has descended into the pelvis.*
>
> *As the cause of slow labour is less apparent and is likely overwun by Nature, the midwife should, when no danger is imminent, do nothing beyond provide a suitable foods, encouragement, and support the power of the birthing woman. She should be allowed to be up and move around, but no intervention to her contractions should take place, […] The duration of the phases are not determined, as different circumstances may shorten or prolong them.*
>
> *The birth of the placenta should in all births be left to nature, and even traction of the umbilical cord should be avoided as it is often fragile and may break[1]."*

[1] Translated to English from the original text.

Contemporary obstetrics in the developed world is substantially different from what it was in the 1840s, a time where morbidity and mortality were common and available interventions were few. Leeches and vaginal douching with oil have been abandoned, as well as bloodletting for preeclampsia. Births are now managed, for the most part in hospitals, in accordance with guidelines, partographs and medical interventions. The improvements are undeniably paramount, but is it possible that we have lost something along the way in our eagerness to organise nature along lines and into systems and actively manage them? In the following, I will attempt to give a comprehensive and critical review on some of the body of knowledge from pre-Friedman to the present day.

2.3 Duration and progression – two sides of the same coin?

The papers in this thesis describe *duration of phases of labour*, rather than progression of labour. These two concepts are, for several reasons, two sides of the same coin:

First: Historically, the partographs or graphical representations of labour did in fact not represent centimetres of cervical dilation, rather traverse times for the different phases of labour, described in the next chapter: "A brief history of the partograph"

Second: Phases, if their starting and ending points are clearly defined, may be more robust than progression. The exact point in time for the rupture of membranes, the birth of the child, the birth of the placenta, can be known with certainty, whereas digital examination will attempt to determine a certain dilation, position, presentation and station at an arbitrary point in time after their occurrence. Furthermore, digital examination of dilation, presentation and station is known to have relatively large inter-observer and intra-observer variability, but determination of station and presentation may be improved with systematic training[8].

Third: In the second stage of labour, duration is a key observation. Progression is clinically evaluated, but difficult to quantify objectively.

Fourth: What if we are indeed digging in the wrong place? As it is elaborated in the following chapters, the first partographs centered on rupture of membranes as a starting point, whereas the start of the active phase of labour in contemporary obstetrics seems to be slipping from 2-3cm (Friedman) to 4cm (WHO 1994)[9] to 5cm (WHO 2020[10]) or 6 cm(Zhang)[11].

Limiting the time of active labour more and more in terms of dilation may give us more robust regression lines and less variation in our statistical analyses, but does it provide useful limits for intervention or care?

If a woman is not allowed into the labour ward or given adequate pain relief before she is defined to be in the active phase of labour, which consequences does it have for providing her with compassionate care? If the latent phase continues to engulf the active stage decade by decade, does the current divisional paradigm into latent and active phase even make sense anymore?

2.4 History of the partograph – from phases to centimetres, and perhaps, back again

In most English language research and textbooks that I was aware of before starting to prepare this thesis, birth is divided into latent and active phases of labour based on definitions instituted by Emanuel A. Friedman through his publications in the 1950s[12-14]. Research and clinical practice in the anglophone world seem to be in relative consensus regarding the division of labour into these phases and stages, and research building upon Friedman's research is normative for labour phase duration, and subsequent interventions taking place when labour duration exceeds these norms. In attempting to get to the bottom of the history of the partograph, I stumbled upon Dr. Astrid Krahls excellent historical review on the latent phase of labour[15]. Reading it made me aware of a schism in the understanding of the partograph's conception:

the Americo-centric view seeing Friedman as the inventor and "father" of the partograph, and the Swiss/German view, considering European publications predating Friedman to be of significant scientific value. In the following I have attempted to expand on some of the historical events leading up to Friedman's initial publication. I believe this review may shed light on some of the paradigm limitations in our current understanding of labour progression and duration.

In the 1940s, the research into rupture of membranes started to stir in Germany and Switzerland. The underlying idea was to determine whether the time of rupture of membranes and duration thereafter had implications for the outcome for mother and child. Willi Wolf published a monograph in 1946, named "Klinik des unzeitigen Blasensprungs[16]", which translates to "Clinical features of untimely membrane rupture". The focus of the publication is to outline causes, consequences, and treatment of what was at the time considered an untimely membrane rupture, *namely at any point before full dilation*. In the chapter outlining the effect on labour progression he presents what, to my knowledge, is the first graphical description of labour progression. It is, however, presented as "teileröffnungszeiten", meaning the number of hours it takes to from a certain number of centimetres dilation to that number +1. The curves represent data from 500 nulliparous women and 500 parous women. Wolf even identifies the acceleration phase, stating: "The cause of the kink in the curve

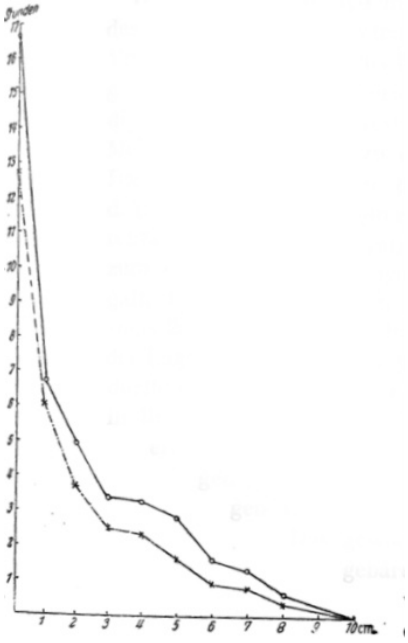

Figure 1- "Teileröffnungszeiten" – Average traversal time per centimeter of dilation. Klinik des unzeitigen Blasensprungs, Willi Wolf, 1946. (Image no longer subject to copyright, Springer)

between three and five centimetres, which is more or less pronounced in all curves, cannot be explained by our current knowledge[2]"

In 1948, dr. Heidi Deuel-Zogg published a paper in which she has graphically plotted the progression of 750 births of Swiss nulli- and multipara from her clinic in Basel in a partograph, in the figures labeled Abb 1 and Abb 2 (Figure 2 and 3)[17]. The x-axis represents time in hours. The y-axis represents birth phases, the first five different degrees of cervical dilation, in an arbitrary scale, see Table 1. The origo is placed at the time of spontaneous rupture of membranes (marked BlSp for Blasensprang).

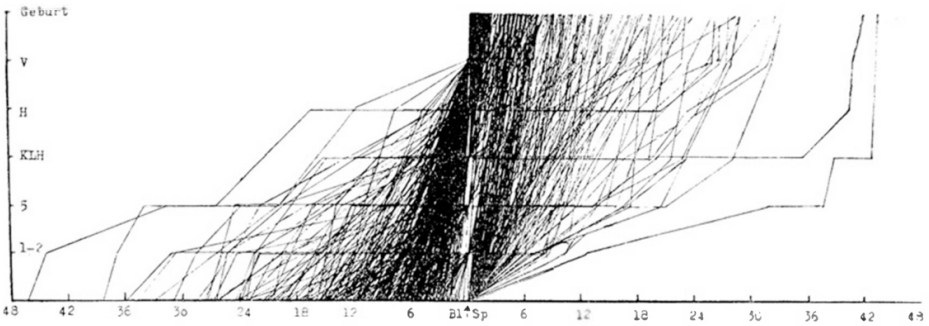

Abb. 1. I-Para

Figure 2 - Progression of labour in nullipara, origin at rupture of membranes, Deuel-Zogg 1948. (Image no longer subject to copyright, Karger)

[2] Translated from German.

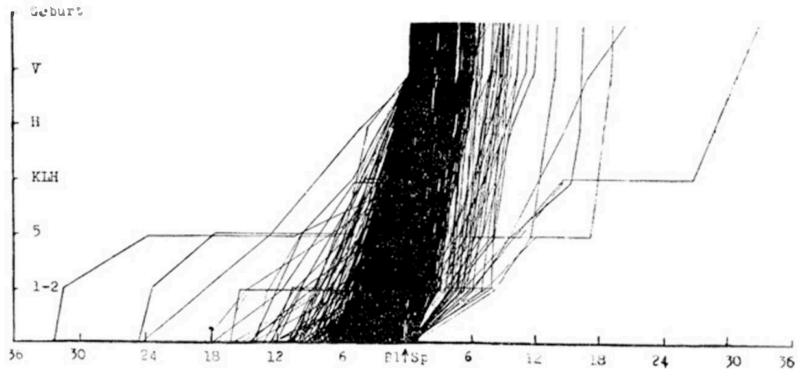

Abb. 3. M-Para

Figure 3 - Progression of labour in parous women, origo at rupture of membranes, Deuel Zogg 1948. (Image no longer subject to copyright, Karger)

Table 1 - Definitions of dilation by Koller / Deuel-Zogg with German full text and English translation

Koller / Deuel-Zogg	German	Translation
1-2	1-2 Franc	2,3-2,7cm
5	5 Franc	3,1 cm
KLH	Kleine handfläche	ca. 6 cm
H	Handfläche	ca. 8 cm
V	Vollöffen	Full dilation
Geburt	Geburt	Birth (of the child)

She furthermore plotted lines of "greater frequency" (solid lines) and a line demarcating pathologically prolonged births (dashed line) for the two groups,

labelled Abb 3 and Abb 4 (Figure 4 and 5), based on outcomes.

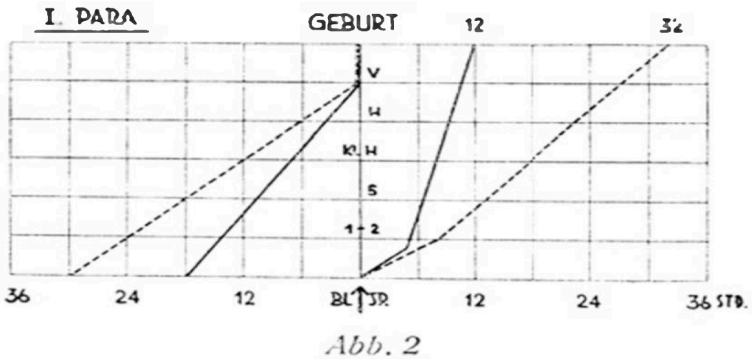

Abb. 2

Figure 4 - Normal and pathological duration based on outcomes, nulliparous women, Deuel-Zogg 1948. (Image no longer subject to copyright, Karger)

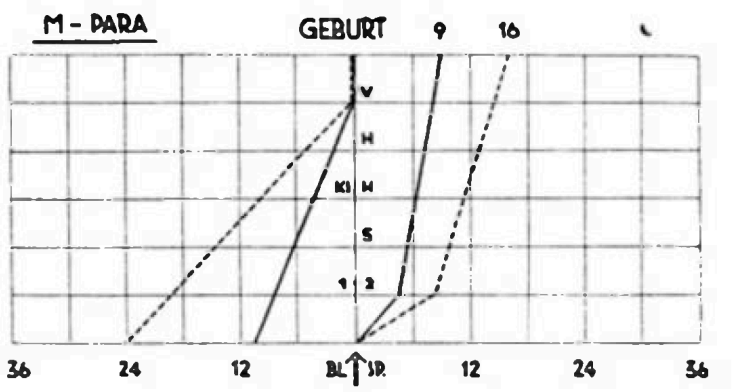

Abb. 4

Figure 5 - Normal and pathological duration based on outcomes, parous women, Deuel-Zogg 1948. (Image no longer subject to copyright, Karger)

She describes percentages of vaginal operative delivery, neonatal mortality and prolonged puerperium due to fever, and groups them according to birth phase duration. The partograph used she credits to Professor Theo Koller. However, the description of the method first appears in print later the same year, where Koller proposes a vertical rather than horizontal partograph, and in turn credits the paper by Deuel-Zogg[17]. According to yet another paper, by Koller & Abt from 1950[18], Koller "briefly presented the idea at a Swiss convention in May 1948", two months before Deuel-Zoggs publication.

In the paper from 1950[18], Koller & Abt suggest using a vertical rather than a horizontal partograph, with origin at admission of the patient later the same year, reasonably arguing that *"it is suited for practical and continuous monitoring of the birth process, regardless of the time of membrane rupture".*

In 1951 Zimmer published an extensive and detailed paper, 18 pages long[19]. In the analyses he uses data from 1814 primiparous and 1299 multiparous women after spontaneous delivery at term. Only births with vertex presentation that were not subject to medication or operative delivery were included. The central theme is also in this publication relating progression of labour to the time of membrane rupture. SI-units in terms of hours and centimetres are used, and statistical methods for describing mean traverse times and standard error per centimetre dilation and standard error. He also performed stratified analyses by maternal age. The perhaps most striking figure is the last one in the paper, in which he presents the labour curves for primi- and multipara with standard deviation.

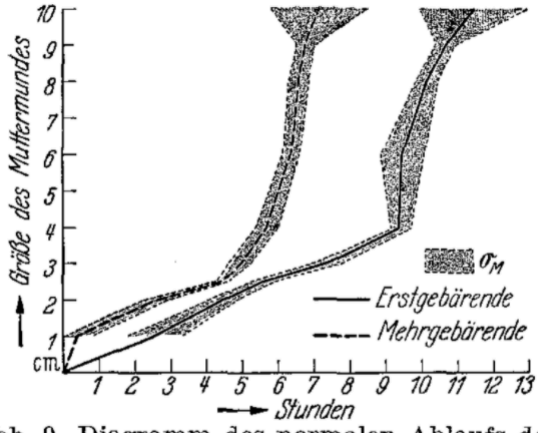

Abb. 9. Diagramm des normalen Ablaufs der Muttermundseröffnung (aus Tabelle 5).

Figure 6 - Diagram of normal cervical dilation with standard deviation in nulliparous and parous women. (Zimmer 1951) (Reprinted with permission from Deutscher Apotheker Verlag)

In 2016, Roberto Romero published an editorial in the American Journal of Obstetrics and Gynecology called "Giants in Obstetrics and Gynaecology"[20], in

which Friedman is interviewed and hailed as the inventor of the labour curve:

Romero writes: "*How was the labor curve "born"? […] A partogram exists in virtually every labor and delivery unit worldwide, and all mothers who are in labor can benefit from this simple but powerful tool first conceived in the mind of such an extraordinary man*." Friedman is interviewed, telling the story of how the idea of the partogram came about while he plotted graphical progressions of labour as he was not allowed to leave his on-call while his first child was born at another hospital. However, Friedman's first child was born in 1952, and it is likely that he was aware of the works by Abt, Koller, Zimmer and Deuel-Zogg, as he references all of them except the latter in his first paper published in 1954[12].

Friedman co-authored a paper with Cohen in 2018 called "The assessment of labor – a brief history", where the Swiss contributions are mentioned, again with the exception of Deuel-Zogg[17]. All pre-Friedman research is trivialised with explanations such as using rupture of membranes as the origo, the use of a non-linear scale for dilation or lack of recognition of sigmoidal shape of the curve.

The sub-section: "The Friedman Era", states: "Friedman determined that measurements of changes in cervical dilatation and fetal station over time were the most useful parameters for the assessment of labor progress[20]. The original dilatation and descent curves were based on and confirmed by direct clinical observations made by one examiner on women in labor."

There is no denying Friedman's substantial contribution to the partograph with his plethora of papers, expanding the knowledge, popularising and propagating it, and implementing it in clinical practice. His other contributions to obstetrics through books and original publications remain paramount.

Interestingly, in his interview with Romero, Friedman states: "I believe that our educational system must be modified because it suppresses curiosity and tends to

perpetuate accepted facts rather than to challenge ideas that have been pronounced as truth.[21]"

Well, one such "truth" in obstetrics is that Friedman is the one true father and inventor of the partograph. I'd like to think that Friedman would condone challenging that idea, even if he were to dislike my conclusion: Continuing along the family metaphor; - the partograph does not have *one* father, but a family, mostly based in Germany and Switzerland. Friedman may have married it and taken it throughout the world, to places it otherwise wouldn't have been, and made famous.

Though, if the partograph were to have had a mother, I propose Dr. Heidi Deuel-Zogg.

2.5 Contemporary thoughts on the pre-Friedman phase

There are certainly aspects to ponder from the pre-Friedman phase. First, before the partographs, labour phases were determined by subjective perception of contractions, rather than cervical dilation. In practice it is not uncommon for the woman's and the birth attendant's stories to diverge as to whether the woman's labour was long. Also, if a subjective definition were to be used, it would give the woman access to care and pain relief at an earlier stage than if the bar is set at a certain number of centimetres of dilation.

The early partographs used rupture of membranes as an origin or starting point. Rupture of membranes is often an easily observable moment, as amniotic fluid gushes out. Furthermore, it is clinically well known that the foetus tends to tolerate labour before rupture of membranes better as it under normal circumstances is surrounded by incompressible amniotic fluid. Also, risk of infection for both mother and foetus rise with time once membranes are no longer intact.

However, in contemporary practice, artificial rupture of membranes to hasten labour or monitor the foetus with a scalp electrode has become so common that spontaneous rupture of membranes no longer provides a useful origin. It begs the question though: Is it the origin that is misplaced, or the very common practice of rupturing intact membranes to hasten labour, all the while knowing that our definition of prolonged labour is disputed?

2.6 Friedmans curves and phases of labour

The Graphic Analysis of Labor

Friedman published his first hallmark paper in 1954, namely "The Graphic Analysis of Labor"[12]. In it, he analyses a serie of 100 nulliparous women, of which 29 delivered spontaneously, 64 by "prophylactic low forceps" and 4 midforceps delivery. All infants were live born, one spontaneously born infant died the first day postpartum, due to subdural hematoma. He describes three cases of "primary inertia" and seven cases of clinically authenticated "secondary inertia". Episiotomy was almost universal. Oxytocin was employed in the ten cases of labour inertia. Twenty-two of the patients had received caudal anaesthesia. Cervical dilation was determined by frequent (30 minutes – 2 hours) rectal examinations, at peak of contraction, in most cases by a single examiner throughout the course of labour. These findings were plotted on square ruled paper.

Based on these results, Friedman analysed the slope of the labour curve and divided it into phases: namely *latent period* or *phase one*, until a dilation of 2 to 2.5 cm. Thereafter follow: Phase two or acceleration period, phase three or steady period, fourth phase or deceleration period. This division of labour into latent and active phases (although the latter term not used in this paper) remains the paradigm until the present day in most scientific literature.

Friedman deduces a curve for normal labour from his series, and presents a case (Figure 7) to illustrate it. He also illustrates two cases of "inertia"(Figure 8 and 9). His conclusions, abbreviated, are that: The efficacy of plotting cervical dilation

against time as a method is demonstrated, the labour curve is sigmoidal in shape, a description of the four phases, primary and secondary inertia are redefined in terms of deviation from the normal, the method may be used to analyse the effect of iatrogenic interventions on the course of labour. And, considering the research done before Friedman, perhaps most important: “The value of this method for the study of individual labours, in progress, is stressed.”

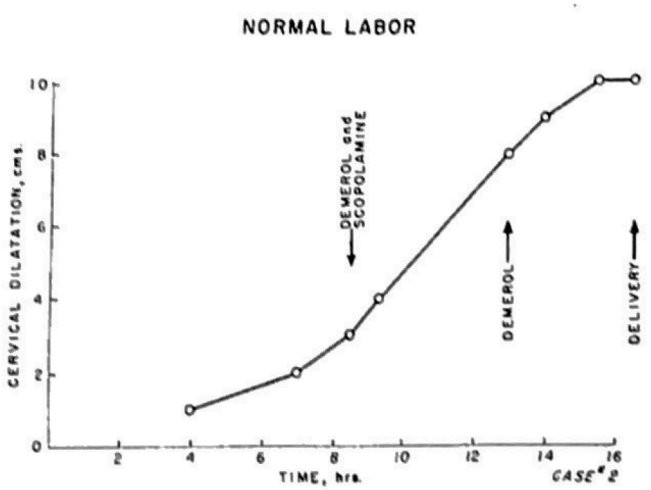

Figure 7 - Normal labour. Primipara at term. Latent phase 7.0 hours, slope 0.3cm per hour: active phase 8.5 hours, maximum slope 1.1cm per hour. The sigmoid character of a normal labor is apparent. (Friedman 1954) Reprinted with permission from Elsevier.

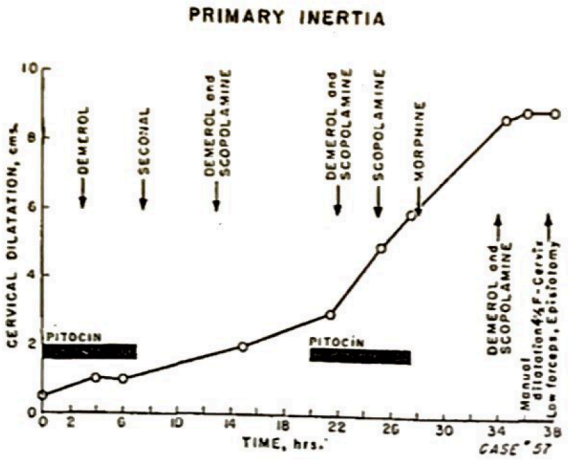

Figure 8 - Primary inertia. (Friedman 1954)
Reprinted with permission from Elsevier.

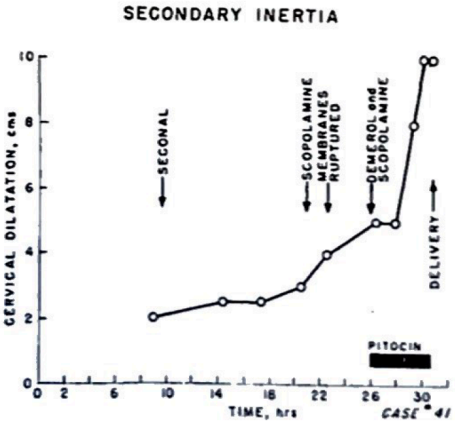

Figure 9 - Secondary inertia. (Friedman 1954)
Reprinted with permission from Elsevier.

Demonstrating the use of this method during labour is indeed Friedman's undeniable contribution to the early history of the partograph. Also, the start of the *active phase of labour*, namely phase two in the words of Friedman, is central in the current paradigm of labour management. However, reading the paper in light of later research, it becomes apparent that these phases are primarily rooted in mathematical analyses rather than in consequential clinical practice: "Normality" and "inertia" are

(re-)defined on the basis mathematical analyses of 100 partograms, and more importantly, the definition of ideal or normal is not made on the basis of absence of adverse outcome.

Friedmans "ideal labour" – ideal for whom?

Friedman expands on the ideas from 1954 in two papers in 1955 and 1956, named "Primigravid labour – a graphicostatistical analysis[13]" and "Labor in multiparas; a graphicostatistical analysis[14]" respectively, of which only the first will be described here. In the first of them, he expands on the analyses from 1954, analysing 500 nulliparous women. The study population is carefully described, and possible causes of inclusion bias disclosed.

However, before the analyses, he excludes the following*: "The maximum allowable limit for the active phase is 11.7 hours. Values greater than this are considerably abnormal, and reflect primary inertia and/or secondary arrest […]".* Thereafter he selects 200 births which he labels "ideal" labours. Explicitly excluded are cases with inertia, precipitate labours occiput posterior, twins, heavy medication, caudal anaesthesia, pitocin, babies <2500g and >4000g. The population allowed to represent the "ideal" is quite restricted, and once again not correlated to adverse outcomes. Also precipitate/fast labours are considered non-ideal, though no clear argument for this is presented.

The remaining part of the paper examines the effect of sedation, caudal anesthesia, pitocin, occiput posterior position, cephalopelvic disproportion, prior abortion, and quite interestingly, - psychological preparation for childbirth defined as financial status, intellectual level, confidence exhibited and *reassurance and personalised attention received (n=140)*. Friedman finds that these groups have shorter latent and active phases of labour, and that their curves "are approaching the ideal". These thoughts have an echo in research done almost 50 years later, investigating the positive effect of continuous support for women during childbirth.

Further research from 1956 until present day

Selecting among the plethora of later publications by Friedman is challenging, as the contributions are immense, however the added dimensions and nuances are certainly substantial. He described computerised analyses of a large number of labour curves (n=10.000), contributed to analyses of deleterious long term neurological effects in children delivered by mid-forceps, and the effects of sedatives on labour outcomes to name a few milestones.

He has also published papers on how to interpret labour curve aberrations and their possible causes and prognostic significance[22, 23]. In a 1971 publication comes a quote which illustrates an evolution in thinking with regards to normality[24]:

> *"Before we can discuss intelligently the detection of aberrant patterns of labor and their management we must be able to characterize normal labour clearly. […] The usual diagnostic criteria in use nowadays invoke arbitrary standards of total duration of labour, beyond which abnormality may be considered to exist. These limits are unfortunate because many serious abnormalities may arise long before the normal duration has been exceeded, and many labors that extend well beyond the normal time may be perfectly normal. Thus, for example, labours lasting more than 24 hours are usually deemed to be abnormal and, therefore, to warrant consultative evaluation. […] The single guideline of duration, therefore, must be considered too coarse and insuffiently definitive to permit us to specify precisely which patients are at risk […]"*

2.7 Philpott and Castle – a practical solution to a lack of health care personnel

Philpott and Castle published two influential papers in 1972[25, 26]. In the first, they outline the necessity of utilising health care personnel in Harare (then Salisbury) in Zimbabwe (then Rhodesia), which at the time had a doctor to patient ratio of 1:80.000. They report a number of obstetric fistulae at the local teaching hospital.

They ascribe this problem to two factors, cephalopelvic disproportion and "inefficient uterine action".

In the same paper, they describe the *alert line* as a tool for transferring women to centralised labour care. The line is superimposed over a horizontal Friedman partogram. The line is started at three cm of dilation, and is crossed if cervical dilation is <1 cm per hour. In their study of 624 women, the authors found that women with progress within the alert line, there were no problems of cephalopelvic disproportion.

In their own words: "*Our Alert Line is both simple and efficient. It separates, when compared to other possible lines, the highest proportion of normal from abnormal patients, allowing time for transfer of those who are abnormal to the Central Unit for active management*."

They furthermore argue that as the start of their alert line at three cm coincides with Friedman's definition of active stage of labour, and as the alert line is only slightly slower than Friedman's statistical limit: "*We believe that it could have universal application in the management of primigravidae*".

In Philpott and Castle's second paper they advise the implementation of an *action line*, arbitrarily displaced four hours from the action line. In the same series of 624 patients as in their first paper, 11% crossed the action line. These were actively managed by transferral to the intensive care ward in the central unit, given routine epidurals, fluids and carbohydrates intravenously, a pelvic assessment for cephalopelvic disproportion, and oxytocin management by intravenous drip. The dose is difficult to determine from the description in the paper.

Out of the 68 patients (11%) which crossed the action line, 19 delivered spontaneously, 35 by vacuum extraction and 14 by CS. Foetal outcomes in all groups were acceptable, the average 5 minute Apgar scores were >8 in all groups and there

were no fresh stillbirths. Compared to outcomes in the same clinic from 1966, all outcomes were improved, yet using comparisons of historical cohorts has significant risk of bias: the change in outcomes may be unrelated to the partogram.

The authors emphasise how the use of the action line has allowed 50% more women whose dilation have crossed the alert line to avoid oxytocin stimulation, thereby reducing the workload in the Central Unit. They also believe that monitoring with this type of partogram has helped the staff in terms of decision making.

These two papers by Philpott and Castle have had a lasting impact on contemporary labour management. Their implementation clear criteria for the use of oxytocin resonate into current obstetrics. And, if using their alert and action lines when applied universally as they suggested, had similar results as in their publication, namely leaving 89% of women to birth safely without intervention, it would be undisputable.

However, in a 2019 systematic review of a compound of 13 studies comprising 20.471 women from all continents, Bonet et al. found that the percentage of women crossing the alert line varies from eight to 76 percent across studies. Furthermore, they report that in none of the studies included in the review, crossing the alert line had adequate accuracy as a diagnostic test for adverse birth outcomes[27].

The idea was propagated in labour wards in the United Kingdom (UK) and later internationally throughout the 1970s and 80s, and became an integral part of the WHO partogram.

2.8 Active management of labour

The research of O'Driscoll et al. has had a major impact on intrapartum care in over the last 50 years.

The first paper was published in 1969 and outlines the results of a regime of *active management* of 1000 consecutive primiparous women at the National Maternity

Hospital in Dublin[28]. The rationale for the study is that "*prolonged labour presents a picture of mental anguish and physical morbidity which often leads to surgical intervention and may produce a permanent revulsion to childbirth […]".*
From the introduction it seems that there has been no clear distinction between active and passive phase of labour, and over the study period of nine months, the local definition of prolonged labour has fallen from 48 to 24 hours.

Start of labour was defined as bloody show, dilation of the cervix (though no definition of dilation is given), spontaneous rupture of membranes in the context of painful uterine contractions. Upon defined labour, an active approach was pursued. Unless progress of dilation (definition of speed not given), membranes were ruptured and if this did not accelerate labour a standardised oxytocin infusion was administered.

Interestingly, whereas active management of labour and Friedman's partogram were implemented in clinical practice over the same time period, and often seen as integrated paradigms, O'Driscoll et al. do not employ Friedman's partogram or definition of onset of labour in any of the early papers on active management. Rather, they criticise Friedman's conclusions twice in the first paper, with regards to approach to labour progress, and interpretation of causal mechanism of prolonged birth[28]. They also disagree on the effects of artificial rupture of membranes, where O'Driscoll claims it expedites labour and Friedman claims it stalls labour[28].

In the results, they show an incidence of prolonged labour, defined as >24 hours of 0.1%. Artificial rupture of membranes was performed in 119 cases (11.9%), oxytocin was used in 35 cases (3.5%), 40 CS (4.0%) and 189 forceps or ventouse deliveries (18.9%). Maternal mortality and morbidity are not reported. There were 25 perinatal deaths in 1010 infants, of which four intrapartum deaths.

O'Driscoll et al. argue that the obstetrician *"should […] forsake the role of passive observer for that of active director, controlling the course of labour"*. They argue for

an objective, or at least obstetrician based decision on whether labour has begun, against the use of sedatives, in favour of early artificial rupture of membranes and use of oxytocin. They advocate for individual attention in a specialised unit for all patients, and that no woman is to be left unattended in labour.

If the excellent results of the Dublin Maternity Hospital were reproducible in other settings at the time, the only sound though crucial argument against the method would be to question whether labours lasting over 24 hours were the genuine problem for the women and their children in the first place. A paper published by O'Driscoll in 1972 sheds some potential light on another possible incentive for active management: In "Abolition of Prolonged Labour" he elaborates on how the delivery unit has five rooms, delivering 6225 babies, with 30 midwives on staff, and at a personnel cost of £4.72, compared to £12 in other institutions[29].

Whereas cost effectiveness in health care undoubtably must be taken into account, the focus on shortening labour in the context of inadequate rooms and staffing may reduce traction in processes of improving conditions in terms of localities and trained birth attendants.

Furthermore, one must acknowledge that the original paper is based on a single centre observational cohort, in part historical comparison to the same centre, and despite implementation of several new interventions, no control group existed outside historical controls.

O'Driscoll et al. published another series of 1000 primiparous patients in the British Medical Journal in 1973, in this series the oxytocin use had increased by a factor of 10, from 3.5% in the original series to 55.0%[30]. Interestingly, in this paper they used a different approach to define labour, namely the time of admission to the labour ward. The conclusions in the paper were similar to those in 1969, albeit more to the side of convincing the reader to accept this method as superior to other management: *"The conclusion is that once labour has started it is possible to regulate the duration with*

almost complete success." Conversely, O'Driscoll seems to consider observational or conservative management as the causal mechanism of negative outcome.

From a contemporary perspective, there are several aspects of the paper with regards to maternal consent, but these must be interpreted in light of historical context. However, O'Driscoll's perspective on labour pain leaves something to be desired, even in his time:

The 1969 paper states:

> *"A generous use of analgesic drugs is characteristic of the passive approach to labour. […] The situation is created in which women demand more and more drugs simply because they are progressively confused.[28]"*

In the 1973 paper:

> *"The subject of pain in labour is highly emotive and widely publicized. None would dispute that relief of pain is desirable or that labour can be conducted without pain. But it is important to consider whether women are sometimes influenced to expect pain for the purpose of having it relieved, and if it is desirable to stimulate popular demand for procedures such as caudal or epidural anaesthesia, which are potentially dangerous.[30]"*

Considering the first sentences of the paper from 1969[28] describe that prolonged labour as a *"picture of mental anguish […] and may produce a permanent revulsion to childbirth"*, this apprehensive approach to pain relief seems contradictory to O'Driscolls aim.

Despite these limitations, active management of labour or components of the treatment package were implemented throughout the UK and many other countries throughout the 1970s and 80s, alongside the Friedman partogram for progress monitoring.

2.9 The active management backlash

In 1994 Thornton and Lilford published a review of observational data, supplemented by evidence from four separate overviews of RCTs in the British Medical Journal on the effects of the different parts of the active management of care package[31]. In this comprehensive paper, they point out how these interventions were rolled out despite a lack of controlled trials. They contrast this against the results of the Dublin papers to the trend of rising CS in the UK from the time of implementation of active management.

They go on to summarise the evidence from trials on amniotomy, early oxytocin, the two combined, and having companionship during labour. Out of these, the only intervention with a clear benefit on CS and operative vaginal delivery, as well as foetal outcome, is the latter: Companionship. The authors deem amniotomy as safe, and with a modest effect on labour duration, whereas early oxytocin only had a modest effect on labour duration in one trial, and no significant reduction of CS.

They describe a poor compliance rate with conservative management arms in the controlled trials. Even in a controlled research setting, the eagerness to pursue intervention over observation prevails, despite lack of evidence of effect of said intervention.

O'Driscoll commented the paper[32], stating that his intentions, and the true purpose of active management have been misunderstood, and states that the purpose was to enhance the experience of childbirth for mothers, particularly first time mothers, whose need is greatest. Furthermore, he argues that CS did not become an issue until much later, and in a different context, and the possibility remains that the adoption of active management of labour by hospitals in the UK has had a restraining influence on CS rates.

Contrasting the two, although the methodology of Thornton is sound and in compliance with contemporary scientific standards, there is a possible causal fallacy from both sides:

1) O'Driscoll attributing a causal effect of active management of labour as a whole on excellent obstetric outcomes in Dublin.
2) Thornton shows the lack of effect of parts of active management on reducing CS. However, by inference through the introduction of the paper, he argues that active management may be causal in the increase, or at least not effective in stalling the CS rates in UK.

A third possibility is that CS in the UK would have risen between 1969 and 1994 regardless of whether births were managed according to the active management principles, given the advent of foetal surveillance with questionable sensitivity and specificity, maternal request, changing birthing population, unwillingness among women and birth attendants to undergo or observe long labours, resource and personnel scarcity to name a few possible factors.

Whether the CS rate would have been higher, lower or the same with a different management regime is counterfactual, and therefore impossible to predict.

In 1996, a heated exchange ensued in the British Journal of Obstetrics and Gynaecology, spurred by a commentary by Karl Olah and Harry Gee, with the title "Active mismanagement of labour[33]". The commentary concludes by stating the following, which was certainly not untrue, but quite sharply worded:

"Unfortunately, we have spent the last 25 years managing labour without knowing what we do. The superficial nature of our understanding must be appreciated and change in practice based on speculative interpretation of complex data should be

viewed with scepticism[3]*. Developments in practice must ultimately be tested by properly conducted clinical trials before widespread implementation."*

2.10 WHO partograph

In 1988 the WHO Maternal Health and Safe Motherhood programme published a series of four documents describing the WHO partograph[9]. The explicit goal was to reduce maternal mortality in developing countries. These documents were re-issued with minor alterations in 1994 to take into account a large multicenter study, see below. The partograph consists of 9 segments, of which one is a modified Philpott partogram with the addition of a latent phase up to 8 hours and a plot of head descent, see Figure 10. The other eight describe foetal heart rate, liquor, moulding of the foetal head, contractions / 10 minutes, oxytocin infusion, maternal pulse, temperature and urine output, protein content and volume.

The publication of the partograph was followed by a Lancet publication describing the application of the partogram in a large multicenter study[34]. The Lancet publication entails a nested single way crossover study in four pairs of hospitals in Thailand, Malaysia and Indonesia, enrolling a total of 35.484 women.

The study showed a significant and relevant reduction of women in labour for >18 hours, and in labour receiving augmentation, but no significant reduction in CS or assisted vaginal delivery. Moreover, 23 maternal deaths were recorded before the intervention and 24 after. Five deaths were intrapartum, and none of the cases were due to prolonged labour, but rather pulmonary embolism, eclampsia and postpartum haemorrhage.

[3] Verbatim.

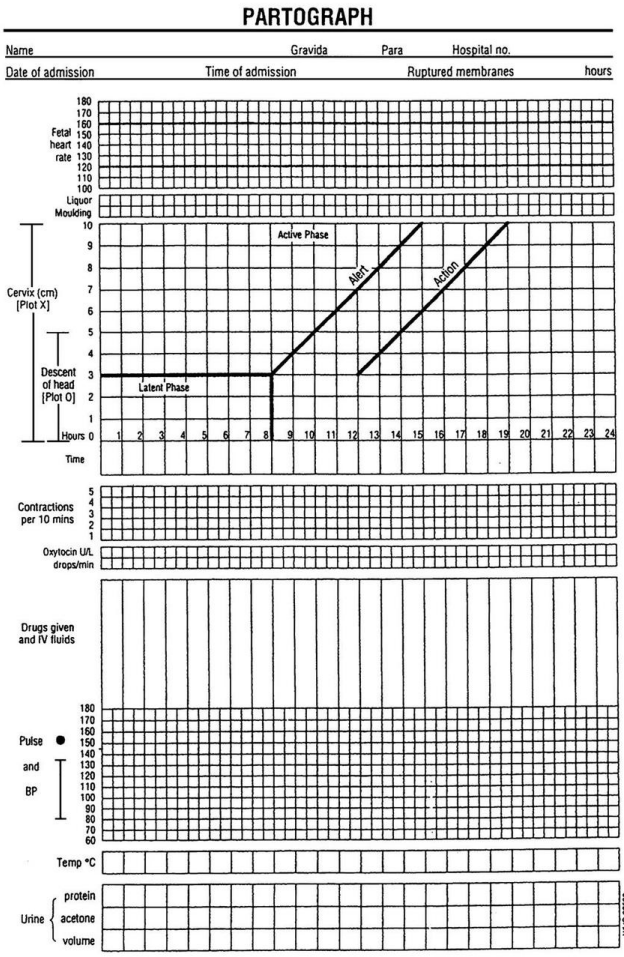

Figure 10 - WHO partograph 1994

The authors nevertheless state: *"Its use in all labour wards is recommended"* and *"Its universal application has the potential not only to reduce fetal and maternal mortality and morbidity, but also to reduce the number of caesarean section"*

One could say that is a relatively broad conclusion from a paper that neither shows reduction in maternal mortality nor CS. Furthermore, we once again see a recommendation of universal implementation coming from a study that has a particular context, namely three countries in southeast Asia. The maternal mortality

in the study was 130/100 000. In the same time period, maternal mortality rates in most western European countries were around or less than a tenth of this figure.

This is not to say that the WHO partograph does not have merit in the context of a developing country, merely that the conclusion of the Lancet study may have oversold its results by claiming universal implementation and effect on potential effect on maternal mortality.

Throughout the next decade, the WHO partograph was disseminated and implemented in a vast number of labour wards throughout the world. The increase in interventions during the latent phase of labour and problems defining the onset of the active phase resulted in another updated version in 2000, in which the latent phase was excluded from the partograph and the start of the active phase was defined as 4 cm of cervical dilation[35]. A further update in 2018 postponed the definition of active labour to 5 cm.

Lavender et al. conducted a meta-analysis in 2013[36] with a 2018[37] update on the effect of partogram use on outcomes for women in spontaneous labour at term. The meta-analysis was done through the Cochrane network, and the 2018 update included neonatal outcomes. Reporting on a number of different outcomes, their main conclusions are that partogram use has little or uncertain effect on outcome, and that universal routine use is not warranted.

2.11 Zhang – a reappraisal of the labour curves

Zhang and collaborators Troendle, Laughon, Kominiarek and others, published several papers between 2002 and 2012 challenging the applicability of Friedman's labour curve in a contemporary labouring cohort. In the first publication from 2002[38], they extracted and analysed labour patterns from 1329 nulliparous women in TGCS 1. They described labour to be slower than in Friedman's analyses, with the active first stage of labour (4-10 cm dilation) lasting ~5.5 hours compared to ~2.5 hours in the Friedman curve. They also did not find a deceleration phase. In 2010 they published a large study comprising the labour progression of 60.000 women which

ended in a vaginal birth of a healthy baby, and on the basis of these data constructed new labour curves (Figure 11)[11].

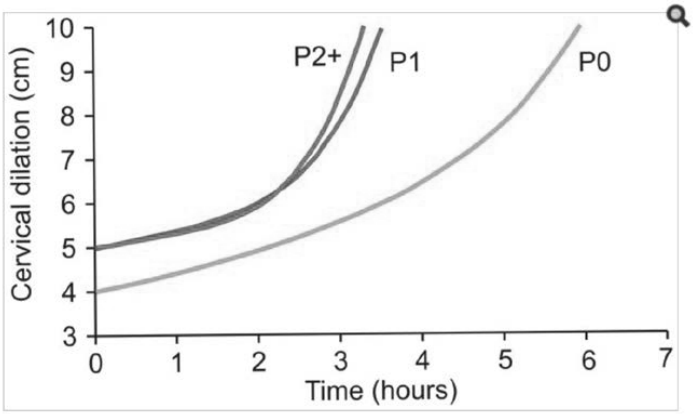

Figure 11 - Average labour curves by parity in singleton, term pregnancies with spontaneous onset of labor, vaginal delivery and normal neonatal outcomes. P0: nulliparas; P1: women of parity 1; P2+: women of parity 2 or higher. (Zhang et al. 2010)

Laughon[39] et al. published a 2012 study comparing two historical cohorts of 39 491 women delivering in the US in 1959-1966 to another cohort of 98 359 in 2002-2008. Based on the attempt to correct for maternal and pregnancy characteristics, she found that the shortened labour duration may be due to changes in obstetrical practice, rather than changes in the birthing population. She concluded that the benefit of extensive intervention needs further evaluation.

Based on the above research and other contributions Caughey et al. published a labour care guideline for The American College of Obstetricians and Gynecologists (ACOG) in 2014, in an attempt to stall rising rates of CS[40]. The guideline was comprehensive and addressed many aspects of labour management, but relevant for labour progression were the following: First, they recommended that active labour should not be defined until six cm of dilation. Second, they suggested that CS for arrest in the active first stage of labour should only be performed in women beyond six cm of dilation with ruptured membranes who did not progress despite four hours

of adequate uterine activity or at least six hours of oxytocin administration with inadequate uterine activity and no progress of cervical dilation.

These guidelines were in turn criticised in a series of papers by Cohen and Friedman[41-43]. Among other arguments, they pointed out that the ACOG guideline was not a result of demonstration of superior outcomes through extensive nor prospective assessment, and theorised that the difference between newer labour progression descriptions were the result of curve-fitting methods rather than true differences from Friedman's description. They furthermore stated that the new guidelines were without concern for potential adverse effects for mother or child.

The need for randomised controlled trials (RCT) of new labour care guidelines and their effect on CS rates as well as maternal and foetal well-being were obvious, and in 2019 Bernitz et al. published a large Norwegian cluster RCT investigating whether the use of the Zhang's guideline reduced the frequency of intrapartum CS compared to Friedman's partograph[44]. They found no significant difference between clusters. They did find longer labours in the clusters employing the Zhang guideline. Secondary analyses found no difference in childbirth experience between groups[45], but further supported the effects of one-to-one care in labour: nulliparous women receiving such care were less likely to receive an epidural[46].

2.12 Oladapo – challenges to a single extrapolated labour curve?

Another interesting study was published in 2018 by Oladapo et al.: They prospectively collected observational data on 5606 women in 13 hospitals in Nigeria and Uganda, women presenting in early, spontaneous labour <6 cm dilation, normal maternal and neonatal outcomes, and plotted their pattern of cervical dilation. They constructed average labour curves and centile charts based on their findings[47].

The average labour curve versus alert line for nulliparous women can be seen in Figure 12. A still of a video found in the supplementary material, namely the

underlying data for the extrapolated regression line, provides insight into the underlying material and its variation, see Figure 13.

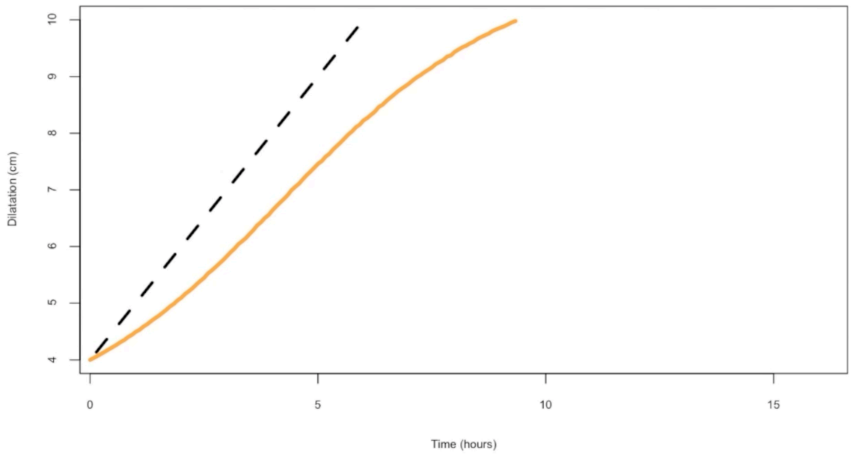

Figure 12 - Average labour curve (solid) from nonlinear mixed models, and alert line (dashed) for nulliparous women, Oladapo 2018. (Open Access)

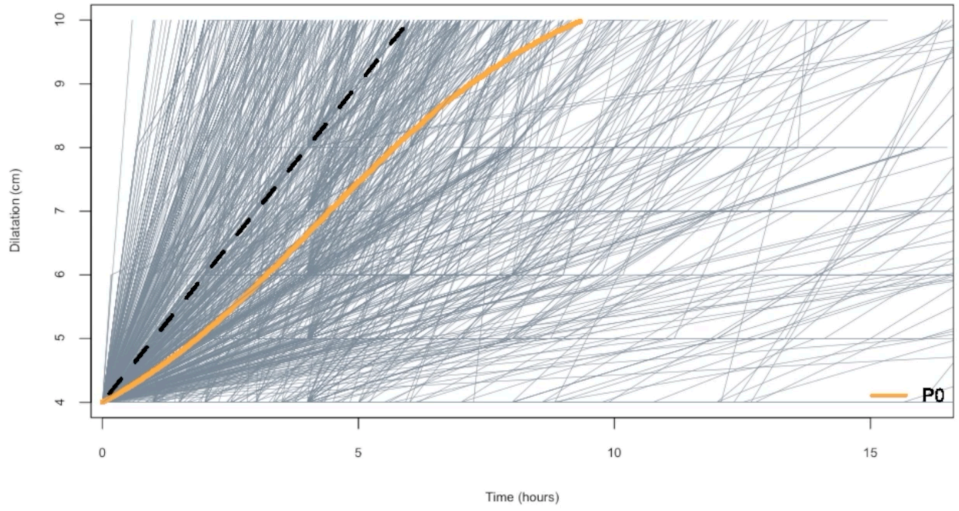

Figure 13 - Individual plots of cervical dilatation, average labour curve (solid orange) from nonlinear mixed models, and alert line for nulliparous women. (Open Access)

The authors conclude that averaged labour curves may not truly reflect the variability associated with labour progression, and their use for decision-making in labour management should be de-emphasized. One could ask whether this conclusion is understated: - does the underlying data support using a linear model to describe labour at all?

Oladapo went on to co-author a systematic review with Bonet the following year, including thirteen studies of 20.471 women, where they do not find support for the use of an alert line to identify women at risk for adverse birth outcomes[27].

These studies lead up to the construction of the WHO labour care guide, published in 2020, and discussed in the Discussion part of this thesis.

All papers in this thesis were done based on labours managed by the WHO 1994 partogram, and the evidence they provide must be viewed in light of the paradigm they were produced under.

3. Second stage of labour

This review has up until this point focused on partograms and the first stage of labour: the progress from a given number of centimetres dilation to full dilation (defined as 10 cm). The second stage of labour is defined from 10 centimetres of dilation until the birth of the child, and is divided into a passive and an active stage: without and with active expulsive efforts on behalf of the woman.

There is also a substantial difference in guidelines from country to country: As examples: The French national guidelines recommend an operative delivery as early as after 30 minutes[48], the Norwegian guidelines recommend an evaluation of operative delivery after one hour regardless of parity and epidural use[49], and the Royal College of Obstetricians and Gynaecologists (RCOG) and ACOG guidelines indicate an operative delivery in nulliparous women with a combined passive/active stage without progress for three hours in the case of regional anaesthesia and two hours without, and two and one hours for parous women respectively[50, 51].

The French guidelines and sources are mostly available in French, but are, as far as I can gather, based on pH-measurement studies from the 1970s[48], whereas the Norwegian guideline in its present form does not quote a clear source of evidence. However, it is likely that the RCT by Yli et al[52] has been influential for selecting one hour as a cut-off. The RCOG guideline quotes Cheng et al. as their evidence, with a retrospective study of 15.759 women in which neonatal morbidity did not increase after three hours of active second stage in the setting of foetal surveillance and timely obstetric intervention. Furthermore, that there were higher rates of maternal morbidity in the >4 hour group, namely CS, operative vaginal delivery, chorioamnionitis and obstetric anal sphincter injury[53].

Other studies show conflicting results: Infante-Torres et al. however, found an impact on neonatal morbidity as well, in a review and meta-analysis including 266.479 women: the children of women with second stages >4 hours had lower five minute

Apgar scores, higher neonatal intensive care transfer rates and composite neonatal morbidity[54]. Leveno et al. argue, based on a review of evidence in 2015, that the long accepted obstetric paradigm that second-stage labour >3 hours in nulliparous women with labour epidural is not safe for the unborn infant[55].

Despite increasing evidence, the guidelines vary so substantially from country to country that the conclusion from a 1991 editorial comment in Australian and New Zealand Journal of Obstetrics and Gynaecology seems to retain precision: *"The optimal management of prolonged second stage of labour remains a confused area of thought and action."*[56]

Oxytocin infusion and a few non-pharmacological interventions have been investigated in the active second stage, either to shorten its duration or reduce the risk of operative delivery.

Whether after thirty minutes or three hours, at some point the birth attendant has to consider an assisted operative delivery or a CS in the second stage to end labour[52]. Caesarean section in the second stage increases the risk for both maternal and perinatal morbidity[57-59], and the risk carries through to future pregnancies and deliveries[60, 61]. Successful operative delivery also carries risks for the mother and child, including and obstetric anal sphincter injuries[62, 63] and neonatal intracranial haemmorhage[64].

A failed operative vaginal delivery resulting in emergency CS carries cumulative risks, the trauma to child and the genital tract thorough the attempted operative delivery, and those from the CS[64, 65]. In other words, determining the right management for a prolonged second stage of labour is of paramount importance.

4. Induction of labour

Induction of labour became part of scientifically documented obstetrical practice in the 1780s[66], initially for a very limited range of indications. However, it is likely that herbs or other remedies were used as abortifacient or inductive agents since prehistoric times, as texts as early Hippocratic oath forbid abortion and descriptions of abortifacient medications are plentiful in ancient medical literature[66].

Contracted pelvis remained the primary indication throughout the 18th and 19th centuries. During this time, methods for induction of labour have included mechanical methods such as amniotomy, membrane sweeping, mechanical dilation of the cervix and direct irritation of the uterus. Medical methods have included ergot preparations, quinine, oxytocin and later prostaglandins in different preparations[66]. In current evidence based medical practice the following remain in use: membrane sweeping, Foley- or Foley derived balloon catheters (e.g. Cook), prostaglandins, amniotomy and oxytocin, and combination regimes of the above. Despite numerous studies comparing different methods, their safety profile, effectiveness and cost-effectiveness, there is no evidence supporting a single panaceal method for labour induction: All methods come with potential benefits and risks[21]: Prostaglandins and oxytocin may increase the risk for tachysystole and uterine rupture, whereas mechanical methods may be somewhat less effective than pharmacological ones in achieving a vaginal delivery[67].

Over the last century, a growing number of indications of induction have entered into clinical management: Pre-eclampsia, premature rupture of membranes, post term pregnancy, suspected macrosomia and maternal request to name a few. As a result, more than one in four births in Norway are now subject to induction, and the trend is similar for other developed countries.

There is ongoing scientific discourse regarding the potential benefits and risks of induction, and whether induction increases the risk of intrapartum caesarean section or reduces the risk of stillbirth. The results are ambiguous.[68-71]

As the majority of studies are observational cohort studies and not RCTs, the bias of confounding by indication is in practice impossible to correct for. Furthermore, the change in CS in RCTs will depend on the base risk for CS in the given population, and are not necessarily useful for extrapolating universal risk for CS. Ultimately, how induced labours are managed in terms of progress will have a potentially substantial impact on CS for failed induction, or an assumed prolonged first stage of labour.

4.1 Duration of labour and induction – why does it matter?

As the WHO partograph does not differentiate between women in spontaneous and induced labour, knowledge about progression and duration of labour in the context of induction is relevant for labour management. In an observational study, one cannot know whether the change in progression or duration is caused by the induction, or the indication for the induction. Nevertheless, when managing labour that has been induced, whether the effect is causal is in fact less relevant: If induced labour has a progression or duration which differs from spontaneous labour, knowledge about the difference will be clinically relevant.

We were aware of two relatively small previous studies which had investigated the progression of labour in spontaneous and induced labours, both conducted on cohorts in the USA. Both were for elective induction of labour, without any medical indication.

Vahratian et al. compared 143 women with Foley catheter cervical ripening and oxytocin induction, 286 women with oxytocin induction, and 1771 women with a spontaneous onset of labour[72]. Women with any pre-existing medical conditions were excluded. After adjusting for potential confounders, women who had an elective induction with cervical ripening had 3.5 times the risk of CS during the first stage,

compared with those admitted in spontaneous labour. Elective induction without cervical ripening, however, was associated with a faster labour progression from four to ten cm (estimated duration 266 compared to 358 minutes, $P < .01$) and did not increase the risk of CS, compared with those in spontaneous labour. Furthermore, women with an unfavourable cervix, requiring Foley catheter as part of the induction process had a CS rate of >40%.

In a similar study Hoffman et al. investigated multiparous women, and found that their labours lasted 99 minutes in induced labour versus 161 minutes in spontaneous labour. However, they found nearly twice as many intrapartum CS in the induction group: 3.9% vs 2.3%, and survival analyses were not used[73].

Certainly, when considering women for elective induction without medical indication, knowing the risk of prolongation and CS has particular interest.

However, with a rising number of inductions for a variety of indications, one in four births in Norway was induced in 2021[74]. Allowing these labours more time if they are indeed more time consuming could reduce the risk of CS. Furthermore, an increasing number of women have preexisting medical conditions. Therefore, a study without exclusions based on indication or maternal condition could potentially yield relevant results for management.

This formed the basis for the research question of paper 1.

5. Oxytocin for labour augmentation

In 1909, the first report of the effect of pituitary extract on rabbit uteri was published, and shortly after it was shown to be as effective as ergot in the treatment of uterine atony[75]. Although not effective on its own, used in adjunct with amniotomy it was proven effective in induction of labour in 1915[76]. Unsafe use of pituitary extract soon became an issue, and a 1922 paper from Canada stated that "the number of fatalities from the use of pitruitin during the last six years has run far into the hundreds"[77]

A standardised preparation of pitruitin was introduced in 1930, and as of 1948 intravenous infusion became the preferred method of administration, which it remains today. In 1955 Vincent de Vignaud received the Nobel Prize in chemistry for his work which resulted in the first synthetic preparation of oxytocin[78].

Although initially used for induction and treatment of postpartum haemorrhage, oxytocin gradually gained momentum in the treatment of prolonged labour in the 20th century. Despite being widely hailed as a mainstay among obstetrical drugs, with paramount effects on induction of labour, augmentation of labour and the treatment of postpartum haemorrhage, oxytocin use is neither risk free nor without side effects. Improper use has been reported in both high and low resource settings.

In a study from 2008, 472 case records of women seeking compensation for suspected medical malpractice during delivery in Sweden were examined[79]. In 71% of cases, incautious use of oxytocin was part of the causal pathway. A 2016 study from Timurgara, Pakistan studying 6379 women, revealed that 9.5% of women had received unregulated labour-inducing medications (oxytocin or prostaglandins) prior to reaching the hospital, resulting in an increased risk of uterine rupture, birth asphyxia and stillbirth[80].

More common maternal side effects include headache, hypotension with resulting reflex tachycardia, nausea, vomiting, fluid retention and more painful contractions than when labouring spontaneously[69, 81]. The effects on the foetus are primarily

secondary to uterine tachysystole and prolonged contractions, with hypooxygenation and risk of foetal asphyxia as a potential result[82, 83].

Efforts have been made to standardise the use of oxytocin, through the introduction of infusion and dose increment intervals[84] and checklists for use. Although several different regimens have been described for administration, two are most commonly mentioned in scientific literature: a low-dose regimen of 1-2 mU/min or a high dose regimen of 4-7mU/min. The low-dose regimen is most commonly used in the Nordic countries.

Selin et al. examined the use of oxytocin in a Swedish cohort in 2009[85]. They found a high prevalence of oxytocin use for augmentation of labour, often with an unstructured implementation and without a diagnosis of prolonged labour.

We were interested to investigate whether a judicious use, through clear indication would influence maternal and foetal outcomes: Would there be fewer CS, particularly for suspected foetal distress? More labours lasting longer than 12 hours? Interventions, or lack thereof, will always be a balancing act in terms of outcome.

These questions formed the basis for Paper 3.

6. Obesity and BMI in pregnancy and labour

6.1.1 Weight, overweight, obesity and BMI

Overweight and obesity are conditions in which an individual's weight is above what is considered healthy. Body mass index, first invented by Adolphe Quetelet in 1932, divides an individual's weight by height squared, in order to obtain comparable numbers across different heights[86].

Despite being described as a "gold standard"[87], the method has medical and statistical caveats: BMI does not take into account whether the weight is made up by fat or muscle mass[88]. Furthermore, waist-to-height ratio has been shown to predict cardiometabolic risk factors with greater accuracy[89]. Other methods for determining body composition on the individual level have been suggested[88].

Despite these caveats, BMI remains the most commonly accepted method, probably in part due to the simplicity of the calculation. BMI and WHO BMI groups have been used as the classification system in all papers included in this thesis[90].

Table 2 - WHO BMI classes, A healthy lifestyle - WHO recommendations 2010.

BMI class	BMI
Underweight	< 18.5
Normal weight	18.5-24.9
Pre-obesity / Overweight	25.0-29.9
Obesity Class I	30.0-34.9
Obesity Class II	35.0-39.9
Obesity Class III	≥40

Weight and lifespan

Returning to the subject of normality as a fickle concept: What is normal weight? Definitions of overweight and obesity have varied over the past decades, and the

current consensus of the WHO may not necessarily reflect outcomes in terms of excess deaths by BMI group: A 2005 study in JAMA with more than 400.000 person years of follow-up showed excess deaths in the underweight and obese groups, but not in the overweight groups. A 2009 study in Lancet found the lowest mortality among those with BMIs between 22.5-25.0, which may provide some support for using 25 as a cutoff for normality in a life span perspective.

However, health is obviously more than survival, and overweight and obesity have been shown to increase risk for conditions including but not limited to cancer[91], diabetes type 2 and cardiovascular disease in the general population, and a wide range of complications in conception, pregnancy and delivery.

Fertility

Women with obesity may experience longer times from cessation of hormone based contraception to pregnancy, compared to normal weight women: A prospective study of 432 women found that median time to pregnancy was 5.3 months for normal weight women, compared to 8.2 months for women with obesity (BMI > 30)[92]. Pregnancy rates in the same study after one year were 59% in obese women compared to 76% in normal weight women. In the case of in vitro fertilisation in the setting of obesity, a meta-analysis found a decreased chance of live birth as compared to normal weight women (RR 0.88) [93].

Maternal complications in pregnancy

A large prospective cohort study from 2004 from Sweden (n=621.221) describes outcomes in obese (BMI 29.1-35.0) and severely obese patients (BMI >35), with normal weight women as a control group. They found an OR of 2.62 for preeclampsia in obese patients, and an almost five-fold increase in risk for severely obese patients, with an adjusted OR of 4.82[94]. The study also found a two- to threefold (or more) increased risk for antepartum intrauterine foetal demise, CS, shoulder dystocia, foetal distress, and large for gestational age babies.

Preterm delivery and increased risk of post term delivery

Somewhat paradoxically, obesity seems associated with both preterm and postterm delivery, through different causal pathways. A 2010 meta-analysis of >1 million women found a relative risk of preterm birth of about 1.24 (95%CI 1.13-1.37)[95]. A subsequent Swedish cohort study of 1.5 million live singleton births found the risk of extreme prematurity (22-27 weeks gestation) to be 0.17% percent in normal weight women, with the risk rising steadily through BMI groups to 0.52% in the women with BMI >40[96]. This study also investigates causal mechanisms: Women with obesity grade 2-3 had increased risk of preterm prelabour rupture of membranes and spontaneous preterm labour. This was theorised to be through mechanisms of increased bacterial growth in the urinary and vaginal tracts and increased inflammation from adipose tissue. However, a substantial disease burden came through the medically indicated inductions for obesity related conditions.

Late term (≥ 41 weeks) and post term birth (≥42 weeks) are also more common in obese women. A retrospective study from the UK of nearly half a million births showed an increase from 6.2% in normal weight women to above 8% in the obesity groups.

Intrauterine foetal demise

Several studies have shown an increased risk of intrauterine foetal death in overweight and obese women[94, 97, 98]. Chu et al. have reviewed these and several other studies in a 2007 meta-analysis, estimating the odds ratio to be 1.47 (95% CI 1.08-1.94) for overweight women and 2.07 (95%CI 1.59-2.74) for obese women[99]. In an American study of nearly 400 000 women, from 20 weeks of gestation, mediation analysis implied that 63% of the effect on intrauterine demise derived from shorter gestational age at delivery[100].

Racial disparity

Overweight and obesity are associated with lower social status and there is also a racial/ethnic difference in prevalence in western countries. Non-Hispanic black women in the USA have a close to doubled relative risk of perinatal mortality

compared to Hispanic and non-Hispanic whites[101]. Considering that obesity, social status, educational level and race are all associated, revealing causal links in this context is fraught with confounding, but one study suggests that maternal obesity may explain 10% of the Black-White disparity in stillbirths[102]. That leaves another 90% unaccounted for.

Post bariatric surgery – improvements and pitfalls

In 2015, a cohort study was published, comparing obstetric outcomes in women having undergone bariatric surgery, compared to control patients matched for age, parity, pre-surgery BMI, educational level, delivery year and smoking[103]. When comparing the 670 patients available for analysis with up to five matched controls, they found lower prevalence of gestational diabetes, birthweight >4.5 kg and large for gestational age ($p<0.001$). However, around twice as many infants in the bariatric surgery group gave birth to small for gestational age babies, and 1.7% had stillborn children compared to 0.7% in the matched control group ($p=0.06$). Weighing these outcomes, it remains disputable whether bariatric surgery improves outcomes in the context of pregnancy outcomes. Johansson et al. have later published and participated in studies with similar methodology showing marked lower risk of preeclampsia[104], but possible higher risk of preterm birth[105], underlining the ambiguity in outcomes.

Prolonged first stage of labour

An American study from 2004 investigated progression of labour in 612 nulliparous women, and found slower progress of dilation from four to ten centimetres in obese women, compared to normal weight women[106]. Some studies have investigated the duration of labour in nulliparous women, and found it to be longer for thosewho are obese than in normal weight women. However, the studies were mostly small case-control studies[107] (n~100) or observational studies ($n < 400$)[108], had other primary outcomes, or were focused on labour duration following induction[109], or a combination of the above.

In 2013, Carlhäll et al. published a cohort study including more than 63.000 women, describing the median duration of labour by BMI group. They found that the median

duration of labour increased by BMI group, from 8.8 hours in normal weight women to 9.8 hours in obesity class III. They found the duration of the second stage to be shorter in obese than in normal weight women, reporting the median duration to be 0.45 hours in class III obesity compared to 0.55 in normal weight women[110, 111].

A Danish study of 1885 women from 2017 found no difference in duration by BMI, group, but the study may have been underpowered[112]. However, this study interestingly found that obese women had CS earlier than normal weight women, perhaps due to risk perception by clinicians.

Are there any silver linings?

In a 2014 study, Hollowell et al. finds that otherwise healthy parous obese women have a lower absolute risk of obstetric intervention or adverse maternal outcome (21%) versus normal weight healthy nulliparous women (53%)[113]. This obviously does not negate the negative effects of overweight and obesity, and may tell us more about a high, or too high intervention rate in nulliparous women. However, it also highlights how, if an overweight or obese woman is managed in a way that allows for a first delivery without CS, it provides her with the best chance of consequent normal deliveries.

Furthermore, even though relative risk for negative outcomes in overweight and obese women may be increased, the absolute risk for many complications and negative outcomes is still low. How outcomes with a high relative risk and low absolute risk are reported requires us to be conscious when interpreting such results and converting them to guidelines and patient information.

Despite all this, clinical experience made us suspect that the active second stage of labour in overweight and obese women was in fact shorter than in normal- and underweight women. Clinicians would enter the room as the woman was about to push, in preparation for possible shoulder dystocia, and be surprised to see the woman deliver quickly. The question emerged: was this perception merely based on

the relief that the birth went better than anticipated, or was it in fact rooted in reality? The secondary findings of the Carlhäll study from 2013 supported this suspicion, but we wanted to explore the second stage with survival analyses, in both nulliparous and parous women to investigate further. This formed the basis for the objective and aim in Paper 2.

7. Ultrasound in labour and before operative delivery

Throughout the history of systematic evaluation of labour progress, evaluation has been based on clinical findings[12, 17, 38]. The diagnosis of prolonged labour and decisions regarding when and how to intervene rely mostly on vaginal digital evaluation of cervical dilatation, foetal head position and foetal head station. However, clinical examination of head station and position is inaccurate and subjective[114, 115], especially in the situation of caput succedaneum.

Ultrasound examinations can be performed before induction of labour[116], at admission in labour ward, in women with prolonged first[117] or second stage and before operative delivery[118, 119].

Studies have shown associations between ultrasound findings and delivery mode and remaining time in labour[117, 120]. Foetal rotation and descent can be followed longitudinally with ultrasound and the use of a sonopartogram has been suggested[121, 122].

7.1.1 Techniques

Ultrasound assessment in labour may be performed using a transabdominal or transperineal approach, depending on the parameter that is the aim of the examination. Several methods have been described, but this description of methods will be limited to those utilised in Paper 4.

7.1.2 Foetal head position

Foetal head position, defined as the rotational position of the foetal head in relation to the maternal pelvis, is best determined by transabdominal ultrasound, in sagittal and axial planes. This allows for identification and localization of foetal landmarks, such as the foetal spine, intracranial midline structures and eye sockets. By determining the localization of these landmarks, the position can be defined[123].

One suggested description of ultrasound defined position is considering the direction of the occiput as the hand of a clock, thereby defining positions (Figure 14)[124]:

> 03.30 hours and < 08.30 hours as occiput posterior

> 09.30 hours and < 02.30 hours as occiput anterior.

≥ 02.30 hours and ≤ 03.30 hours as left occiput transverse

≥ 08.30 hours and ≤ 09.30 hours as right occiput transverse

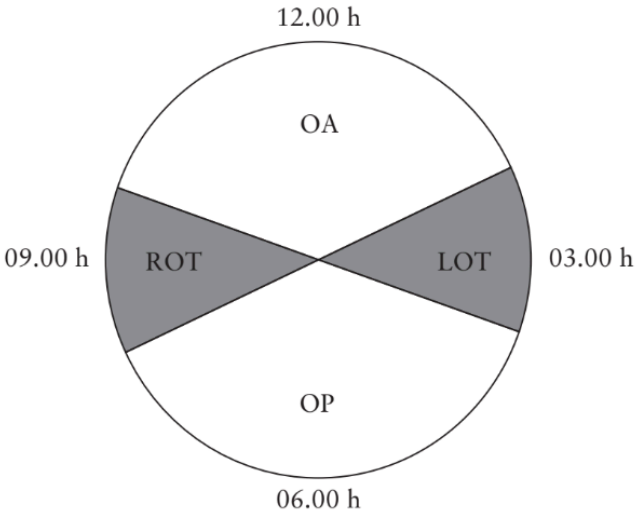

Figure 14 - Classification of foetal occiput position based on positions. OA, occiput anterior. OP, occiput posterior. LOT, left occiput transverse, ROT, right occipur transverse.[116]

7.1.3 Foetal head station

Sonographic assessment of the foetal head station can be performed by transperineal ultrasound in the axial or midsagittal plane. The ultrasound probe is placed between the labia majora or more caudally, at the level of the posterior fourchette, with the woman in a semirecumbent position. The legs should be flexed at the hips and knees

at 45° and 90° degrees, respectively. In order to obtain measurements of quality, the examinations need to be performed with an empty bladder.

7.1.4 Angle of progression

The angle of progressions is defined as the angle between the long axis of the pubic symphysis and a line from the lowest edge of the pubis drawn tangential to the lowest bony part of the foetal skull (Figure 15). It was first described in 2009 and has been found to be an accurate and reproducible parameter for assessment of foetal head descent.[125, 126]

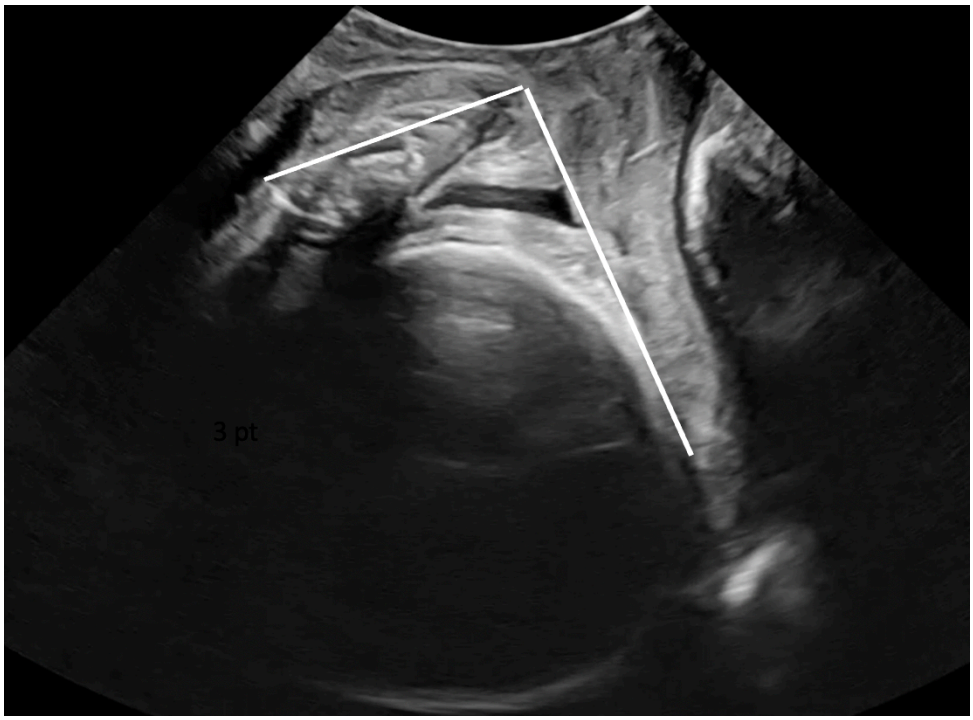

Figure 15 - Measurement of angle of progression, unpublished image (Eggebø TM, 2020)

7.1.5 Head–perineum distance (HPD)

Head-perineum distance (HPD) was first described by Eggebø et al.[127] In order to perform this measurement, the ultrasound transducer should be placed transversely in

the posterior fourchette, and the soft tissue compressed completely against the underlying bony structures (Figure 16). The transduced should be adjusted until the skull contour is as clear as possible, implying that the plane of the ultrasound is perpendicular to the foetal skull. Head perineum distance can then be measured in the frontal plane as the shortest distance from the outer bony limitation of the foetal skull to the perineum. Head perineum distance cannot be compared directly with the clinical assessment of foetal head station relating to the ischial spines (-5 to +5), as it does not follow the curve of the birth canal[128]. Head perineum distance is given in millimetres. Tutschek et al. found head station 0 to correspond to a head perineum distance of 36 mm[129].

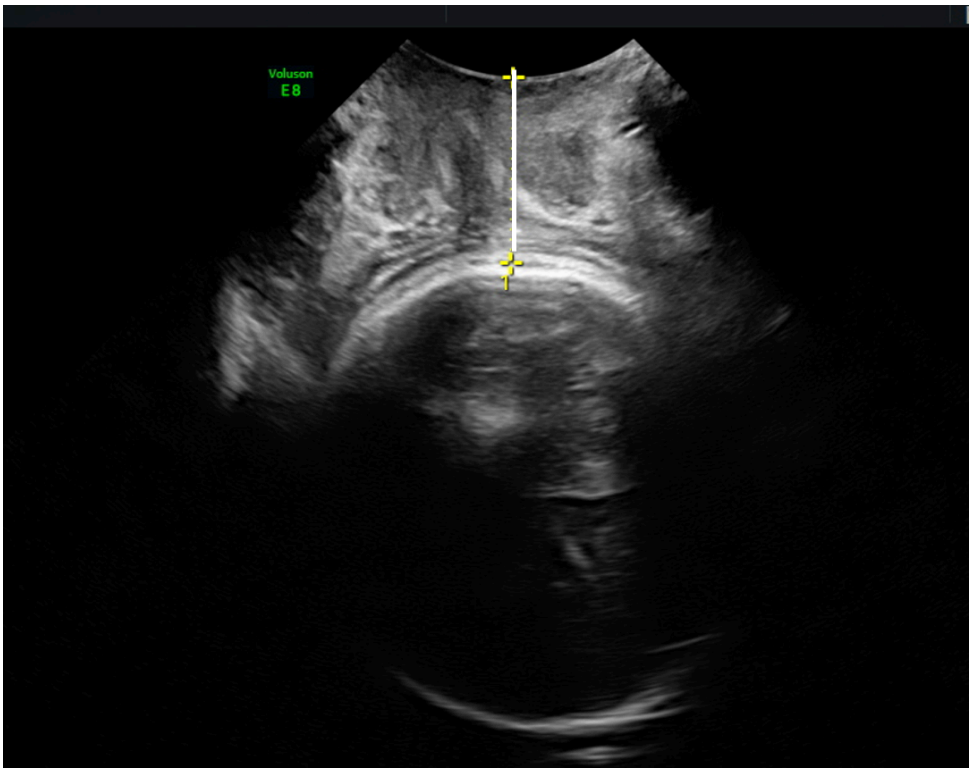

Figure 16 - Head perineum distance, unpublished image (Eggebø TM, 2015)

7.1.6 Intrapartum ultrasound in the second stage of labour

It is reported that failed operative deliveries are reported to occur in around 6% of vacuum extractions, and that factors affecting successful delivery without foetal and maternal complications rely on accurate assessments of foetal position and station, on operator skill[130, 131]. Furthermore, unsuccessful attempts at operative delivery and prolonged operative delivery are associated with adverse outcomes for mother and infant[64, 65, 132]. The Norwegian national guideline states that an attempted operative delivery should not exceed 20 minutes[49].

Intrapartum ultrasound as a prognostic tool has previously been investigated in the case of prolonged first stage of labour[117], but documentation on its potential use in the active second stage of labour is limited.

Ramphul et al. published a multicenter randomised controlled trial in 2014[133]. They investigated a cohort of 514 nulliparous women and compared ultrasound plus clinical assessment to clinical assessment alone before instrumental delivery. They found that ultrasound assessment prior to instrumental delivery reduced incorrect diagnosis of the foetal head position, but had no effect on maternal and neonatal complications, failed instrumental delivery, or CS rate.

This study did not consider the duration of operative delivery, and we wanted to explore the predictive value of ultrasound in this setting.

This formed the basis for the research outlined in Paper 4.

8. Classification systems – useful beyond comparing CS rates

8.1.1 How to avoid comparing apples to bananas

Hospitals and clinicians tend to compare their outcomes, and particularly, CS rate is a common such point of comparison. Rightly so, as it is considered an indicator of quality of care, although a precise ideal percentage has been abandoned in contemporary practice[134].

At a birth facility level, CS rates have traditionally been monitored using the percentage of CS across all deliveries. However, this single number is difficult to interpret, compare and use for implementing changes in practice because of differences between, for instance, primary and tertiary level hospitals, or characteristics of the birthing population.

There is substantial difference in risk of CS by factors such as parity, induction, foetal lie, multiple pregnancy etc., which called for a better system for comparison. Several such classification systems have been proposed and published:

8.1.2 Robson – or the Ten Group Classification System (TGCS)

In 2001, Michael Robson published a review paper named "Classification of cesarean section"[135]. In it he outlines a system for categorising different groups of labouring women into ten mutually exclusive groups. He argues that the principles for such classification systems have to be "simplicity, clinical relevance, total accountability, replicability, and verifiability". Robson derived his parameters from the following categories: Category of pregnancy, obstetric record, course of labour and gestational age. From the parameters in these categories, ten mutually exclusive groups of women emerge, see following paragraphs.

8.1.3 Other women-based systems

Robson was not the first to suggest women-based categories. Cleary et al. suggested using a standardised subgroup of the birthing population for comparison between units, namely Caucasian women, between 20 and 34 years old, above 155 cm in height, a singleton cephalic foetus >37 weeks, excluding cases with pre-existing diseases or pregnancy complications[136]. Although perhaps suited for a comparison between UK hospitals at the time, it is not applicable throughout the world, nor to compare groups of women within the same institution. Lieberman suggested a form of matrix-model, combining some of the women's characteristics and certain indications for CS[137]. There are also other women-based classification systems published after Robson's 2001 publication, such as Denk's eight group system from 2006[138], which is quite similar to Robson's.

8.1.4 Consolidation, evaluation and propagation by WHO

In a 2014 review paper, Betrán et al. compared 27 different classification systems in a scoring system using parameters such as ease, clarity, mutual exclusive groups, total inclusivity, reproducibility and implementability, concluding that women-based classifications in general and Robson's classification in particular, would best fulfil current needs to create an internationally useful CS classification system[139]. WHO issued a statement in 2016, where it proposed the Robson classification system as "a global standard for assessing, monitoring and comparing CS rates within healthcare facilities over time, and between facilities", and also issued an implementation manual[140].

The classification of groups and corresponding sub-groups is summarised in Table 3:

Table 3 - TGCS classification (Robson 2001)

1	Nulliparous women with a single, cephalic pregnancy, ≥ 37 weeks, spontaneous onset of labour.
2	Nulliparous women with a single, cephalic pregnancy, ≥ 37 weeks, induced labour or delivered by CS before labour.
2a	Labour induced.
2b	Pre-labour CS.
3	Parous women without previous CS, with a single, cephalic pregnancy, ≥ 37 weeks, spontaneous onset of labour.
4	Parous women without previous CS, with a single, cephalic pregnancy, ≥ 37 weeks, induced labour or delivered by CS before labour.
4a	Labour induced.
4b	Pre-labour CS.
5	All parous women with at least one previous CS, women with a single, cephalic pregnancy, ≥ 37 weeks.
5.1	With one previous CS.
5.2	With two or more previous CSs.
6	All nulliparous women with a single breech pregnancy.
7	All multiparous women with a single breech pregnancy, including women with previous CS(s).
8	All women with multiple pregnancy including women with previous CS(s).
9	All women with a single pregnancy with a transverse or oblique lie, including women with previous CS(s)
10	All women with a single cephalic pregnancy <37 weeks, including women with previous CS(s)

8.1.5 What's in a name? Robson Groups or Ten Group Classification System?

As it turns out, women-based classifications, unlike indication-based classification systems, have applications far beyond comparing CS rates between hospitals/institutions. It can be useful in comparing groups of labouring women, and we employed the system invented by Robson in three out of four papers in this thesis. Whether or not to use the eponym was discussed, and although there were arguments in favour of using the eponym, the name Ten Group Classification System (TGCS) provides a descriptive name which may be more accessible than using the "Robson classification".

8.1.6 Why did we employ a classification system in this research?

The focus of the research in this thesis may in some ways reflect a more inclusive version of Cleary's definition[136]. TGCS groups 1-4 are the most common groups in obstetrics, and, TGCS 1 and 3 are, for the lack of a better word, the most "normal", where the lowest percentage of intervention could or should be expected.

Breech (TGCS 6 - 7) is in Norwegian obstetrics considered a variation of normal, and the option of vaginal birth is offered/recommended if there are no contraindications. However, the CS rate is higher for TGCS 6-7 than in TGCS 1-4. Women with one previous CS (TGCS 5) are offered/recommended trial of labour after CS in Norway, but the CS rate is higher than in TGCS 1-4. Women with multiple pregnancy (TGCS 8) will often be managed differently than TGCS 1-4. Prematurely labouring women often have precipitious deliveries and women with a transverse/oblique lie which are not correctable by external cephalic version are routinely delivered by CS.

9. Aims of the studies

Overall aim: Investigate effects of maternal and iatrogenic factors on duration of phases of labour.

Paper 1: Compare the duration of active stage of labour in induced and spontaneously labouring women.

Paper 2: Explore the duration of the active second stage of labour in relation to BMI.

Paper 3: Investigate the effect of a protocol for more judicious use of oxytocin for prolonged labour on maternal, labour and foetal outcomes.

Paper 4: Assess whether ultrasound measurements of foetal station and position can predict duration of vacuum extraction, mode of delivery and outcomes for the foetus in nulliparous women with a prolonged active second stage of labour.

10. Ethical considerations

Paper 1, 2 and 3 were all based on cohort studies performed on de-identified data from the NATUS electronic birth journal. Attempting to individually seek consent to use the deidentified data of >20 000, or in the case of paper 2, >100 000, would have been futile. We find that the knowledge produced through the research and implications for care outweigh the possible negative implications of the research.

Paper 4 was based on an observational study using ultrasound in the active second stage of labour. Oral and written consent was obtained, and births with any signs of foetal distress were excluded. Having an ultrasound performed intrapartum is a sensitive issue, but we find that the benefits outweighed the risks posed to women and their children: the examination itself and a delay in operative delivery of 10-15 minutes.

All research was done in compliance with the Helsinki declaration, and were approved by the Regional committees for Medical and Health Research Ethics in Norway (REK).

Paper 1: REK 2014/1925

Paper 2: REK 2020/109526

Paper 3: REK 2014/1912

Paper 4: REK vest 2012/1865, 3348/ 2013 in Italy, Research Ethics Committee 15/LO/1341, project identification 169478 in the UK, Number 2012/808 in Sweden; and H-4-2014-038 in Denmark.

11. Study design, materials and methods

11.1 Paper 1 – Duration of labour in spontaneous and induced labours

11.1.1 Study design and materials

Paper 1 was an observational cohort study comparing estimated duration of labour in spontaneously labouring women with induced labours. We based our analyses on the NATUS electronic birth journal at Stavanger University Hospital, using data from January 2010 to December 2013. During this time, 19.524 women delivered, of which 16.660 were in TGCS groups 1-4. For inclusions and exclusions, see flow chart (Figure 17).

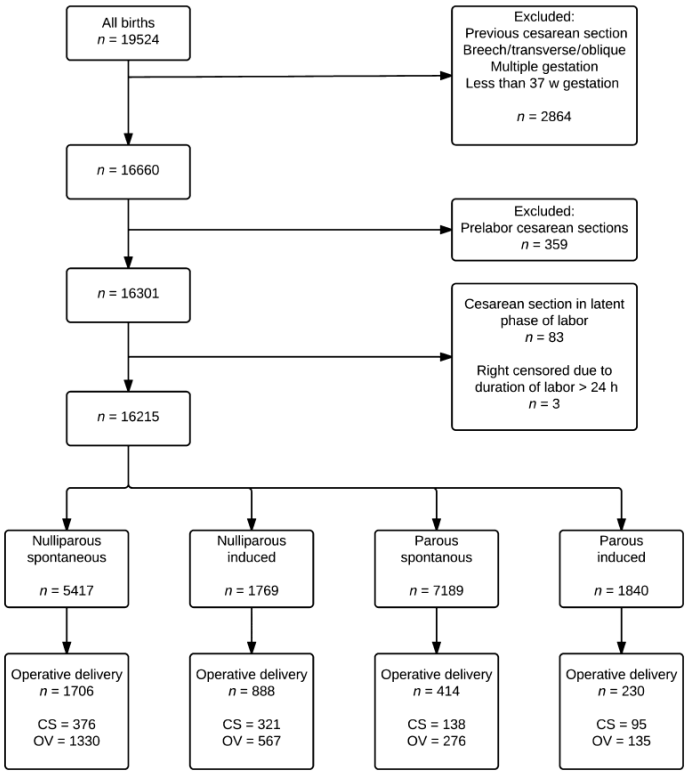

Figure 17 - Flow chart of the study population (Østborg, 2016)

Start of active labour was defined as effaced cervix, with four cm dilation and regular contractions, as per the WHO recommendation in the study period, for both nulliparous and parous women. In women admitted in active labour, the midwife estimated the start of labour based on clinical findings upon admission and the woman's report of onset of regular and painful contractions.

Estimated due date was determined by a second trimester ultrasound scan with measurement of biparietal diameter or femur length (eSnurra)[141], or, in rare cases, from last menstrual period when no ultrasound was available. Induction of labour was categorised into post-term pregnancies, hypertensive disorders, prelabour rupture of membranes, maternal request, or others. One week post term, women were evaluated with cardiotocography (CTG) and ultrasound, and induction would be considered. In the case of prelabour rupture of membranes, induction was routinely performed if labour did not ensue spontaneously within 24 hours.

Method of induction was determined according to Bishop score[142]: In women with a Bishop score <6, misoprostol was used as an induction agent, 25µg vaginally every 4 hours, up to a maximum dose of 100µg daily, over a maximum of two days, or until Bishop score ≥6. In women with Bishop score ≥6, amniotomy was performed with a single use AmniHook, and oxytocin was added after four hours unless labour ensued. Failure of induction was concluded if amniotomy was considered impossible or unsafe after a full regimen of misoprostol, or if oxytocin administered up to 40mU/minute failed to bring the patient into active labour.

During labour, progress was monitored with a partograph with an alert line (1cm/hour) and action line displaced by four hours, as per WHO recommendation in the study period. Prolonged labour was defined as crossing the action line, and oxytocin in the first stage was only started in the setting of prolonged labour. Artificial rupture of membranes was not routinely performed, but always before administration of oxytocin. During the second stage of labour, oxytocin could be

administered at the discretion of the birth attendant if contractions or progress were deemed insufficient.

Oxytocin was administered as an infusion of 5 international units (IU) of oxytocin in 500ml solution, and the starting rate was 6mIU/minute with dose increments of 3mIU/min every 15 minutes to a maximum of 40mIU/minute, until progress of labour or 3-5 regular contractions per 10 minutes was achieved. A combination low dose ropivacaine/fentanyl was routinely used for epidural anaesthesia, spinal anaesthesia was rarely used.

Operative delivery was considered after 60 minutes of active pushing, regardless of parity or anaesthesia, as recommended in national guidelines.

11.1.2 Statistical considerations and methods

We used chi-square test to compare categorical variables, and Mann-Whitney U-tests to compare continuous variables. The duration of the active phase of labour was estimated using survival analyses. Births with missing information about the the start of active phase of labour or CS in the latent phase were left-censored. Births with active phase of labour > 24 hours or an operative delivery were right-censored.

Comparison was done between TGCS 1 and 2a, and TGCS 3 with 4a. One minus survival plots were created, and the groups were compared using the log rank test. In multivariate Cox regression analyses, maternal age, BMI, gestational age and birthweight >4000g were included as possible confounders. We performed competing risk regression on the survival data according to the method of Fine and Gray[143] in order to evaluate the potential impact from the competing event of operative deliveries.

Amniotomy, oxytocin augmentation and epidural analgesia were initiated after the start of active phase of labour and therefore considered mediators rather than confounders, and therefore not included in the regression analysis. P-values <0.05 were considered significant.

11.2 Paper 2 - Put your weight behind it – effect of BMI on the active second stage of labour: A retrospective cohort study.

11.2.1 Study design and materials

Paper 2 was an observational cohort study comparing the estimated duration of the active second stage of spontaneously labouring women by BMI groups.

The analyses were performed on data from consolidated NATUS datasets from three Norwegian University hospitals: Stavanger University Hospital, Bergen University Hospital (Haukeland sjukehus) and Trondheim University Hospital (St. Olavs Hospital).

Data was extracted from January 2012 through December 2019. During this time, 109 989 women delivered, of which 50.771 were in TGCS groups 1 and 3. For inclusions, exclusions, and remaining cases available for analysis, see flow chart (Figure 18). Pre-pregnant BMI was missing in 18.192 cases, and upon excluding patients with missing information about the duration of the second stage, left-censoring women with CS before the second stage, and right-censoring women with active second stages of ≥120 minutes, we were left with n=21.783 women in TGCS 1 and n=26.159 in TGCS 3 available for survival analyses (Figure 18).

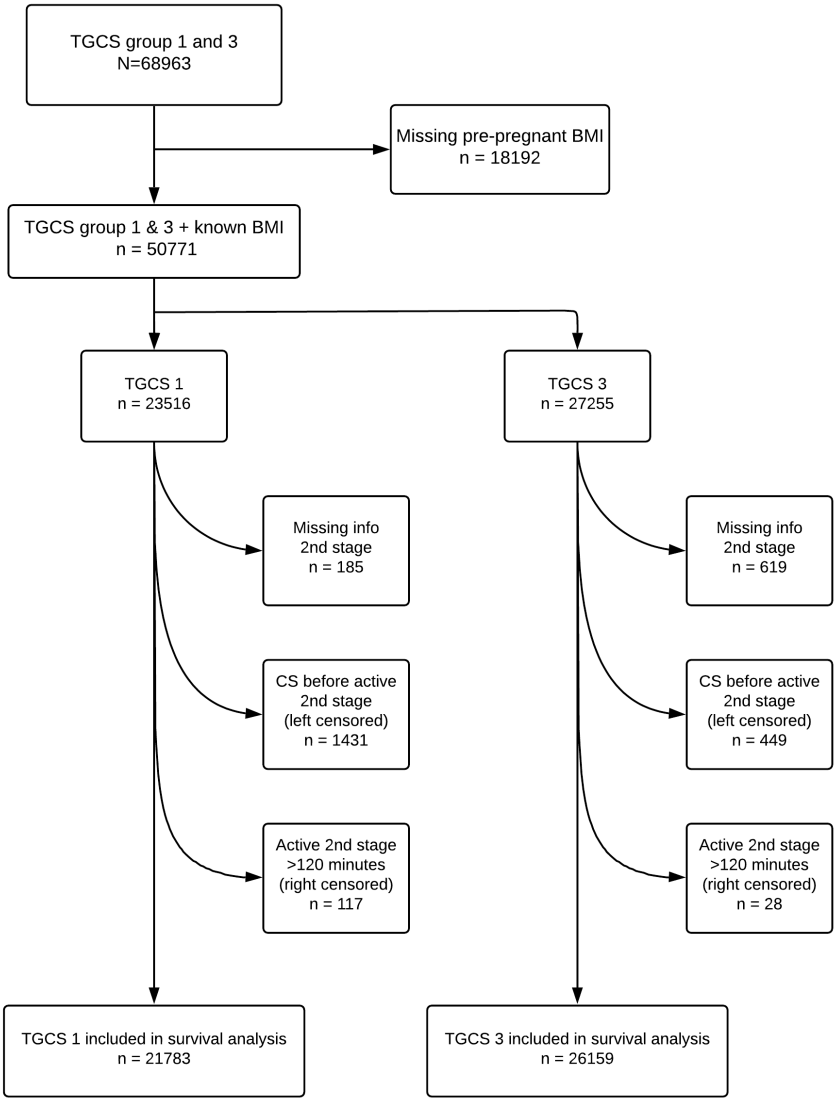

Figure 18 - Flow chart illustrating the study population (Østborg et al. 2022)

The women were stratified into BMI groups according to the WHO classification. Pre-pregnant BMI <18.5 was categorised as underweight, BMI 18.5-24.9 as normal weight, BMI 25.0-29.9 as overweight, BMI 30.0-34.9 as obesity class one, BMI 35.0-

39.9 as obesity class two and BMI ≥40.0 as obesity class three. The main outcome measure was the estimated median duration of the active second stage of labour.

The start of the first stage of labour was defined according to the former WHO classification[9] during the study period as an effaced cervix, regular contractions and four cm dilatation. The second stage was defined when the woman had a fully dilated cervix, and the active second stage was defined as the time from active expulsive effort started until the delivery of the foetus.

Monitoring of labour progress, guidelines for artificial rupture of membranes, indication for start of oxytocin augmentation and dosage/dose increments, epidural use, as well as indication for operative delivery in the second stage were the same as in Paper 1.

11.2.2 Statistical considerations and methods

The associations between maternal age, epidural analgesia and oxytocin augmentation on BMI and the duration of the active second stage are illustrated in a directed acyclic graph (Figure 19).

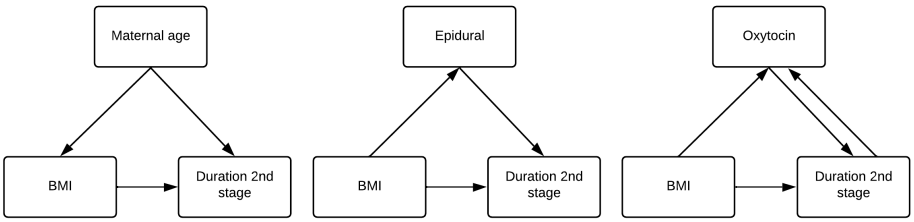

Figure 19 - Directed acyclic graph (DAG) illustrating how maternal age, epidural analgesia and oxytocin augmentation (Østborg et al., 2022)

Maternal age is the only confounder with effect on both the independent and dependent variables. The causal associations are different for epidural analgesia and oxytocin augmentation. High BMI may be associated with higher frequencies of epidural analgesia and more use of oxytocin augmentation. Slow progress is an

indication of oxytocin augmentation, but oxytocin may also lead to a shorter active second stage.

The duration of the active phase of the second stage of labour was examined using survival methods. TGCS group 1 and 3 were analysed separately. Median duration with interquartile range was estimated using Kaplan-Meier methods. We considered oxytocin augmentation and epidural analgesia to be mediators, and stratified the analyses of estimated median duration in women with and without epidural analgesia and with and without oxytocin augmentation. One minus survival plots were created from Cox regression analyses and stratified into BMI groups.

11.3 Paper 3 - Judicious use of oxytocin augmentation for the management of prolonged labour

11.3.1 Study design and materials

Paper 3 was an observational cohort study comparing outcomes before and after the implementation of a protocol for use of oxytocin augmentation in the first stage of labour. The analyses were based on data from the NATUS structured birth journal at Stavanger University Hospital, from January 2009 to December 2013.

In 2009, the WHO partograph was introduced for routine use, and start of the active phase of labour was defined upon regular contractions and an effaced cervix dilated to four cm. At this point, a clear definition of prolonged labour did not exist in the department, and oxytocin augmentation could be started at the discretion of the birth attendant, when the birth attendant felt that the labour was progressing slowly.

On 1st of January 2010 a protocol for judicious use of oxytocin was implemented in the department. Prolonged labour in the first stage was defined when cervical dilation crossed the 4-hour action line, and oxytocin could only be administered in the first stage when a diagnosis of prolonged labour had been made.

Analyses aimed to compare outcomes in the period before and after the implementation of the judicious protocol for oxytocin augmentation. The main outcome variable was the frequency of intrapartum CS. Secondary outcomes were use of oxytocin augmentation, intrapartum CS due to foetal distress or dystocia, operative vaginal delivery, sphincter rupture, estimated postpartum haemorrhage >1000 mL, duration of labour >12 hours, Apgar score <7 at five minutes, umbilical cord arterial pH <7.00, and umbilical cord arterial pH <7.10.

Estimated due date, indication and methods of induction, type of epidural analgesia, time until consideration of operative delivery in the second stage (>60 minutes) were the same as described in Paper 1 and 2.

The dosage and dosage increments and times for oxytocin augmentation in the judicious protocol implemented January 1st 2010 is equal to the protocol described in Paper 1.

Routinely, the third stage of labour was actively managed, and 5IU of oxytocin administered. Blood loss was visually estimated, and blood-soaked compresses collected and weighed when possible. Estimated blood loss >1000 mL was defined as severe postpartum haemorrhage. Obstetric anal sphincter injury was defined as partial or complete tear of the anal sphincter muscle (3rd and 4th degree tears).

11.3.2 Statistical considerations and methods

The linear-by-linear association trend test was used in categorical data analyses, and continuous variables were compared using one-way analysis of variance with Bonferroni correction. P-values <0.05 were considered significant.

11.4 Paper 4 - Sonographic prediction of outcome of vacuum deliveries: a multicenter, prospective cohort study

11.4.1 Study design and materials

Paper 4 was a prospective cohort study of nulliparous women at term with prolonged second stage of labour. The study was an international multicenter study in seven European maternity units. Women eligible for inclusion were nulliparous women with a live singleton foetus in cephalic presentation, gestational age ≥37 and <42 weeks. The second stage of labour was differentiated into a passive stage <2 hours, and an active stage with active expulsive effort. Women were included and examined once with ultrasound upon diagnosis of prolonged second stage of labour. This was defined as ≥45 minutes of pushing and vacuum extraction was considered a potential treatment option. Exclusion criteria was suspicion of foetal compromise due to non-reassuring cardiotocography (CTG).

The transperineal measurements were done between contractions, and all ultrasound measurements were done online 2-dimensionally in the labour room. The woman and the birth attendant were blinded to ultrasound results. The ultrasound operator was not involved in clinical decisions or management of labour.

11.4.2 Ultrasound methods

Transabdominal scan.

Foetal head position was categorised into occiput anterior (OA) position or non-OA position (posterior or transverse position). The position was described as a clock face

with 12 hourly divisions; positions: ≥ 10 o'clock and ≤ 2 o'clock were classified as OA (Figure 20).

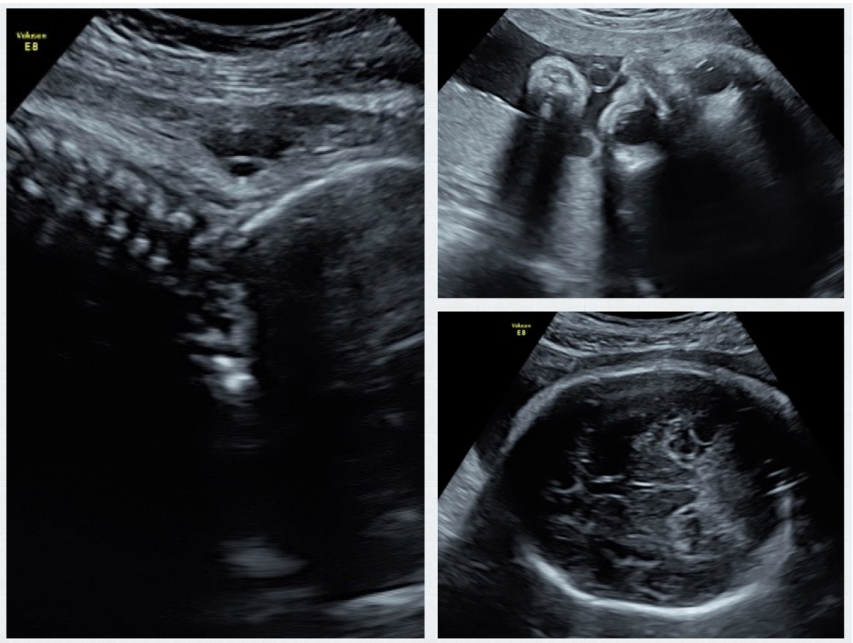

Figure 20 - Left, Sagittal scan, occiput anterior. Top right: Transverse scan, occiput posterior position, bottom right: Transverse scan, transverse position. (Kahrs et al. 2018)

Transperineal scan

A transperineal scan was used to measure the angle of progression and the head-perineum distance.

Angle of progression was measured in the sagittal plane as the angle between the longitudinal axis of the pubic bone and a line joining the lowest edge of the pubis to the lowest convexity of the foetal skull (Figure 21, left panel)

Head-perineum distance was measured in a transverse transperineal scan (in the axial plane) as the shortest distance from the outer bony limit of the foetal skull to perineum (Figure 21, right panel)

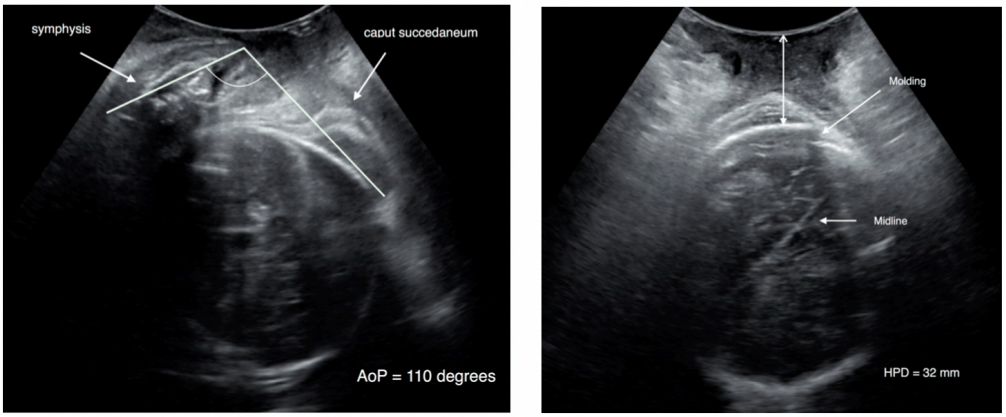

Figure 21 - Left: Sagittal transperineal image illustrating measurement of angle of progression. Right: Transverse transperineal image illustrating measurement of head-perineum distance (double arrow). Head midline and molding are seen. (Kahrs et al. 2018)

Technical equipment

A metal vacuum cup was the preferred device used in Stavanger and Trondheim, Norway; Lund, Sweden; London, UK; and Copenhagen, Denmark. In Bologna and Parma, Italy, a Kiwi OmniCup was used. BMI was calculated from maternal height and prepregnant weight. Cord blood was obtained by direct puncture of the umbilical artery without clamping of the cord. Umbilical artery pH <7.10 was used as the cut-off level. The main outcome measure was duration of vacuum extractions. Secondary outcomes were frequencies of spontaneous deliveries, vacuum extractions, cesarean deliveries, and umbilical artery blood samples after birth (pH and base excess).

11.4.3 Statistical considerations and methods

Choice of main outcome measure

Prolonged attempts at operative vaginal delivery are associated with adverse outcomes, and was chosen as a main outcome for both reasons of feasibility and clinical relevance. Failed operative vaginal delivery is a relatively rare event, and was

for this reason not chosen as the main outcome, as achieving a large enough study population seemed futile.

Power analysis

Our preliminary clinical experience assessing head-perineum distance prior to vacuum delivery suggested that we should set 25 mm for the power calculation, a level corresponding approximately to +2 ACOG classification. The main outcome of the study was the duration of vacuum extraction. The main predictor variable was head-perineum distance with a predefined cut-off at 25mm to discriminate between the groups. To identify a hazard ratio as low as 1.5 with 80% power, 2-sided test, with alpha 5%, one third of the women with distance >25 mm and two thirds with distance 25mm, we determined that 220 women should be included when expecting 10% censoring.

Statistical methods

Variables were compared using chi square test and linear regression. To evaluate differences in the time interval from start of vacuum extraction to complete delivery according to head-perineum distance and angle of progression, we used Kaplan-Meier methods and Cox regression analyses. The Kaplan-Meier method was used to generate survival plots, and we used head-perineum distance 25 mm as cut-off value in accordance with the power analysis. Cox regression was used to calculate hazard ratio as an estimate for relative risk of delivery. Women with a spontaneous vaginal delivery were not included in the survival analyses and cesarean deliveries were censored at the time of the decision to perform a caesarean delivery.

The association between head-perineum distance and delivery mode was analysed at five different cut-off levels: ≤20, 21-25, 26-30, 31-35, >35. In a previous study 36 mm was found to correspond to station 0 by clinical examinations[129]. Therefore, we focused on 35mm as the cut-off level and present test characteristics related to this level. The association between angle of progression and delivery mode was analysed

at cutoff levels: <120, 120-129, 130-139, 140-149, ≥150 degrees. The associations between spontaneous and caesarean delivery related to head-perineum distance and angle of progression as continuous variables were evaluated using receiver operating characteristic (ROC) curves.

The area under the curve was considered to have discriminatory potential if the lower limit of the confidence interval was >0.5. P <.05 was considered statistically significant.

12. Results

12.1 Paper 1

Out of the 19 524 women who gave birth during the study period, 16 660 (85.3%) were in TGCS 1-4, and 359 (2.2%) of these were excluded from the study due to prelabour CS (TGCS 2a and 4a). Fifty-three women were left-censored due to lack of information about the start of the active phase of labour, and thirty due to CS in the latent phase of labour. Three women were right-censored due to a labour duration recorded as more than 24 hours, and 3238 were right-censored due to operative deliveries.

When comparing the groups, we found that the women in the induction groups differed from their spontaneously labouring counterparts in the following aspects: They were older, had higher BMI and higher gestational age. The induced births were more often augmented, had a higher frequency of epidural analgesia, and the babies had higher birth weight. The rates of operative vaginal delivery and CS were higher in the induction groups. For a summary and comparison of groups in the study population, see Table 4.

Table 4 - Characteristics of the study population. (Østborg et al. 2016)

	TGCS 1 n = 5424	*TGCS 2a n = 1778*	*p-value*	*TGCS 3 n = 7205*	*TGCS 4a n = 1846*	*p-value*
Characteristics related to the mother						
Maternal age (years)	27 (7)	28 (7)	< 0.01	31 (6)	32 (6)	< 0.01
Pre-pregnant BMI (weight/m^2)	22.3 (4.4)	23.6 (5.9)	< 0.01	23.0 (4.7)	24.0 (6.3)	< 0.01
Gestational age (weeks)	283 (10)	287 (14)	< 0.01	282 (9)	283 (18)	< 0.01
Characteristics related to labour						
Delivery method						
Spontaneous	68.5%	49.5%	< 0.01	94.1%	87.2%	< 0.01
Operative vaginal	24.5%	31.9%	< 0.01	3.8%	7.3%	< 0.01
CS	7 %	18.6%	< 0.01	2.1%	5.5%	< 0.01
Augmentation	32.9%	62.5%	< 0.01	6.4%	37.2%	< 0.01
Epidural anaesthesia	43.3%	70.5%	< 0.01	19.0%	44.4%	< 0.01
Characteristics of the newborn						
Birth weight (g)	3450 (570)	3525 (675)	< 0.01	3618 (595)	3700 (710)	< 0.01
Head circumference (cm)	35 (2)	36 (2)	< 0.01	35 (2)	36 (2)	< 0.01

The p-values from Mann-Whitney U-test or chi-squared test. Values are means or median with interquartile range given in parentheses or percentages.

The median duration of the active phase of labour in nulliparous women with spontaneous start was 368 minutes, whereas in nulliparous induced women it was 355 minutes. The corresponding durations in parous women were 165 and 135 minutes, respectively.

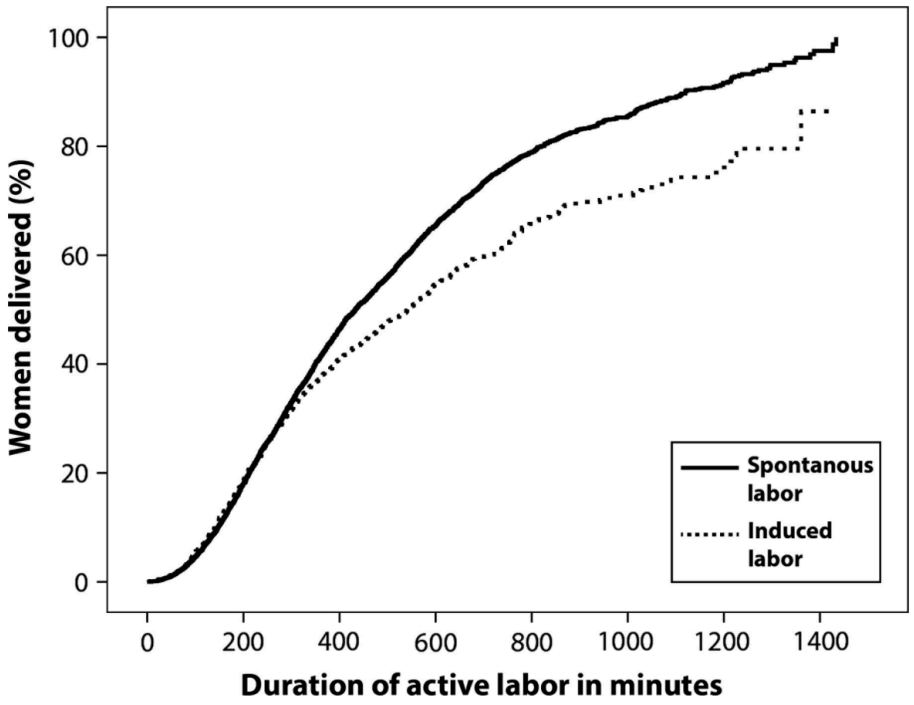

Figure 22 - Kaplan–Meier plot (1-survival) illustrating duration of active phase of labour in nulliparous women. (Østborg et al. 2016)

The estimated median duration active phase was longer in all groups when using Kaplan-Meier analyses. In spontaneously labouring nulliparous women, the estimated median duration was 433 minutes (95% CI 419–446) versus 541 minutes (95% CI 502–580) in induced labour. In parous women the corresponding values were 168 minutes (95% CI 164–172) in women with spontaneous start and 142 minutes (95% CI 135–149) in women with induced labour. One minus survival plots for nulliparous women with spontaneous and induced labours ($p < 0.01$; log rank test) are illustrated in Figure 22. After 12 hours in active labour 12.6% (95% CI 11.8–13.5%) remained undelivered among nulliparous women with spontaneous onset vs. 13.4% (95% CI 11.9–15.1%) in nulliparous women with induced labour.

The active phase of labour was significantly longer in spontaneous than induced labours in parous women as illustrated in Figure 23 ($p = 0.02$, log rank test), however the lines were crossing. Until six hours of active labour, induced labours had shorter

duration, but after six hours, induced labours lasted longer. Figure 23 illustrates the difference, however the numeric differences between the groups did not differ substanatially nor did they differ in any clinically relevant manner. In spontaneously labouring women, 2.4% (95% CI 2.1–2.8%) were undelivered after 12 hours, vs 3.7% (95% CI 3.0–4.4%) in women undergoing induction.

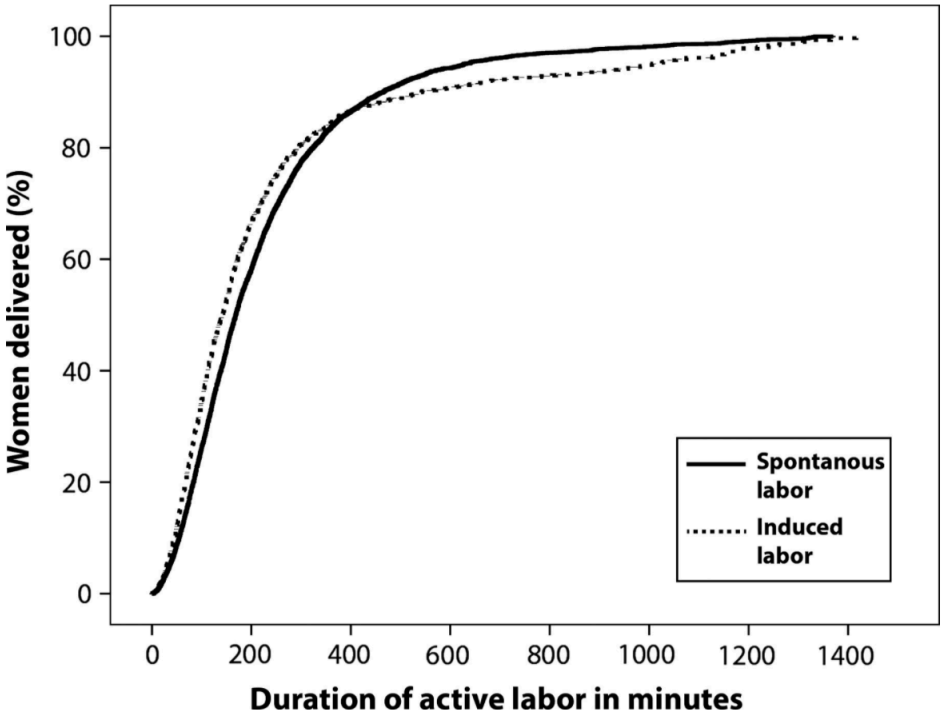

Figure 23 - Kaplan–Meier plot (1-survival) illustrating duration of active phase of labour in parous women. (Østborg et al. 2016)

When applying Cox regression analysis, the duration of the active phase of labour in nulliparous women was longer in induced labours than in spontaneous labours. The unadjusted hazard ratio was 0.76 (95% CI 0.71–0.82) for induced labours compared to spontaneous labours.

Increasing BMI, maternal age and gestational age, as well as birth weight >4000 grams were all factors associated with a longer duration of the active phase of labour.

When adjusting for these factors, the hazard ratio for duration of the active phase of labour in induced compared with spontaneous labours was 0.88 (95% CI 0.82–0.95) Details of these analyses are presented in Table 5. We performed a competing risk regression analysis that incorporated the competing event of operative deliveries. In this analysis, the adjusted hazard ratio for delivery was 0.74 (95% CI 0.68–0.80) for induced labours vs. spontaneous labours. As the data violated the proportional hazard assumption in parous women, we refrained from performing Cox regression analyses on these data.

Table 5 - Hazard ratio for duration of active phase of labour in nulliparous women. (Østborg et al. 2016)

	Unadjusted values		Adjusted values	
	HR	95% CI	HR	95% CI
Spontaneous labours	1.0		1.0	
Induced labours	0.76	0.71–0.82	0.88	0.82–0.95
Maternal age	0.96	0.96–0.97	0.97	0.96–0.97
BMI	0.97	0.97–0.98	0.99	0.98–0.99
Gestational age	0.97	0.97–0.98	0.98	0.97–0.98
Birthweight >4000 g	0.54	0.49–0.60	0.64	0.57–0.71

One minus survival plot from the study population differentiated into operative and spontaneous vaginal deliveries is presented in Figure 24. The duration was significantly longer in operative deliveries. Induced labours were differentiated into indications of induction and results presented as one minus survival plots for nulliparous women in Figure 25 and parous women in Figure 26. Labour duration was shorter in nulliparous women with induced labours due to prelabour rupture of

membranes, but showed no significant difference between other indications. In parous women the indication of induction had a minor effect on labour duration.

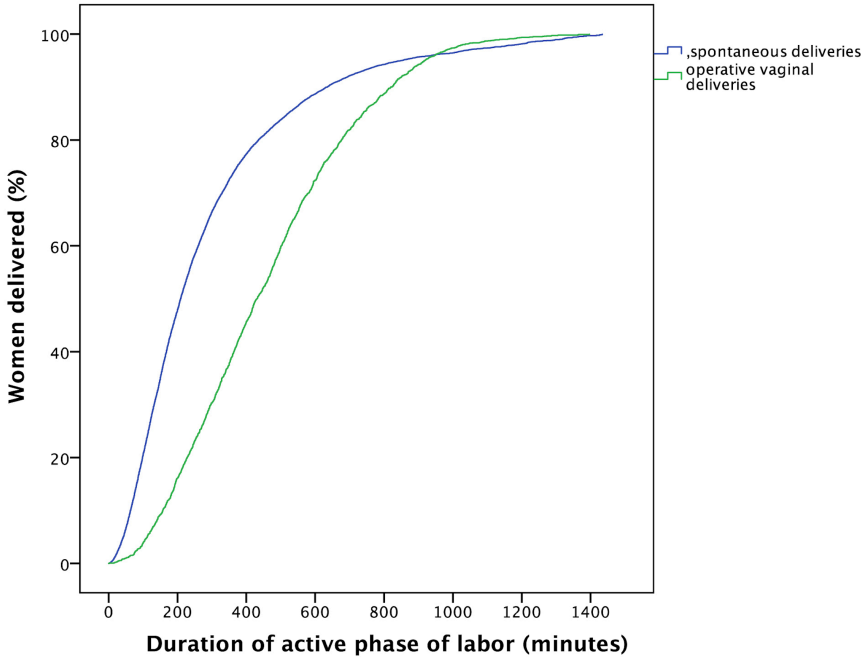

Figure 24 - Kaplan–Meier plot (1-survival) comparing duration of active phase of labour in spontaneous and operative deliveries, total study population. (Østborg et al. 2016)

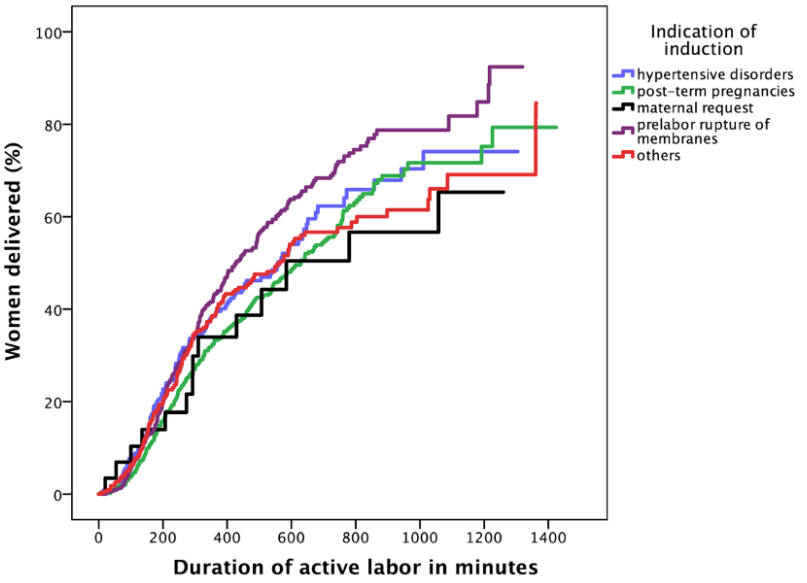

Figure 25 - Kaplan–Meier plot (1-survival) illustrating duration of active phase of labour in nulliparous women with induced labour differentiated by indication for induction. (Østborg et al. 2016)

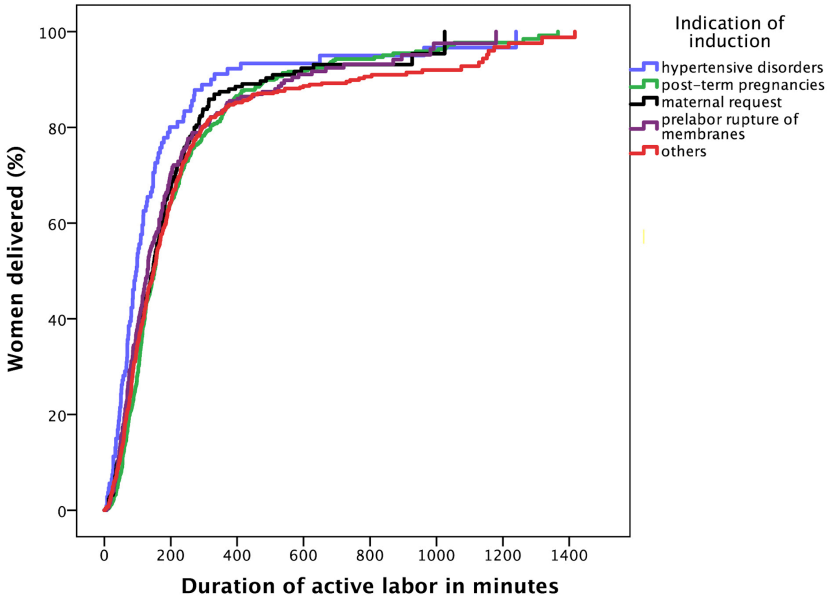

Figure 26 - Kaplan-Meier plot (1-survival) illustrating duration of active phase of labor in parous women with induced labour differentiated by indication for induction. (Østborg et al. 2016)

12.2 Paper 2

After inclusion, exclusions and censoring as described in materials and methods, we had 21.783 women in TGCS 1 and 26.159 women in TGCS 3 available for analysis. Maternal, labour and newborn characteristics are presented for TGCS 1 in Table 6 and TGCS 3 in Table 7.

Table 6 - Maternal, labour and newborn characteristics, TGCS 1 (Østborg et al. 2022)

	BMI < 18.5 Underweight	BMI 18.5 - 24.9 Normal weight	BMI 25.0 - 29.9 Overweight	BMI 30.0 - 34.9 Obesity Class I	BMI 35.0 - 39.9 Obesity Class II	BMI ≥ 40.0 Obesity Class III
TGCS 1 n = 23516	1169 (5.0)	16039 (68.2)	4454 (18.9)	1368 (5.8)	360 (1.5)	126 (0.5)
Maternal age	27.2 (4.5)	28.7 (4.4)	28.6 (4.7)	28.5 (4.7)	27.9 (4.5)	28.2 (4.9)
Birthweight	3330 (426)	3480 (426)	3576 (438)	3583 (465)	3606 (476)	3604 (472)
Caucasian	726 (62.1)	11943 (74.5)	3621 (81.3)	1166 (85.2)	317 (88.1)	105 (83.3)
Oxytocin augmentation	384 (32.8)	5978 (37.3)	1857 (41.7)	583 (42.6)	16(2 45.0)	64 (50.8)
Epidural analgesia	551 (47.1)	8152 (50.8)	2603 (58.4)	882 (64.5)	253 (70.3)	100 (79.4)
Spontaneous vaginal delivery	840 (71.9)	11287 (70.4)	2966 (66.6)	909 (66.4)	250 (69.4)	85 (67.5)
Instrumental vaginal delivery	274 (23.4)	3664 (22.8)	1032 (23.2)	289 (21.1)	61 (16.9)	25 (19.8)
Intrapartum CS	55 (4.7)	1088 (6.8)	456 (10.2)	170 (12.4)	49 (13.6)	16 (12.7)
CS during active second stage	9 (0.8)	255 (1.6)	95 (2.1)	33 (2.4)	10 (2.8)	1 (0.8)

Values are mean (standard deviation) or n(%).

Table 7 - Maternal, labour and newborn characteristics, TGCS 3 (Østborg et al. 2022)

	BMI < 18.5 Underweight	BMI 18.5 - 24.9 Normal weight	BMI 25.0 - 29.9 Overweight	BMI 30.0 - 34.9 Obesity Class I	BMI 35.0 - 39.9 Obesity Class II	BMI ≥ 40.0 Obesity Class III
TGCS 3 n = 27255	1129 (4.1)	17617 (64.6)	5927 (21.7)	1910 (7.0)	490 (1.8)	182 (0.7)
Maternal age	30.5 (4.4)	31.7 (4.3)	31.7 (4.5)	31.3 (4.7)	31.3 (4.9)	31.3 (4.9)
Birthweight	3446 (432)	3622 (442)	3719 (455)	3761 (492)	3766 (442)	3802 (494)
Caucasian	835 (74.0)	14053 (79.8)	4674 (78.9)	1584 (82.9)	408 (83.3)	162 (89.0)
Oxytocin augmentation	55 (4.9)	1141 (6.5)	460 (7.8)	201 (10.5)	57 (11.6)	27 (14.8)
Epidural analgesia	227 (20.1)	3782 (21.5)	1400 (23.6)	607 (31.8)	179 (36.5)	96 (52.7)
Spontaneous vaginal delivery	1090 (96.5)	16792 (95.3)	5616 (94.8)	1787 (93.6)	457 (93.3)	170 (93.4)
Instrumental vaginal delivery	25 (2.2)	537 (3.0)	184 (3.1)	58 (3.0)	18 (3.7)	5 (2.7)
Intrapartum CS	14 (1.2)	288 (1.6)	127 (2.1)	65 (3.4)	15 (3.1)	7 (3.8)
Caeserean during active second stage	1 (0.1)	44 (0.2)	14 (0.2)	6 (0.3)	2 (0.4)	0 (0)

Values are mean (standard deviation) or n(%).

We found that shorter estimated median duration of the active phase of the second stage was associated with higher BMI in both TGCS groups. In TGCS group 1, the estimated median durations (interquartile range) were 44(26-75), 43(25-71), 39(22-70), 33(18-63), 34(19-54) and 29(16-56) minutes in BMI groups 1 to 6, respectively. In the TGCS group 3, the corresponding values were 11(6-19), 10(6-17), 10(6-16), 9(5-15), 8(5-13) and 7(4-11) minutes, as shown in Table 8 and 9.

Table 8 - Estimated median duration of active second stage in minutes (interquartile range) in TGCS 1 using Kaplan-Meier method. (Østborg et al. 2022)

TGCS group 1	n	Overall	Epidural -	Epidural +	Oxytocin -	Oxytocin +
BMI < 18.5 Underweight	1102	44 (26-75)	37 (22-63)	55 (32-84)	34 (22-54)	76 (51-98)
BMI 18.5 - 24.9 Normal weight	14997	43 (25-71)	35 (21-58)	54 (31-84)	34 (20-53)	68 (43-98)
BMI 25 - 29.9 Overweight	4042	39 (22-70)	30 (17-54)	49 (26-82)	29 (17-48)	65 (37-97)
BMI 30 -34.9 Obesity Class I	1214	33 (18-63)	24 (14-44)	43 (22-78)	25 (15-44)	61 (30-93)
BMI 35 - 39.9 Obesity Class II	319	34 (19-54)	25 (18-48)	39 (21-63)	25 (17-45)	46 (30-80)
BMI ≥ 40 Obesity Class III	109	29 (16-56)	19 (15-37)	32 (17-56)	21 (15-38)	38 (19-77)

Table 9 - Estimated median duration of active pushing phase in minutes (interquartile range) in TGCS group 3. (Østborg et al. 2022)

TGCS group 3	n	Overall	Epidural -	Epidural +	Oxytocin -	Oxytocin +
BMI < 18.5 Underweight	1076	11 (6-19)	10 (6-17)	15 (9-28)	11 (6-18)	41 (20-74)
BMI 18.5 - 24.9 Normal weight	16975	10 (6-17)	10 (6-15)	14 (8-25)	10 (6-16)	25 (13-55)
BMI 25 - 29.9 Overweight	5668	10 (6-16)	9 (5-14)	12 (8-22)	9 (5-15)	19 (10-42)
BMI 30 -34.9 Obesity Class I	1808	9 (5-15)	8 (5-13)	11 (7-20)	8 (5-14)	16 (8-32)
BMI 35 - 39.9 Obesity Class II	460	8 (5-13)	8 (4-12)	9 (5-15)	8 (4-12)	15 (8-51)
BMI ≥ 40 Obesity Class III	172	7 (4-11)	7 (4-10)	7 (4-13)	7 (4-11)	6 (4-17)

Figure 27 and 28 show the probability of delivery in accordance with duration of the active phase illustrated as one minus survival plots in nulliparous and parous women respectively.

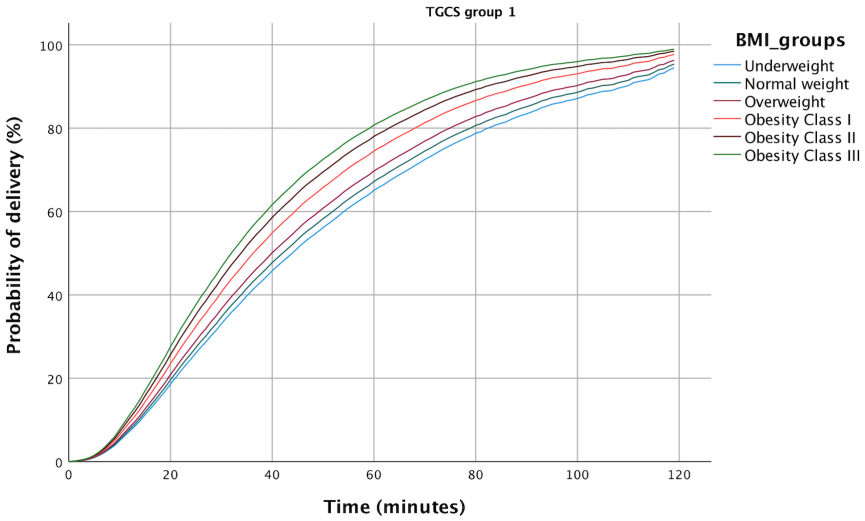

Figure 27 - One-minus survival plots showing probability of delivery during active second stage differentiated into BMI groups for TGCS group 1. (Østborg et al. 2022)

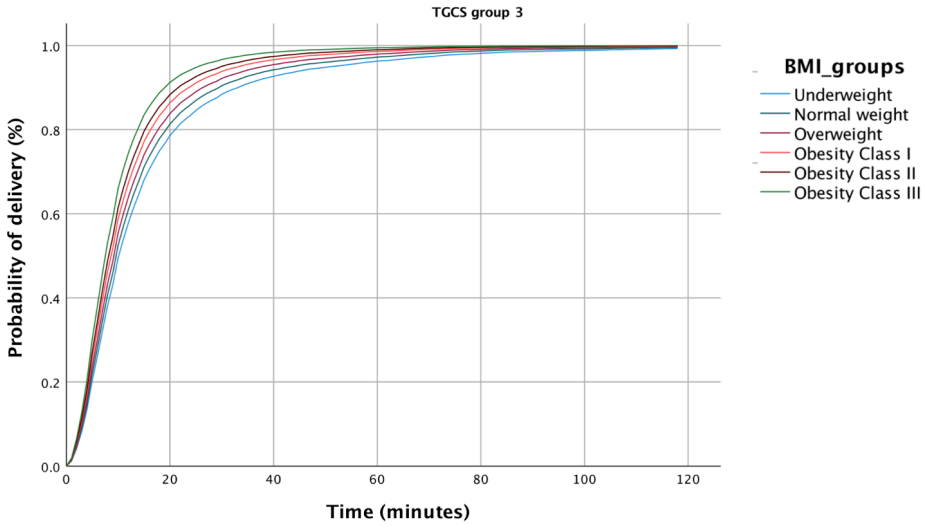

Figure 28 - One-minus survival plots showing probability of delivery during active second stage differentiated into BMI groups for TGCS group 3

In TGCS group 1 the overall estimated median duration was 42 (95% CI 41.5–42.5) minutes in women with known BMI vs. 40 (95% CI 39.2–40.8) minutes in women with missing information about BMI. Corresponding values in TGCS group 3 were 10 (95% CI 9.9–10.1) minutes vs 11 (95% CI 10.9–11.1) minutes.

12.3 Paper 3

In total, 24.134 women delivered at the hospital during the study period, out of which the study population (TGCS 1, 2a, 3 and 4a) comprised 20.277 women. Of these 6897 (28.6%) were nulliparous with spontaneous onset of labour (TGCS group 1), 2144 (8.9%) were nulliparous with induced labour (TGCS group 2a), 8967 (37.2%) were parous with spontaneous onset of labour (TGCS group 3), and 2219 (9.2%) were parous with induced labour (TGCS group 4a). The overall CS rate was 13.8%, of which 5.0% were pre-labour CS and 8.8% were intrapartum CS. The characteristics of the study population are presented in Table 10.

Table 10 - Characteristics of the study population (n = 20 227) from 2009 to 2013. (Rossen et al. 2015)

Year	2009	2010	2011	2012	2013	p-value
n	3926	4144	4113	4091	3953	
Nulliparous women (%)	46.1	44.7	45.0	43.8	44.0	0.04[a]
Maternal age (years)	29.6	29.8	29.6	29.9	30.0	<0.01[b]
Gestational age (days)	282.0	281. 9	281.5	281.4	281.3	<0.01[b]
BMI (kg/m2)	23.9	24.0	23.8	23.8	23.7	0.07[b]
Infant birth weight (g)	3567	3572	3569	3557	3578	0.30[b]
Induction of labour (%)	18.6	18.9	21.4	24.0	24.9	<0.01[a]

[a]Linear trend analyses
[b]One-way ANOVA.

The mean maternal age had a rising trend throughout the study period ($p < 0.01$) and the mean gestational age was lower in 2012 and 2013 than in 2009, 2010 or 2011 ($p < 0.05$). The frequency of induced labour increased significantly and substantially over the study period, from 18.6% at the start of the study period to 24.9% in the final year. No significant change in maternal BMI or birthweight was observed. Changes in the use of oxytocin augmentation during the study period are presented in Table 11 There was a significant reduction of oxytocin in all TGCS groups over the study period.

Table 11 - Use of oxytocin in the study population, and in TGCS 1, 2a, 3 and 4a) from 2009 to 2013 in percent. (Rossen et al. 2015)

Year	2009	2010	2011	2012	2013	p-value[a]
All groups	35.5	25.9	26.5	23.6	23.6	<0.01
TGCS 1	45.9	30.7	35.8	31.2	34.4	<0.01
TGCS 2a	79.1	73.7	64.1	59.0	55.2	<0.01
TGCS 3	12.3	5.8	7.6	5.6	6.7	<0.01
TGCS 4a	62.3	57.6	37.6	34.5	24.0	<0.01

[a]Linear trend analyses.

The overall frequency of intrapartum CS declined from 6.9% to 5.3% ($p < 0.05$) and intrapartum CS performed due to suspected foetal distress fell from 3.2% to 2.0% ($p = 0.01$).

In subgroup analyses, the rate of intrapartum CS among nulliparous women with induced labour (TGCS group 2a) declined from 26.5% to 15.7% ($p < 0.01$).

Moreover, there was a trend towards a reduced frequency of intrapartum CS performed due to suspected foetal distress in all groups, which only reached statistical significance among nulliparous women (TGCS groups 1 and 2a). The frequency of intrapartum CS due to prolonged labour remained unchanged. The frequency of

women who were in active labour for more than 12 hours increased from 4.4% to 8.5% ($p < 0.01$). In subgroup analyses, the increase was statistically significant among nulliparous women only (TGCS groups 1 and 2a).

An increase in estimated severe postpartum haemorrhage (>1000mL) from 2.6% to 3.7% ($p = 0.01$) was observed in the study population over the study period. The increase in estimated mean haemorrhage was not significant: 354, 352, 352, 359 and 371 mL, from the first to the last year of the study period, respectively.

The frequency of infants with umbilical artery pH <7.1 in was reduced from 4.7% to 3.2% ($p < 0.01$), but the reduction in infants with pH <7.0 did not reach statistical significance ($p = 0.10$). There was a trend towards a reduced frequency of children with umbilical artery pH <7.1 in the pooled group that reached statistical significance in TGCS group 1 ($p < 0.05$). Changes in labour and foetal outcomes in the total study population are presented in Table 12.

Table 12 - Labour and foetal outcomes in the study population from 2009 to 2013. (Rossen et al 2015)

Year	2009	2010	2011	2012	2013	p-value[a]
Intrapartum CS	6.9	5.9	6.0	6.7	5.3	<0.05
CS due to foetal distress	3.2	2.7	2.8	2.4	2.0	0.01
CS due to dystocia	2.2	1.8	2.1	2.5	1.7	0.75
Epidural analgesia	34.3	34.8	36.5	35.2	36.4	0.06
Duration of labour >12h	4.4	5.8	7.0	8.0	8.5	<0.01
Operative vaginal delivery	14.8	14.0	13.5	14.0	15.5	0.42
Sphincter rupture	2.3	1.4	1.7	2.0	1.5	0.10
PPH >1000 mL[b]	2.6	3.2	3.2	3.3	3.7	0.01
Apgar score after 5 min < 7	0.8	0.7	0.8	1.0	1.0	0.17
pH umbilical cord < 7.00	0.7	0.8	0.5	0.6	0.4	0.10

pH umbilical cord < 7.10	4.7	4.8	4.2	3.5	3.2	<0.01

[a]Linear trend analysis

[b]PPH – Postpartum haemorrhage

12.4 Paper 4

From November 2013 through July 2016, 223 women were included in the study:

- Stavanger Uni. Hospital (n=135)
- University Hospital of Bologna, Italy (n=34)
- Trondheim Uni. Hospital, Norway (n=16)
- Queen Charlotte's and Chelsea Hospital, UK (n=14)
- Lund University Hospital, Sweden (n =9)
- Hvidovre University Hospital, Copenhagen, Denmark (n=9)
- University Hospital of Parma, Italy (n=6)

One woman was excluded because information about the main outcome was missing, leaving 222 women in the study population. See Figure 29 for a flow chart illustrating delivery methods.

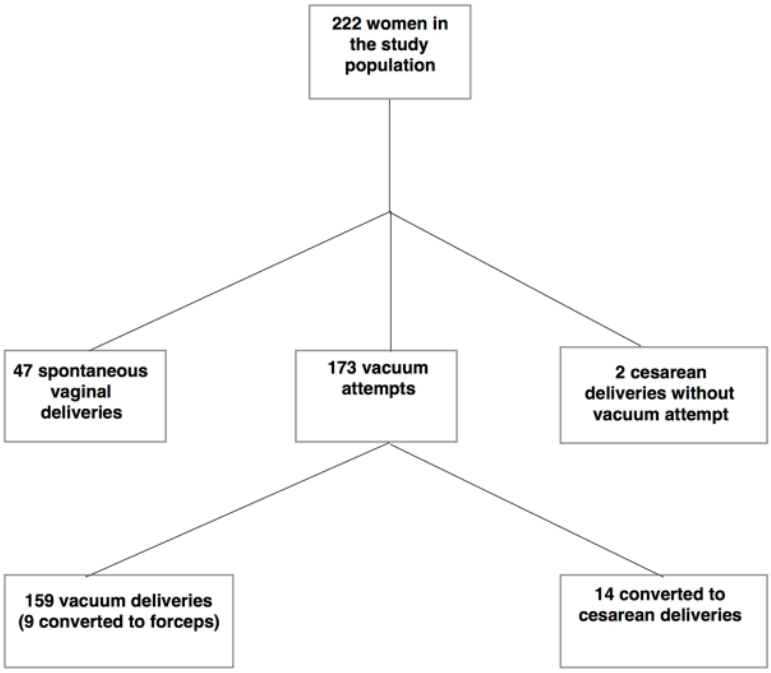

Figure 29 - Flow chart of study population and delivery methods (Kahrs et al. 2017)

Head-perineum distance was successfully measured in all women. Angle of progression was successfully measured in 182/222 (82%). Characteristics of the study population are presented in Table 13.

Table 13 - Characteristics of the study population. (Kahrs et al. 2017)

	HPD ≤25 n = 99		HPD >25 n = 123	
	Median or n (%)	Range	Median or n (%)	Range
Maternal characteristics				
Maternal age (years)	29	20-43	30	17-41
Pre-pregnant BMI	23	18-39	24	18-39
Gestational age (weeks)	40	38-42	40	37-42
Labour characteristics				
Induction of labour	30 (30)		43 (35)	-
Epidural analgesia	80(81)		95 (77)	-
Oxytocin augmentation	72 (73)		98(80)	-
Characteristics of the newborn				
Birthweight (g),	3660	2570-4665	3650	2152-4930
Apgar score 5 minutes	10	7-10	10	5-10
pH in umbilical artery (n=184)	7.24	7.09-7.43	7.24	6.90-7.40
Birth characteristics				
Blood loss (mL)	400	100-2000	400	100-3400
3rd and 4th degree anal sphincter tears	8 (8)		6 (5)	

HPD, head-perineum distance

Duration of vacuum extraction

We performed survival analyses in women with an attempted vacuum extraction. In women with head-perineum distance ≤25 mm, the duration of operative delivery was significantly shorter (log rank test <0.01), see Figure 30. The estimated median duration in women with head-perineum distance >25 mm was 8.0 (95% CI 7.1-8.9) minutes vs. 6.0 (95% CI 5.2-6.8) minutes in women with head perineum distance ≤25 mm. The HR in Cox regression analyses was 0.56 (95% CI 0.41-0.78) and adjusted value 0.58 (95% CI 0.41-0.82).

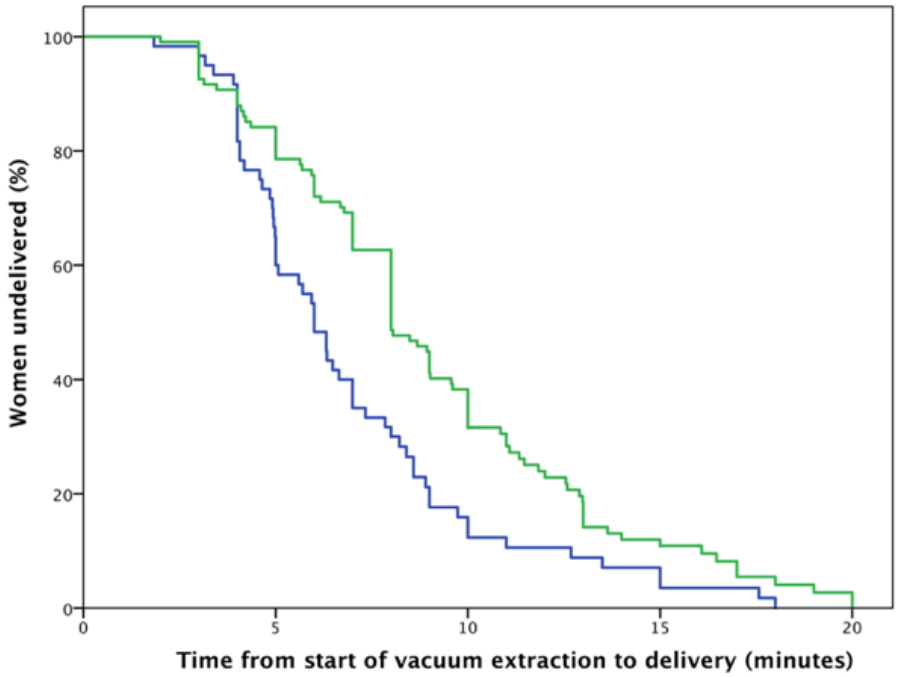

Figure 30 - Kaplan-Meier plot of time from start of vacuum extraction to delivery within 20 minutes differentiated into those with head-perineum distance 25 mm (blue) and >25 mm (green). Women who were delivered by CS were censored at time of decision to convert to CS. (P < .01; log rank test) (Kahrs et al. 2017)

Head-perineum distance and angle of progression were both analysed as continuous variables in separate analyses. Both variables were significantly associated with the duration of operative vaginal deliveries after adjusting for covariates. Adjusted HR was 0.98 (95% CI 0.97-0.996) for decreasing angle of progression and 0.96 (95% CI 0.94-0.98) for increasing head-perineum distance. The Cox analysis is shown in Table 14.

Table 14 - Cox regression analyses for predicting duration of vacuum extraction in nulliparous women with prolonged second stage of labour. Hazard ratios with CI intervals not crossing 1.0 were assumed significant. (Kahrs et al. 2017)

	Unadjusted HR	(95% CI)	Adjusted HR	(95% CI)
Head-perineum distance*	0.96	0.94-0.98	0.96	0.94-0.98
BMI*	1.05	1.04-1.09	1.05	1.01-1.10
Maternal age*	0.99	0.97-1.03	1.00	0.96-1.03
Foetal position (n=212)				
Occiput anterior (reference)	1.00	-	1.00	-
Non-occiput anterior	0.46	0.32-0.68	0.56	0.38-0.84
Induction of labour				
No (reference)	1.00	-	1.00	-
Yes	0.97	0.69-1.36	1.10	0.76-1.60
Epidural analgesia				
No (reference)	1.00	-	1.00	-
Yes	0.69	0.47-1.03	0.73	0.49-1.10
Augmentation with oxytocin				
No (reference)	1.00	-	1.00	-
Yes	0.75	0.52-1.09	0.87	0.59-1.29

HR, hazard ratio; *analysed as continuous variable

Delivery mode

The frequency of CS was 1% (1/99) in women with head perineum distance ≤25mm vs. 12% (15/122) in women with distance >25 mm ($p < .01$). Using head-perineum distance >35 mm as cutoff value, the sensitivity in predicting CS was 56% (95% CI, 33-77%), the false positive rate was 16% (95% CI, 11-21%), with a positive predictive value of 22% (95% CI, 12-33%), and a negative predictive value of 96% (95% CI, 92-98%). A graphical representation of the distribution of delivery mode by head perineum distance can be seen in Figure 31 and by angle of progression in Figure 32.

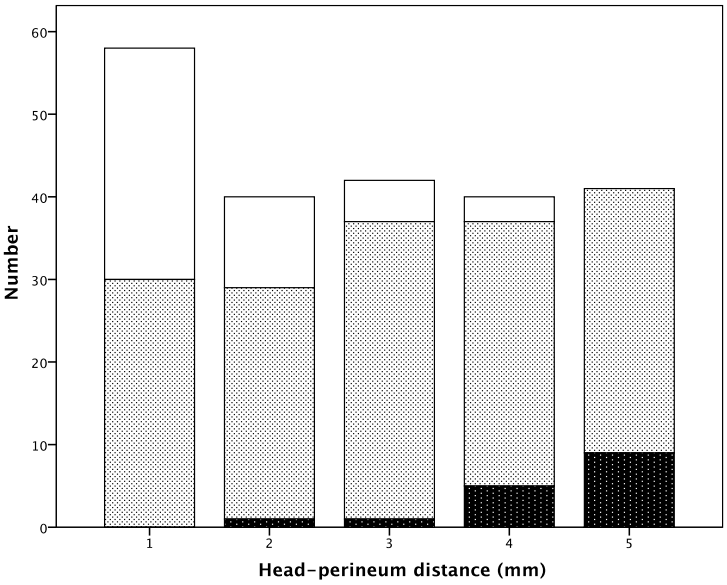

Figure 31 - Distribution of spontaneous (white), operative vaginal (light grey), and CS (dark grey) deliveries in relation to HPD in nulliparous women with prolonged second stage of labour. (Kahrs et al. 2017)

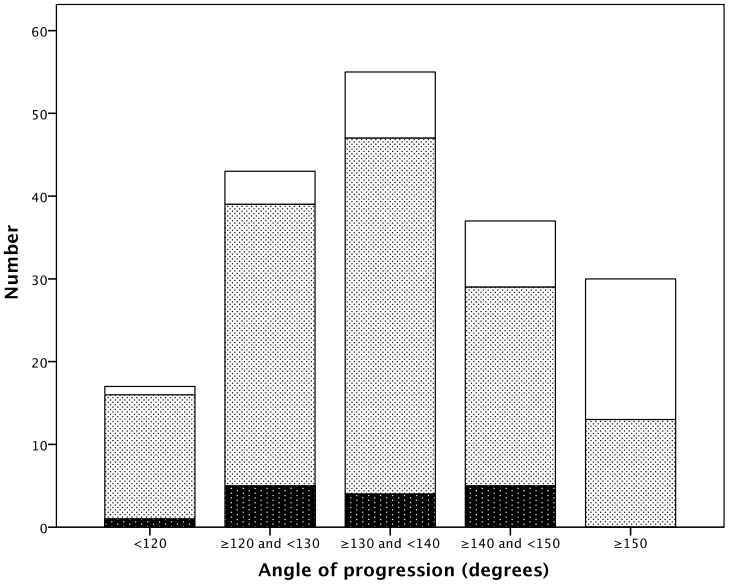

Figure 32 - Distribution of spontaneous (white), operative vaginal (grey hatch), and CS (black hatch) deliveries in relation to angle of progression in

nulliparous women with prolonged second stage of labour. (Kahrs et al. 2017)

In women with head-perineum distance ≤35 mm, 7/181 (3.9%) were delivered by CS vs. 9/41 (22.0%) in women with head-perineum distance >35 mm ($p < 0.01$). Foetal position assessed by ultrasound was OA in 73% of cases and non-OA in 23%, whereas 4% of cases were missing information about foetal position. Of the foetuses in OA position 6/162 (3.7%) were delivered by CS. In contrast, 10/50 (20.0%) of the foetuses in a non-OA position were delivered by CS. ($p < 0.01$). Just 3/138 (2.2%) of foetuses in OA position and head-perineum distance ≤35 mm were delivered by CS. In the cases where the foetuses were in non-OA position combined with head-perineum distance >35 mm, 6/17 (35.3%) were delivered by CS.

Umbilical artery pH was measured in 184/222 (83%) of cases. Only one neonate had pH <7.0 (pH 6.90 and BE -18). This baby was delivered by vacuum and head-perineum distance before start of vacuum delivery was 38 mm. pH <7.10 occurred in 10 neonates, and head-perineum distance was >35mm in 8/40 (20.0%) compared to 2/144 (1.4%) in cases with head-perineum distance ≤35 mm ($p <0.01$).

13. Discussion

13.1 Findings and interpretations

As shown throughout the introduction, norms and guidelines for normal labour duration have been influenced by several factors which are not purely medical in nature: logistics, economy, availability of care and birth helper preference to name a few. Nevertheless, managing labour without a framework for defining normal duration is nearly unthinkable in modern obstetric practice. In lieu of the critique of the paradigm of active phase of labour in the introduction, one may ponder the value of Papers 1 and 3. However, given that this paradigm is the dominant one in management of labour today, they may provide useful insight, nonetheless.

In Paper 1 we found that the duration of the active phase of labour was longer when the woman was nulliparous and had undergone induction of labour, compared to when she was in spontaneous labour. Whether the causal mechanism is the induction itself or the indication bringing about the induction is unclear. Nevertheless, once the induction has taken place, the paper provides insight into what difference in labour duration one can expect.

We received a critical review of this paper upon submission, stating that women undergoing induction would be diagnosed as being in labour at an earlier stage. That may indeed be the case, however that doesn't change that induced women are managed by the same partograph as spontaneously labouring women in many facilities, and that no induction specific partograph or definition of normal duration is established.

The data derives from a single centre, which is a weakness. Also, national guidelines recommending operative delivery after one hour of active pushing may cause a shorter duration than in other contexts. Furthermore, and as has been discussed in the introduction, there is no way of knowing precisely how long labours terminated by

operative delivery would have lasted if allowed to run their natural course. Compared to simple mean or median durations, survival analyses ameliorate error, but does not correct them. Survival analyses *estimate* the duration in the case of censoring, but it is an estimate, not an observed point in time.

So what is it good for? In a context of rapidly increasing rates of induction in high-resource countries: Being aware that labour in nulliparous women have longer estimated duration than those with a spontaneous onset may nudge the birth attendant to approach labour management in induced women with more patience.

The results of paper 2 imply that the duration of active second stage of labour is inversely correlated with BMI in both nulliparous and parous women. The study is large, multicentre, and has clear definitions for start and end of the time periods observed. BMI was missing in 26 percent of cases, which could have introduced bias, but analysis of the difference in the active stage in the cases missing BMI was not clinically relevant when compared to those with known BMI. Once again, external validity is questionable given that national guidelines may shorten the active second stage of labour. However, the results align well with the results from the study by Carlhäll et al, which may point to validity beyond the Norwegian setting.

Analysing observational data is fraught with risk of confounding. Determining whether factors are confounding or mediating is central as to whether to correct for them. We found DAGs to be a useful tool in this process: they visualise whether a factor influences both dependent and independent variables. For instance, maternal age was clearly a confounder as it impacted both BMI and duration of the active second stage, whereas in epidural analgesia and oxytocin the causal pathways are different (see Figure 19 under Statistical considerations).

The same considerations for error in survival analyses as in Paper 1 are present here: Survival analyses provide partial but not complete correction by estimation.

However, both the research into, and communication with, overweight and obese women is permeated by perceived or proven increased relative risk for negative outcomes. Women who are overweight or obese experience shame and are deterred from seeking health care[144] more than their normal weight counterparts throughout pregnancy. Furthermore, birth attendants are also affected by the perceived risk, and this is known to affect management in labour[145-147]. Therefore: providing women and their caregivers with an aspect of labour in which overweight and obese women excel compared to their normal weight counterparts may imbue both parties with a bit of much needed optimism.

Paper 3 advises more patience in the management of labour through the use of a clear indication and judicious dose increments in administration of oxytocin. We found a trend towards reduction in intrapartum CS for foetal distress after implementation of the judicious protocol. Several other outcome measures are also improved over the time period.

Comparing temporal cohorts such as these is not without risk: Other factors may have changed with or without our knowledge over the study period. One is known and important: The rate of blood transfusions fell throughout the study period, but this coincided with a defined cut-off haemoglobin limit for blood transfusion. Another is the rate of inductions, which rose from 18.6% to 24.9%, with a potential and unknown effect on outcome variables.

Nevertheless, the paper clearly illustrates the need for a consensus on diagnosis of prolonged labour and dosage of oxytocin, rather than subjective feelings on part of the birth attendant and indiscriminate dosing of a potent drug. In other medical contexts, it is nearly unthinkable to administer an arbitrary dose of a drug with no clear-cut indication. Obstetrics should certainly aspire to a similar standard. However, the judicious protocol for oxytocin also had drawbacks: Twice as many women spent more than 12 hours in active labour (8.5% vs 4.4%). This may be part of the

mechanism for a similar rise in postpartum haemorrhage > 1000mL over the study period, from 2.6% to 3.7%.

Paper 4 addresses a clinical situation and assessment which is well known and, in some cases, dreaded by clinicians: Prolonged second stage of labour and assessing the prognosis for a vaginal birth, whether spontaneously or aided by vacuum or forceps. A misdiagnosis of the foetal head station or position leading to improper application of the instrument increases risk of failure, and a failed operative vaginal delivery will result in a CS with increased risk for mother and child[64]. Ultrasound can provide additional information, and paper 4 examines and provides evidence for its value as a prognostic tool.

However, ultrasound can never replace assessing the clinical situation as a whole: The mother, her partner, the pregnancy, the rest of the course of labour, pain or pain relief, preferences, language barriers, the tension in the room, clinical examination and so many other factors should be taken into consideration when decisions on management of prolonged second stage is made. Ultrasound is merely an addition to our assessment, and despite its ability to give us absolute values and measurements, is but one of many factors to consider when making clinical decisions.

13.2 From 3 to 4 to 5 to 6 – sign of a dysfunctional paradigm?

As previously stated, all papers comprising this thesis have been conducted according to the WHO guideline of 1994. However, over the course of time from Friedman to ACOG's guideline, we see a slide of the start of active labour from 3 to 6 cm, with WHO's new labour care guide at 5 cm. Is the phenomenon of labour so variable from woman to woman that a universal inflection point for an acceleration phase can not be defined? It also poses another problem: definition of active labour has been a key to care, pain relief and one-to-one attention in the labour ward: By pushing the start of active labour to progressively higher dilation, are we depriving women of care at a point in their labour where they need care, pain relief and companionship?

As Krahl points out in her historical analysis of the latent phase of labour[15]:

> *"Today's culture of care for women in the early opening period or early phase of labour reflects the interaction of traditional perspectives, medical definitions and clinical frameworks. The organisation of the delivery unit does not provide for the care of women in the early phase of childbirth. Midwives often try to exclude women from the delivery room routine for as long as possible so that they do not tie up the capacity in the delivery unit too early and their labour progress does not have to be measured and treated too early according to the tight time schedule. Midwives repeatedly get into the conflict of not being able to care for women according to their needs."*

Up until the invention and implementation of partograms, definition of labour was centred on how women perceived their contractions, and aid given accordingly. It is not rare to hear stories where the woman and the birth attendant have completely different perceptions on when labour started.

Whichever way future labour guidelines are developed and implemented: It is vital to the birth experience that they promote supportive care, and do not dissuade birth attendants from giving adequate support and pain relief to women for lacking a certain centimeter of cervical dilation.

13.3 WHO labour care guide

In 2020 WHO released their new guideline, the WHO Labour Care Guide[10]. It is an attempt to integrate the knowledge and research attained since the publication of the 1994 partograph. Interestingly, the first table of the Labour Care Guide Chart is Supportive care, with companionship as first parameter to be monitored. The last is shared decision making. The labour progress monitoring part has been moved to the middle, and modified from a line-based system to maximum traversal times per

centimetre dilation. The latter despite no clear evidence from RCTs as to whether it decreases the CS rate[44]. The LCG itself is accompanied by several documents outlining recommended use and background material.

An interesting aspect to note is that the LCG still recommends the use of abdominal palpation of the head, in fifths above the pelvic inlet, as means to determine foetal descent. This was first suggested by Crichton in 1974[148], and found to be unreliable by Buchmann et al. in 2007[149]. Furthermore, in our clinical practice we have yet to encounter birth attendants who find this method easy and reliable to use, and even less so in the context of maternal obesity.

Unlike the 1994 partograph, the 2020 LCG has not in itself been subjected to any RCT. It is a meticulous attempt to implement accrued knowledge from the two last decades. Nevertheless, upon its publication and recommended universal implementation, its potential effects on maternal and neonatal outcomes remain unknown. In 2021, a study investigating its usability, feasibility, and acceptability was published, with a usability score of 67.5% and overall user satisfaction of 75.7%[150]. The qualitative part of the analysis is interesting: One midwife notes that the lack of graphical representation of birth progress as a disadvantage: *"[T]he previous one [partograph] would tell if the baby is in distress by just looking."* Another midwife notes: *"It is difficult where one staff member has 10 mothers. It is quite difficult, almost impossible, the monitoring will not be done well. […]"*

The second midwife makes an important point, especially for low resource settings: Over the course of 12 hours, which may very well be the observation time, correct use of the LCG requires 300 separately documented observations. For one staff member with 10 mothers to care for: 3000. One may wonder, in its quest for completeness, has the LCG become too elaborate? Will it improve labour care or merely become a tool that gets in the way of care because paperwork will consume the birth attendant's time and energy?

The PICRINO study may provide answers[151]: A Swedish, multi-center, cluster RCT comparing outcomes for mother, child, obstetrical complications, birth experience and health economics. Inclusion in the study will start in 2023. From a scientific viewpoint this study should most certainly have preceded the WHOs recommendation of universal implementation, and will hopefully provide insight and possibly corrections to the LCG.

13.4 Moving beyond oxytocin as the one hammer to fix all nails, screws and bolts?

The knowledge of correctible causal mechanisms impacting labour duration are limited. Presence and companionship are well documented as described in the introduction, as well as walking and upright positions in the first stage of labour[152].

Maternal positioning in the hands and knees posture in late pregnancy and labour has also been investigated through several trials, and a Cochrane review has found it to be effective for alleviating back pain[153]. However, only one of the trials included in the review was done during labour to evaluate its efficacy in correcting non-occipitoanterior positions[154]. Though there was a trend towards a positive effect in the intervention group, the study did not find any significant difference. Walker et al. found no difference in maternal positioning in the active second stage on duration in another Cochrane meta-analysis[155].

Over the last five years, a movement concept known as Spinning Babies has gained popularity[156]. Despite lack of evidence base, workshops are being held throughout the world on a daily basis, for birth attendants and parents-to-be. The inventors claim that performing exercises in pregnancy and during labour will promote decent and rotation of the foetal head.

Such movements pose little risk to mother and child, but it would be interesting to know if the effects could be quantified, and whether particular positions or movements could improve particular malpositions. In 2017 we attempted to

undertake a pilot study on one such position, the sidelying release, on prolonged labour with occiput posterior position, but the study fell through for logistical reasons. Maybe the lack of evidence in a procedure without risk is unproblematic, but pinpointing potentially effective positions and movements would make for more precise treatment.

13.4.1 Novel pharmacological approaches

Oxytocin has been the mainstay drug for managing prolonged labour throughout the last century. Its effect on labour duration is well documented, as is its risks and side effects, as described in the introduction.

Oxytocin increases the duration and frequency of contractions. However, contractions are only one side of the coin: cervical dilation is the other in the first phase of labour. Antispasmodics have been employed in the management of prolonged labour, despite limited evidence. The theoretical basis for their use is that the cervix consists of a mix of smooth muscle and connective tissue, the smooth muscle component may be relaxed by the use of antispasmodics.

A Cochrane review from 2013 reviewed the effect of 21 RCTs investigating antispasmodics in the first stage of labour found an increased rate of cervical dilation, though the level of evidence was poor[157]. RCTs and reviews published after this review have found labour durations to be shortened by little less than an hour with the administration of butylscopolamine in active labour[158, 159]. However, these studies did not employ the drug in the setting of prolonged labour, so one may ask the question of what they were treating in the first place.

In November 2022 the study protocol for the BUSCLAB study was published: A RCT trial investigating the effect of butylscopolamine on prolonged labour[160]. The study defines prolonged labour as crossing the alert line, which may be a somewhat tight definition of normality, but the indication is clear, and the intervention is targeted. Furthermore, in January 2023, a Norwegian nationwide multicenter RCT was launched, the SAINT trial: investigating whether butylscopolamine and/or

bicarbonate can facilitate normal labour progression in primiparous women undergoing induction of labour[161].

Hopefully these studies can add some evidence-based tools to our labour toolbox, beyond oxytocin.

13.5 Conclusion

Through our studies we have found that the active phase of labour was longer in induced nulliparous women, the active second stage of labour was shorter with increasing BMI, that a judicious protocol for oxytocin augmentation may be beneficial for mothers and offspring but prolongs labour, and that ultrasound provided prognostic information in the setting of a prolonged second stage of labour.

A multitude of factors have the potential to influence labour duration in women, and this thesis has only scratched the surface. The awareness of the effects of factors such as induction of labour and BMI on the duration of labour phases could make our interventions more precise. In the case of oxytocin augmentation, its use may benefit from clear guidelines of indication and dosage to minimise the risk of iatrogenic injury. And, if operative delivery is considered for prolonged labour, knowing the precise position and station of the foetus is paramount, and prognostic tools may serve as an adjunct to clinical examination and in decision making.

The overall aim of this thesis was certainly broad, perhaps too broad: Investigating effects of maternal and iatrogenic factors on duration of phases of labour. Induction, BMI and oxytocin are but a few in a myriad of factors which influence labour – leaving a whole universe of other aspects to be explored. Hopefully though, this thesis and the papers enclosed may have shed some light in places which were less elucidated before.

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Duration of the active phase of labor in spontaneous and induced labors

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Key words
Labor duration, induction, cesarean delivery, nulliparous women, parous women

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Abstract

Introduction. The aim of the study was to compare the duration of active phase of labor in women with spontaneous or induced start of labor. *Material and methods.* An observational cohort study was performed at Stavanger University Hospital in Norway between January 2010 and December 2013. During the study period 19 524 women delivered. Data for the study were collected from an electronic birth journal. Women with previous cesarean section, multiple pregnancy, breech or transverse lie, preterm labor or prelabor cesarean section were excluded. Analyses were stratified between nulliparous and parous women. Active phase of labor was defined when contractions were regular, with cervix effaced and dilated 4 cm. The main outcome measure was duration of active phase of labor. *Results.* The active phase was longer in induced labors than in labors with spontaneous onset in nulliparous women. The estimated median duration using survival analyses was 433 min (95% confidence interval 419–446) in spontaneous vs. 541 min (95% confidence interval 502–580) in induced labors [unadjusted hazard ratio 0.76 (95% confidence interval 0.71–0.82) and adjusted hazard ratio 0.88 (95% confidence interval 0.82–0.95)]. In parous women, a one minus survival plot showed that induced labors had shorter duration before six hours in active labor, but after six hours, induced labors had longer duration. The overall difference in parous women was small and probably of little clinical importance. *Conclusion.* The active phase of labor was longer in induced than in spontaneous labors in nulliparous women.

Abbreviations: BMI, body mass index; TGCS, Ten Group Classification System; WHO, World Health Organization.

Introduction

There is ongoing discussion within the obstetrical community regarding the normal progression and duration of labor (1). Labor dystocia is one of the main indications for unplanned cesarean deliveries, thus knowledge of the normal range of progression and duration is of utmost importance for a precise diagnosis and clinical management (2). The World Health Organization (WHO) recommends defining the start of the active phase of labor as when the cervix is effaced and dilated 4 cm in women with regular contractions (3). Accordingly, the time span between this event and delivery of the fetus constitutes the duration of active phase of labor.

Key Message

The active phase of labor was longer in induced labors than in labors with spontaneous onset in nulliparous women. In parous women the difference was small and probably of little clinical importance.

However, in a contemporary cohort, a number of interventions take place which shorten labor duration and will therefore interfere with calculation of mean and median duration. For this reason, survival analyses might be used when conducting such studies to ameliorate the effects of interventions on studies of duration (4). It has been documented in previous studies that duration of labor is influenced by factors such as parity (5), age (6), ethnicity (5), body mass index (BMI) (7), fetal position (8), use of oxytocin (9,10) and epidural analgesia (11).

Induction of labor is becoming increasingly common in obstetrics. Different induction methods have been compared with regard to safety and efficacy (12). Retrospective studies indicate an increased risk of operative interventions in induced labors (13,14), but it is unclear whether these interventions are due to the induction itself or to confounding by indication (15–17). Some studies indicate that prolonged labor has potential adverse effects on mother and fetus and duration of labor following labor induction warrants investigation (18). Two previous studies compared median duration of time elapsed for each centimeter of cervical dilation in induced and spontaneous labors (19,20). The use of survival analyses might add information.

The Ten Group Classification System (TGCS) was described in 2001 and originally used to assess cesarean delivery rates in different groups of laboring women (21). We aimed to compare the duration of active phase of labor in nulliparous and parous women with spontaneous or induced start of labor (TGCS 1–4) using survival analyses.

Material and methods

The labor ward at Stavanger University Hospital serves as the only delivery unit in the region for a population of 320 000 people, with around 4800 deliveries yearly. Information related to pregnancies and deliveries was collected prospectively and recorded in an electronic birth journal (*Natus*), and continuously maintained using standardized procedures for data entry and quality control. The study period was from 1 January 2010 to 31 December 2013. The study was in accordance with the Helsinki Declaration and was approved by the regional ethics committee in western Norway (REK 2014/1925).

Selection of the study population is presented in Figure 1. Women with a previous cesarean section, multiple pregnancy, breech or transverse lie, preterm labor or prelabor cesarean section were excluded (corresponding to TGCS 5–10). The main outcome was duration of labor defined as time from start of active phase until delivery of the fetus. Women were considered to be in active labor once the cervix was effaced, dilated 4 cm, and the woman was experiencing regular contractions. In spontaneously laboring women who were admitted when labor had progressed beyond 4 cm, the admitting midwife estimated start of labor based on clinical findings upon admission and from the woman's report of when contractions became regular and painful. Estimated date of delivery was determined by a second trimester ultrasound scan (eSnurra) (22) or from menstrual data when no ultrasound results were available. Indication for labor induction was categorized into post-term pregnancies, hypertensive disorders, prelabor rupture of membranes, maternal request and others. Labor induction in post-term women was considered one week past term in women with prelabor rupture of membranes more than 24 h and after a specialist consultation for other indications. In women with Bishop score <6, misoprostol was used as induction agent, and 25 μg was administered vaginally every four hours up to a maximum dose of 100 μg/day over a maximum of two days. In women with Bishop score ≥6, amniotomy was performed and oxytocin added after four hours if regular contractions were not established.

The progress of labor was monitored using a partograph with an alert line (1 cm cervical dilation/hour) and an action line displacement of four hours as recommended by the WHO, and prolonged first stage diagnosed when the action line was crossed. This definition was used in both nulliparous and parous women, and augmentation with oxytocin during the first stage was only carried out in women with a diagnosis of prolonged labor. During the second stage, augmentation with oxytocin could be started at the discretion of the birth attendant when the contractions were considered insufficient. Amniotomy was not routinely performed during the active phase of labor but always prior to oxytocin augmentation. Oxytocin was administered as an intravenous infusion of 5 IE (0.01 mg) oxytocin in 500 L saline and the infusion rate started at 6 mU/min (30 mL/h), with a dose increment of 3 mU/min (15 mL/h) every 15 min to a maximum of 40 mU/min (180 mL/h) until progress of labor or regular contractions at a rate of 3–5/10 min was achieved. A combination of low-dose ropivacaine/fentanyl was used for epidural analgesia.

Operative vaginal delivery was considered in all women after 60 min of active pushing, in accordance with national guidelines (23). The preferred device for operative vaginal delivery in the department is the Malmstrom metal cup.

Statistical analyses

A chi-square test was used to compare categorical variables, and continuous variables were compared using

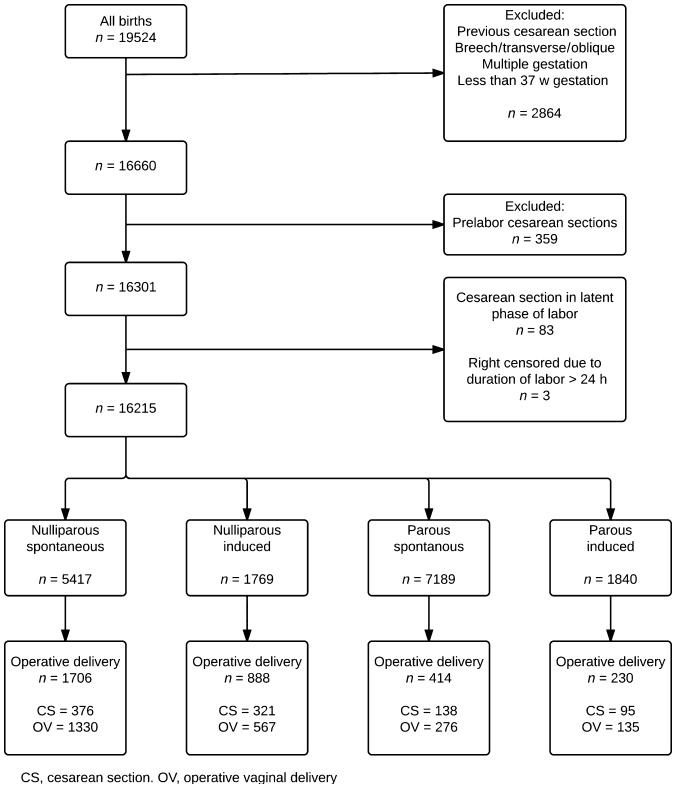

Figure 1. Flow chart of study population.

Mann–Whitney *U*-tests. The duration of active phase of labor was evaluated using survival analyses. Women with missing information about start of active phase of labor or cesarean section performed during the latent phase were left-censored. Women with active phase of labor >24 h or an operative delivery were right-censored. The analyses were performed by comparing TGCS 1 with 2a and 3 with 4a. Kaplan–Meier (one minus survival) plots were created and the groups compared using the log rank test. In multivariable Cox regression analyses, maternal age, BMI, gestational age and birthweight >4000 g were included as possible confounders. To evaluate the potential impact from the competing event of operative deliveries, we performed competing risk regression on the survival data according to the method of Fine and Gray. Amniotomy, oxytocin augmentation and epidural analgesia were initiated after start of active phase and considered mediators and not confounders, and were therefore not included in the regression analysis. The assumptions of proportional hazards for the Cox regression analyses were checked using log minus log plots. Statistical analyses were performed with IBM SPSS STATISTICS FOR WINDOWS v. 21.0 (IBM Corp., Armonk, NY, USA).

Results

Of a total of 19 524 women who delivered at the hospital during the study period, 16 660 (85.3%) were in TGCS 1–4 and 359 (2.2%) women were excluded due to prelabor cesarean section. Fifty-three women were left censored due to lacking information about the start of active phase of labor and 30 women due to cesarean section performed in the latent phase. Three women were right-censored due to a labor duration recorded as more than 24 h and 3238 women were right-censored due to operative deliveries (Figure 1).

The women in the induction groups differed from their spontaneously laboring counterparts by being older, having higher BMI and a higher gestational age (Table 1).

Table 1. Characteristics of the study population.

	Nulliparous women			Parous women		
	Spontaneous start (TGCS 1) *n* = 5417	Induced (TGCS 2a) *n* = 1769	*p*-value	Spontaneous start (TGCS 3) *n* = 7189	Induced TGCS 4a) *n* = 1840	*p*-value
Characteristics related to the mother						
Maternal age in years; median (IQ-range)	27 (7)	28 (7)	<0.01	31 (6)	32 (6)	<0.01
Prepregnant BMI (weight/m^2): median (IQ-range)	22.3 (4.4)	23.6 (5.9)	<0.01	23.0 (4.7)	24.0 (6.3)	<0.01
Gestational age in days; median (IQ-range)	283 (10)	287 (14)	<0.01	282 (9)	283 (18)	<0.01
Characteristics related to labor						
Delivery method						
Spontaneous (%)	68.5%	49.5%	<0.01	94.1%	87.2%	<0.01
Operative vaginal (%)	24.5%	31.9%	<0.01	3.8%	7.3%	<0.01
Cesarean section (%)	7.0%	18.6%	<0.01	2.1%	5.5%	<0.01
Augmentation (%)	32.9%	62.5%	<0.01	6.4%	37.2%	<0.01
Epidural analgesia (%)	43.3%	70.5%	<0.01	19.0%	44.4%	<0.01
Duration of active second stage (minutes); median (IQ-range)	38 (38)	37 (42)	0.56	10 (12)	10 (13)	0.24
Characteristics related to the newborn						
Mean birthweight (g); median (IQ-range)	3450 (570)	3525 (675)	<0.01	3618 (595)	3700 (710)	<0.01
Head circumference (cm); median (IQ-range)	35 (2)	36 (2)	<0.01	35 (2)	36 (2)	<0.01

The *p*-values from Mann–Whitney *U*-test or chi-squared test. Values are median with interquartile range given in parentheses, or percentages.

The women in this group gave birth to babies with higher birthweight, and there was more use of oxytocin and epidural analgesia. The rates of both cesarean section and operative vaginal delivery were higher in the induction groups.

The median duration of active phase of labor in nulliparous women with spontaneous start was 368 min vs. 335 min in nulliparous women with induced labors. The corresponding durations in parous women were 165 min vs. 134 min. Using Kaplan–Meier analyses the estimated median duration of active phase was longer in all groups. In nulliparous women with spontaneous onset of labor, the estimated median duration was 433 min (95% CI 419–446) vs. 541 min (95% CI 502–580) in induced labor. The corresponding values in parous women were 168 min (95% CI 164–172) in women with spontaneous start and 142 min (95% CI 135–149) in women with induced labor. Figure 2 illustrates 1-survival plots for nulliparous women with spontaneous and induced labors ($p < 0.01$; log rank test). After 12 h in active labor 12.6% (95% CI 11.8–13.5%) were undelivered among nulliparous women with spontaneous start vs. 13.4% (95% CI 11.9–15.1%) in nulliparous women with induced labor.

In parous women the duration of the active phase of labor was significantly longer in spontaneous than in induced labors as illustrated in Figure 3 ($p = 0.02$, log rank test), but the lines were crossing. The duration of labor at different times can be assessed from the Figure. Before six hours in active labor, induced labors had shorter duration, but after six hours, induced labors were longer. The difference in 1-survival plots illustrated in Figure 3 did not differ substantially. The frequencies of undelivered women after 12 h were 2.4% (95% CI 2.1–2.8%) vs. 3.7% (95% CI 3.0–4.4%) among spontaneous and induced labors, respectively.

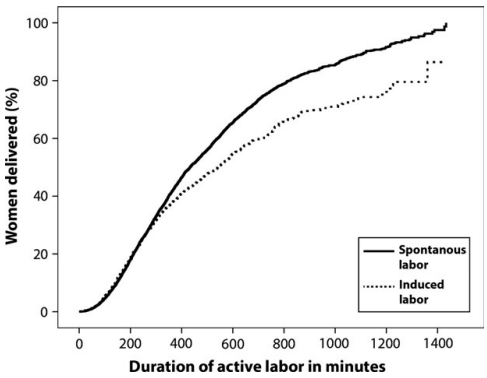

Figure 2. Kaplan–Meier plot (1-survival) illustrating duration of active phase of labor in nulliparous women.

Using Cox regression analysis the duration of active phase of labor in nulliparous women was longer in induced labors. The unadjusted hazard ratio was 0.76 (95% CI 0.71–0.82) for induced compared with spontaneous labors. Increasing maternal age, gestational age and BMI, and birthweight >4000 g were all factors associated with longer duration of the active phase of labor. The adjusted hazard

Table 2. Hazard ratio for duration of active phase of labor in nulliparous women.

	Unadjusted values		Adjusted values	
	HR	95% CI	HR	95% CI
Spontaneous labors	1.0		1.0	
Induced labors	0.76	0.71–0.82	0.88	0.82–0.95
Maternal age	0.96	0.96–0.97	0.97	0.96–0.97
BMI	0.97	0.97–0.98	0.99	0.98–0.99
Gestational age	0.97	0.97–0.98	0.98	0.97–0.98
Birthweight >4000 g	0.54	0.49–0.60	0.64	0.57–0.71

BMI, body mass index; HR, hazard ratio.

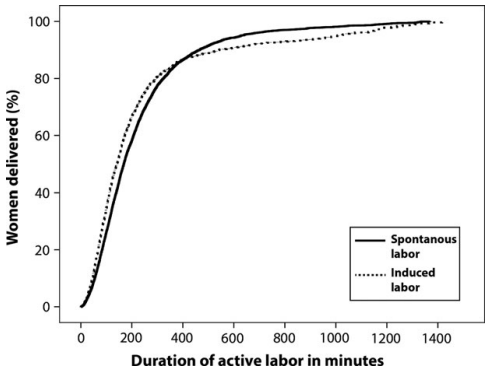

Figure 3. Kaplan–Meier plot (1-survival) illustrating duration of active phase of labor in the parous women.

ratio for duration of active phase of labor in induced compared with spontaneous labors was 0.88 (95% CI 0.82–0.95). Details are presented in Table 2. In the competing risk regression analysis that incorporated the competing event of operative deliveries, the adjusted HR for delivery was 0.74 (95% CI 0.68–0.80) for induced labors vs. spontaneous labors. We refrained from comparing induced and spontaneous labors in parous women using Cox regression analysis due to violation of the proportional hazard assumption when the lines are crossing in the 1-survival plot (Figure 3).

One minus survival plot from the study population differentiated into operative and spontaneous vaginal deliveries is presented in Figure S1. The duration was significantly longer in operative deliveries. Induced labors were differentiated into indications of induction and results presented as one minus survival plots in Figures S2 and S3. Labor duration was shorter in nulliparous women with induced labors due to prelabor rupture of membranes, but showed little variance among other indications. In parous women the indication of induction had a minor effect on labor duration.

Discussion

We found that the active phase of labor was longer in induced labors than in labors with spontaneous onset in nulliparous women. Induced contractions may be less effective than spontaneous contractions. We also observed a difference in parous women but it was small and probably of little clinical importance.

The strengths of our study are the large number of women included, prospectively gathered data, an unselected population, and clear guidelines for defining the start of active phase of labor in the hospital. Furthermore, a consistent definition and diagnosis of prolonged first stage of labor was used, and oxytocin augmentation was performed in accordance with the WHO partograph. The use of TGCS to categorize laboring women into well-defined groups allows for simple comparison with other labor wards.

Survival analyses are a useful method when interpreting data with a high number of interventions. Cases with interventions are not excluded but are censored at the time of intervention. However, survival analyses do have limitations and rely on rather strong assumptions such as independent censoring. To assess the potential impact of differences in operative deliveries between the groups, we therefore also performed a competing risk regression analysis for survival data. This analysis suggested that our estimates based on ordinary Cox regression were conservative. Still, the results should be interpreted with caution since we are not able to directly measure the outcome in the absence of operative deliveries. We found that the duration of the active phase of labor was longer in women with an operative vaginal delivery than in women with spontaneous vaginal delivery (Figure S1) and the frequencies of operative deliveries varied between groups (Figure 1). Confounding by indication of induction is supposed to influence cesarean section rates (15) but might also influence duration of labor. Only the induction due to preterm rupture of membranes in nulliparous women differed substantially from other indications in our study (Figure S2). Epidural analgesia and oxytocin augmentation might influence duration but could not be included in the Cox regression analysis because they were started during the active phase and should be considered mediators and not confounders. The importance of epidural analgesia and oxytocin augmentation is difficult to investigate because slow progress is an indication for starting these interventions. It is also important to note that our study is observational and does not imply causality between induction and longer duration of labor in nulliparous women, merely an association.

Among the women with spontaneous delivery, some arrive in the labor ward in the late active phase. The midwives ask these women when the contractions started and

estimate the start of active phase based on this. This time is recorded as start of active phase and not the time of arrival. We realise that this estimation may be imprecise and is a limitation of the study. We suppose that these women would tend to have shorter active phase of labor (24). By excluding these women we would introduce a bias. We therefore think the best way to handle this challenge is to rely on the self-report on contractions. Figure 2 illustrates that this possible bias would probably not lead to changes in the main results and conclusion. The difference between the groups appears after 250 min, and thus short labor durations have little impact on the findings and main conclusions.

The study was conducted within a single hospital, which is a limitation, and the study population was not based on a power calculation. The time period was selected as a period strictly using the WHO recommendation of the start of active phase of labor and the use of labor augmentation with oxytocin. Zhang et al. found that labor progression from 4 to 6 cm was slower than previously described, and that the start of active phase of labor might be defined at 6 cm cervical dilation (1,25). Vahratian et al. showed that electively induced labors in nulliparous women with cervical ripening had slower latent and early active phases (20). Thus, we think our main findings will only have external validity in settings using the WHO definition of the start of active phase of labor. Furthermore, Norwegian national guidelines recommend considering operative vaginal delivery after 60 min of active pushing regardless of parity and epidural use (23), which differs from other guidelines, i.e. guidelines from the National Institute for Health and Care Excellence (26). This reduces the external validity of the study for hospital units with a longer duration of bearing down. The Friedman partograph with WHO alert and action lines (3,27) and its definition of start of active labor has been used for labor management of both nulliparous and parous women throughout the study period. Accordingly, the results are not necessarily representative of a cohort managed with a parity-specific partograph.

Advantages and disadvantages related to labor induction are frequently a part of the obstetrical discourse. Induction of labor one week past term might reduce the frequencies of intrauterine fetal death but, according to some studies, induction of labor leads to a higher cesarean delivery frequency (13,14). However, a recent meta-analysis reported reduced frequencies of cesarean sections in induced labors (17). It is clinically important in counseling nulliparous women before induction to balance the pros and cons, and they should also be informed that the length of active phase of labor seems to be longer in induced labors. Induction is known to take time, but often it is presumed that it is the establishment of active labor, rather than the active phase that takes time. This knowledge is also important when it comes to the logistics and management of a labor and delivery suite regarding labor ward design, planning and bed management.

There is no established definition of labor dystocia, though it is one of the main indications of unplanned cesarean sections (10). The active management of labor concept recommends the active phase of labor to be limited to 12 h (28). A high proportion of nulliparous women needs augmentation with oxytocin to achieve the active management concept (10); thus we think it is important to report the frequencies of undelivered women after 12 h.

A reduction of interventions in uncomplicated deliveries is warranted. The risks of complications associated with long duration of active phase of labor such as postpartum hemorrhage (29) have to be weighed against potential adverse effects of augmenting labor with oxytocin such as fetal distress (10,30) and anal sphincter injuries (31). Childbirth satisfaction is another important outcome, and in some studies long duration is associated with lower maternal satisfaction (32), which might lead to cesarean section due to maternal request in later pregnancies. However, a systematic review shows that rather than labor duration, the most important factors in women's satisfaction with childbirth are personal expectations, support from caregivers, quality of the caregiver–patient relationship and involvement in decision making (33,34).

In conclusion, we found that the duration of the active phase of labor seems to differ in spontaneous and induced labors in nulliparous women. Clinicians might take this into account when counseling women before labor induction and management during prolonged labor.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Kaplan–Meier plot (1-survival) comparing duration of active phase of labor in spontaneous and operative deliveries (total study population).

Figure S2. Kaplan–Meier plot (1-survival) illustrating duration of active phase of labor in nulliparous women with induced labor differentiated in indication of induction.

Figure S3. Kaplan-Meier plot (1-survival) illustrating duration of active phase of labor in parous women with induced labor differentiated in indication of induction.

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RESEARCH ARTICLE

Intrapartum Care

Put your weight behind it—Effect of body mass index on the active second stage of labour: A retrospective cohort study

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Abstract

Objective: To explore the duration of the active phase of the second stage of labour in relation to maternal pre-pregnant body mass index (BMI).

Design: Retrospective cohort study.

Setting: Labour wards of three Norwegian university hospitals, 2012–2019.

Population: Nulliparous and parous women without previous caesarean section with a live singleton fetus in cephalic presentation and spontaneous onset of labour, corresponding to the Ten Group Classification System (TGCS) group 1 and 3.

Methods: Women were stratified to BMI groups according to WHO classification, and estimated median duration of the active phase of the second stage of labour was calculated using survival analyses. Caesarean sections and operative vaginal deliveries during the active phase were censored.

Main outcome measures: Estimated median duration of the active phase of second stage of labour.

Results: In all, 47 942 women were included in the survival analyses. Increasing BMI was associated with shorter estimated median duration of the active second stage in both TGCS groups. In TGCS group 1, the estimated median durations (interquartile range) were 44 (26–75), 43 (25–71), 39 (22–70), 33 (18–63), 34 (19–54) and 29 (16–56) minutes in BMI groups 1–6, respectively. In TGCS group 3, the corresponding values were 11 (6–19), 10 (6–17), 10 (6–16), 9 (5–15), 8 (5–13) and 7 (4–11) minutes. Increasing BMI remained associated with shorter estimated median duration in analyses stratified by oxytocin augmentation and epidural analgesia.

Conclusion: Increasing BMI was associated with shorter estimated median duration of the active second stage of labour.

KEYWORDS
birth, body mass index, caesarean, delivery, labour, obesity, overweight, second stage, underweight

This article includes Author Insights, a video abstract available at https://vimeo.com/bjogabstracts/authorinsights17186.

Abbreviations: BMI, body mass index; WHO, World Health Organization; HR, hazard ratio; TGCS, Ten Group Classification system.

Linked article This article is commented on by Whitney A. Booker, pp. 2175 in this issue. To view this mini commentary visit https://doi.org/10.1111/1471-0528.17185

1 | INTRODUCTION

According to the World Health Organization (WHO) in 2016, 37% of women in the USA, 29% in the UK, 21% in France and 23% in Norway were obese,[1] and rates of obesity are rising throughout the world.[2–4] In Norway, 51% of the population was classified as overweight in 2019.[5] Obesity in pregnancy is associated with gestational diabetes, pre-eclampsia, miscarriage, birth defects, macrosomia, preterm delivery and stillbirth.[6–11] Obesity also poses challenges in safe delivery of the fetus, as cardiotocographic monitoring is impaired[12] and the risk of operative delivery is increased.[13–17] However, a recent study found that nulliparous low-risk normal weight women were more likely to require obstetric intervention or care than otherwise healthy multiparous women with body mass index (BMI) >35.[18] Furthermore, a recent study did not find any difference in neonatal outcome for women undergoing trial of labour compared with planned caesarean section in this group.[19]

Outcomes in labouring women are known to depend on parity, spontaneous or induced onset, previous caesarean section, fetal lie, multiple pregnancy and gestational age. To obtain comparable groups for these variables, the Ten-Group Classification System (TGCS) provides a useful framework.[20–22]

Labour is divided into a latent phase and an active phase, and the active phase is differentiated into the first, second and third stage. The second stage is defined from the a fully effaced cervix until the birth of the child. The second stage is divided into a passive phase and an active phase when the mother performs active expulsive effort.

Studies have shown that obesity is associated with slow progress in the latent phase,[23] and slow progress and arrested labour during the first stage of labour.[23–25] The duration of the second stage of labour and BMI has been investigated in a few previous studies, with conflicting findings. One study found no significant difference in duration,[26] but another study found shorter second stage in obese women.[27] A recent study found longer second stages in obese women; however, that study did not employ survival analyses[28] and neither of those studies differentiated between second stage and active second stage.

The precise moment when the woman reaches full dilation is unknown, and the diagnosis is first made upon vaginal examination, which may occur sometime after full dilation. Therefore, the true length of the passive second stage is not known with certainty. However, the start and end of active second stage can be recorded with certainty, as expulsive efforts and the birth of the child are objectively observable events.

Obese women have an increased risk for several adverse outcomes;[17] the awareness of this may influence the attitude of the birth attendant, which in turn may affect both the birth experience and delivery outcome.[29] Clinical experience indicates that obese women may have a shorter active second stage, and we believe this information could result in a more positive approach to delivery in both the birth attendant and the women themselves. We wanted to explore the duration of the active second stage in TGCS groups 1 and 3 differentiated into BMI groups.

2 | METHODS

We performed a retrospective cohort study in women who delivered at Stavanger University Hospital, Haukeland University Hospital, Bergen and Trondheim University Hospital in Norway between 2012 and 2019. Data were collected and stored in the hospital's electronic birth journals (Natus-CSAM).

In all, 109 989 women with a gestational age ≥22 weeks delivered at the hospitals during the study period. Women with a singleton pregnancy, cephalic presentation, spontaneous onset of labour, pregnancy length ≥37 weeks and without previous caesarean section were included in the study population. The women were differentiated into nulliparous (TGCS 1) and parous women (TGCS 3) and stratified into BMI groups according to WHO classification.[17] Pre-pregnant BMI <18.5 was categorised as underweight, BMI 18.5–24.9 as normal weight, BMI 25.0–29.9 as overweight, BMI 30.0–34.9 as obesity class 1, BMI 35.0–39.9 as obesity class 2 and BMI ≥40.0 as obesity class 3. The main outcome measure was estimated median duration of the active second stage of labour.

The start of the first stage of labour was defined according to the former WHO classification during the study period as an effaced cervix, regular contractions and 4-cm dilation.[30,31] The second stage was defined when the woman had a fully dilated cervix, and the active second stage was defined as the time from active expulsive effort started until the delivery of the fetus.

Labour progress during the first stage of labour was monitored in accordance with the WHO recommendations before 2018,[32] with an alert line (1 cm cervical dilation/hour) and an action line displaced at 4 hours.[33,34] According to the national guidelines, augmentation with oxytocin during the first stage could only be started if the action line was crossed, and after amniotomy.[31] Zhang's guideline was used in the first stage of labour at Stavanger University Hospital in 2015 and 2016.[35] During the second stage, oxytocin augmentation could be started at the discretion of the birth attendant when the contractions were considered insufficient. Also in accordance with national guidelines, the duration of the second stage was not recommended to exceed 3 hours and an operative delivery should be considered both in nulliparous and parous women after 60 minutes of active pushing.[31]

Oxytocin was administered as an intravenous infusion of 5 mU/minute, with dose increments of 2.5 mU every 15 minute to a maximum of 30 mU/minute, until progress of labour or regular contractions at a rate of 3–5/10 minute was achieved. A low-dose mobile epidural analgesia (bupivacaine or ropivacaine combined with fentanyl) was the first choice for pain relief.

2.1 | Statistical analyses

Median duration of the second stage of labour and interquartile ranges were estimated using survival analyses. Caesarean sections and operative vaginal deliveries during the active phase were censored. Women with a caesarean section in the first stage of labour were left censored and women with an active phase of second stage ≥120 minutes were right-censored and not included in the survival analyses. We considered oxytocin augmentation and epidural analgesia to be mediators, and stratified the analyses of estimated median duration in women with and without epidural analgesia, and with and without oxytocin augmentation.

One minus survival plots were created from Cox regression analyses and stratified into BMI groups. TGCS group 1 and 3 were analysed separately.

We calculated the unadjusted hazard ratio (HR) as an estimate of relative risk of delivery using Cox regression analyses. The normal weight group with BMI of 18.5–24.9 kg/m^2 was used as the reference group. We also performed analyses adjusted for maternal age. The assumptions of proportional hazards for the Cox regression analyses were checked using log minus log plots. Statistical analyses were performed with IBM SPSS statistics for Windows v.26.0 (IBM Corp.).

3 | RESULTS

During the study period, 68 963 women in TGCS 1 and 3 gave birth in the three hospitals. We excluded 18 192 women with missing BMI, leaving 50 711 women available for analysis, 23 516 in TGCS group 1 and 27 255 in TGCS group 3. The study population and selections into the survival analyses are presented as a flow chart (Figure 1). Maternal, labour and fetal characteristics are presented in Tables 1 and 2.

Increasing BMI was associated with shorter estimated median duration of the active phase of second stage in both TGCS groups. In TGCS group 1, the estimated median durations (interquartile range) were 44 (26–75), 43 (25–71), 39 (22–70), 33 (18–63), 34 (19–54) and 29 (16–56) minutes in BMI groups 1–6, respectively (Table 3). In TGCS group 3, the corresponding values were 11 (6–19), 10 (6–17), 10 (6–16), 9 (5–15), 8 (5–13) and 7 (4–11) minutes (Table 4). Figure 2 shows the probability of delivery in accordance with duration of the active phase illustrated as one minus survival plots. Tables 3 and 4 show the estimated median durations stratified into women with and without epidural analgesia, and in women with and without oxytocin augmentation. Increasing BMI was associated with shorter estimated median duration in both TGCS groups in the stratified analyses as well.

The overall estimated median duration was 40 (95% CI 39.2–40.8) minutes in women with missing BMI information versus 42 (95% CI 41.5–42.5) minutes in women with known BMI in TGCS group 1. Corresponding values in group 3 were 11 (95% CI 10.9–11.1) versus 10 (95% CI 9.9–10.1) minutes.

The unadjusted calculated HR as an estimate of relative risk of delivery increased with increasing BMI. The HR was 0.94 (95% CI 0.88–1.01) for the underweight group compared with normal weight women in TGCS group 1. The HR was 1.07 (95% CI 1.03–1.12) for the overweight group compared with normal weight women, and 1.23 (95% CI 1.15–1.31), 1.36 (95% CI 1.20–1.54) and 1.48 (95% CI 1.19–1.1) for obesity classes 1–3, respectively. Corresponding HR in TGCS group 3 was HR 0.92 (95% CI 0.86–0.98) for the underweight group, 1.09 (95% CI 1.05–1.12) for the overweight group and 1.19 (95% CI 1.13–1.25), 1.28 (95% CI 1.16–1.41) and 1.45 (95% CI 1.25–1.69) for obesity classes 1–3. Maternal age did not show a confounding effect in adjusted analyses.

4 | DISCUSSION

We found that higher BMI was associated with shorter estimated median duration of the active second stage in labour, in both TGCS group 1 and 3. In TGCS group 1, the estimated median duration was 14 minutes shorter in women with obesity class 3 than in normal weight women, and in TGCS group 3 the corresponding difference was 3 minutes. The association between higher BMI and estimated duration remained similar when stratifying women into groups with and without epidural analgesia and oxytocin augmentation.

A strength of the study was that the population was large, and that the women were included from three university hospitals over a period of 8 years. The second stage was managed according to the same national guidelines and the data were collected in the same structured electronic birth journal across all participating hospitals. The use of survival analyses reduces the risk of error due to operative delivery.

Only pre-pregnant BMI was recorded, not the BMI at the time of delivery. Information about pre-pregnant BMI was missing in 26% of cases. Overweight or obese women might be less inclined to give information about their weight to caregivers, but the missing data may also be due to lack of entry into the electronic birth journal. However, when analysing the overall estimated duration of the active second stage in the women with missing BMI, there were only small differences from the population available for analysis. Although Norwegian hospitals adhere to the national guidelines, exceptions may have occurred in the management of individual women, either intentionally or unintentionally. Another source of bias is that a greater proportion of women in high BMI groups were delivered by caesarean before reaching the second stage. However, more than 85% of nulliparous women in all BMI groups did reach the active second stage. Furthermore, the caesarean section rate was similar in obesity groups 1–3, and the bias may therefore only partly explain the differences in estimated duration of the active second stage.

Several previous studies have reported slower cervical dilation and increased duration of the first stage of labour in overweight and obese women.[23–25,36,37] Analysing mean or median duration of labour carries a risk of error, as all operative deliveries shorten the duration. Ellekjaer et al. investigated nulliparous women in a Danish cohort and found

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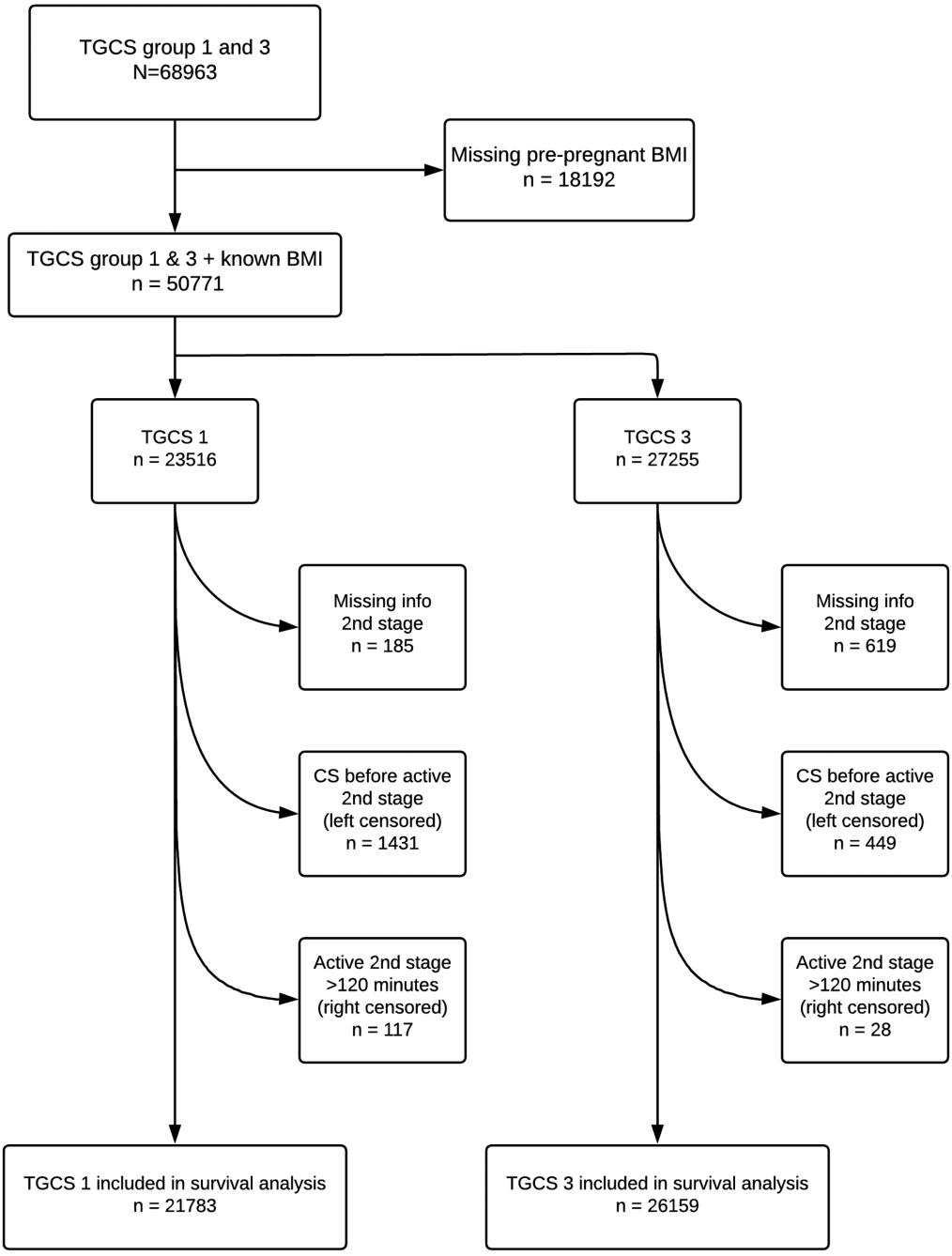

FIGURE 1 Flow chart illustrating the study population and women included in the survival analyses

no difference in the total length of active labour.[38] However, they also found that caesarean sections were performed earlier in labour for overweight and obese women and concluded that this may have influenced their results. Not attempting to correct for operative interventions could lead to the false conclusion that labour is shorter in obese women.

TABLE 1 Maternal, labour and newborn characteristics in TGCS group 1

	Underweight	Normal weight	Overweight	Obesity class 1	Obesity class 2	Obesity class 3
n = 23 516	1169 (5.0)	16 039 (68.2%)	4454 (18.9)	1368 (5.8)	360 (1.5)	126 (0.5)
Maternal age	27.2 (4.5)	28.7 (4.4)	28.6 (4.7)	28.5 (4.7)	27.9 (4.5)	28.2 (4.9)
Birthweight, g	3330 (426)	3480 (426)	3576 (438)	3583 (465)	3606 (476)	3604 (472)
Caucasian	726 (62.1)	11 943 (74.5)	3621 (81.3)	1166 (85.2)	317 (88.1)	105 (83.3)
Oxytocin augmentation	384 (32.8)	5978 (37.3)	1857 (41.7)	583 (42.6)	162 (45.0)	64 (50.8)
Epidural analgesia	551 (47.1)	8152 (50.8)	2603 (58.4)	882 (64.5)	253 (70.3)	100 (79.4)
Spontaneous delivery	840 (71.9)	11 287 (70.4)	2966 (66.6)	909 (66.4)	250 (69.4)	85 (67.5)
Instrumental delivery	274 (23.4)	3664 (22.8)	1032 (23.2)	289 (21.1)	61 (16.9)	25 (19.8)
Intrapartum CS	55 (4.7)	1088 (6.8)	456 (10.2)	170 (12.4)	49 (13.6)	16 (12.7)
CS active 2nd stage	9 (0.8)	255 (1.6)	95 (2.1)	33 (2.4)	10 (2.8)	1 (0.8)

Note: Values are mean (standard deviation) or *n* (%).

Abbreviations: BMI, body mass index; CS, caesarean section; TGCS, Ten Group Classification System.

TABLE 2 Maternal, labour and newborn characteristics in TGCS group 3

	Underweight	Normal weight	Overweight	Obesity class 1	Obesity class 2	Obesity class 3
n = 27 255	1129 (4.1%)	17 617 (64.6%)	5927 (21.7)	1910 (7.0%)	490 (1.8%)	182 (0.7%)
Maternal age	30.5 (4.4)	31.7 (4.3)	31.7 (4.5)	31.3 (4.7)	31.3 (4.9)	31.3 (4.9)
Birthweight, g	3446 (432)	3622 (442)	3719 (455)	3761 (492)	3766 (442)	3802 (494)
Caucasian	835 (74.0)	14 053 (79.8)	4674 (78.9)	1584 (82.9)	408 (83.3)	162 (89.0)
Oxytocin augmentation	55 (4.9)	1141 (6.5)	460 (7.8)	201 (10.5)	57 (11.6)	27 (14.8)
Epidural analgesia	227 (20.1)	3782 (21.5)	1400 (23.6)	607 (31.8)	179 (36.5)	96 (52.7)
Spontaneous delivery	1090 (96.5)	16 792 (95.3)	5616 (94.8)	1787 (93.6)	457 (93.3)	170 (93.4)
Instrumental delivery	25 (2.2)	537 (3.0)	184 (3.1)	58 (3.0)	18 (3.7)	5 (2.7)
Intrapartum CS	14 (1.2)	288 (1.6)	127 (2.1)	65 (3.4)	15 (3.1)	7 (3.8)
CS active 2nd stage	1 (0.1)	44 (0.2)	14 (0.2)	6 (0.3)	2 (0.4)	0 (0)

Note: Values are mean (standard deviation) or *n* (%).

Abbreviations: BMI, body mass index; CS, caesarean section; TGCS, Ten Group Classification System.

TABLE 3 Estimated median duration of active pushing phase in minutes (interquartile range) in TGCS group 1

	n	Overall	Epidural –	Epidural +	Oxytocin –	Oxytocin +
BMI <18.5 Underweight	1102	44 (26–75)	37 (22–63)	55 (32–84)	34 (22–54)	76 (51–98)
BMI 18.5–24.9 Normal weight	14 997	43 (25–71)	35 (21–58)	54 (31–84)	34 (20–53)	68 (43–98)
BMI 25–29.9 Overweight	4042	39 (22–70)	30 (17–54)	49 (26–82)	29 (17–48)	65 (37–97)
BMI 30–34.9 Obesity class 1	1214	33 (18–63)	24 (14–44)	43 (22–78)	25 (15–44)	61 (30–93)
BMI 35–39.9 Obesity class 2	319	34 (19–54)	25 (18–48)	39 (21–63)	25 (17–45)	46 (30–80)
BMI ≥49 Obesity class 3	109	29 (16–56)	19 (15–37)	32 (17–56)	21 (15–38)	38 (19–77)

Abbreviations: BMI, body mass index; TGCS, Ten Group Classification System.

Labour duration can be studied with survival methods with censoring of operative deliveries, as previously suggested by Vahratian et al.[39] In this way, the risk of this type of error is reduced.

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TABLE 4 Estimated median duration of active pushing phase in minutes (interquartile range) in TGCS group 3

	n	Overall	Epidural –	Epidural +	Oxytocin –	Oxytocin +
BMI <18.5 Underweight	1076	11 (6–19)	10 (6–17)	15 (9–28)	11 (6–18)	41 (20–74)
BMI 18.5–24.9 Normal weight	16 975	10 (6–17)	10 (6–15)	14 (8–25)	10 (6–16)	25 (13–55)
BMI 25–29.9 Overweight	5668	10 (6–16)	9 (5–14)	12 (8–22)	9 (5–15)	19 (10–42)
BMI 30–34.9 Obesity Class 1	1808	9 (5–15)	8 (5–13)	11 (7–20)	8 (5–14)	16 (8–32)
BMI 35–39.9 Obesity class 2	460	8 (5–13)	8 (4–12)	9 (5–15)	8 (4–12)	15 (8–51)
BMI ≥49 Obesity class 3	172	7 (4–11)	7 (4–10)	7 (4–13)	7 (4–11)	6 (4–17)

Abbreviations: BMI, body mass index; TGCS, Ten Group Classification System.

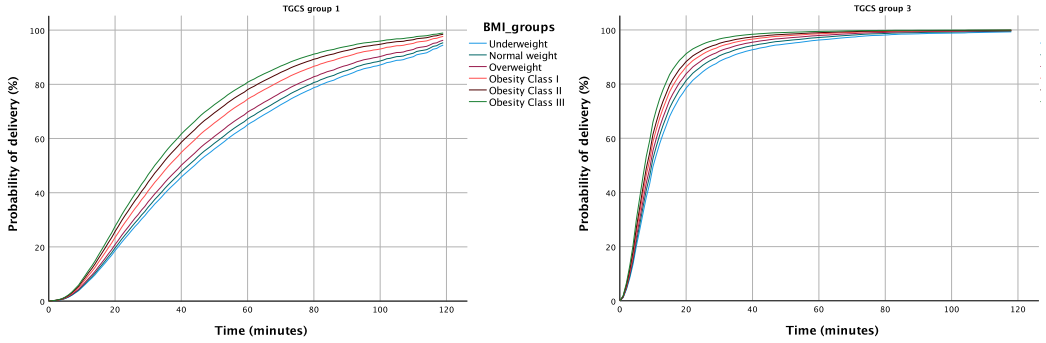

FIGURE 2 One-minus survival plots showing probability of delivery during active pushing phase differentiated into BMI groups. TGCS 1 (left) and TGCS 3 (right)

The second stage of labour has been the subject of fewer studies. One study reports no difference of duration in the second stage with increasing BMI,[26] and one study found that the second stage was prolonged with increasing BMI in multiparous women, but not in nulliparous women.[36] Carlhäll et al.[27] studied a large, contemporary Swedish cohort. They found that the estimated duration of the active phase of labour increased significantly with increasing BMI using survival analyses. As a secondary finding, they reported a shorter median duration of the second stage in obese women. However, survival methods were not employed in the analysis of the second stage, and they did not differentiate between the passive and active second stage.

Epidural analgesia and oxytocin augmentation influence duration of labour, and it is debated how to manage these variables when investigating labour duration. A previous study found an increased duration of the active second stage in women with epidural analgesia,[40] and this is in accordance with our findings. We considered oxytocin and epidural analgesia to be mediators rather than confounders. The associations between maternal age, epidural analgesia and oxytocin augmentation on BMI and the duration of the active second stage are illustrated in a directed acyclic graph (Figure 3). Maternal age is the only confounder with effect on both the independent and dependent variables. The causal associations are different for epidural analgesia and oxytocin augmentation.

High BMI may be associated with higher frequencies of epidural analgesia. Slow progress is an indication of oxytocin augmentation but this may also lead to shorter active second stage. Therefore, we stratified our analyses into groups with and without epidural analgesia and oxytocin augmentation and found similar associations in the stratified analyses (Tables 3 and 4).

The external validity of our results may be a matter for discussion. Norway, like the other Scandinavian countries, has a low caesarean section rate. However, to minimise this potential bias, we used survival methods. Furthermore, the mean BMI in Norway is lower than in USA and UK, but is similar to that in Germany, France and Italy.[1] The majority

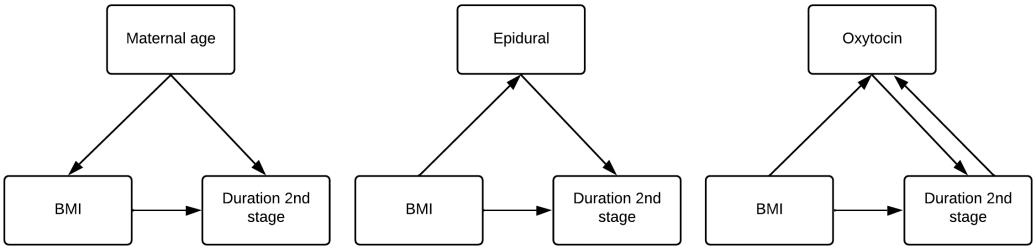

FIGURE 3 Directed acyclic graph (DAG) illustrating how maternal age, epidural analgesia and oxytocin augmentation may be associated with BMI and the active second stage of labour

of women in our study were Caucasian (Tables 1 and 2), and another study found that black women had a shorter second stage than did women of other ethnicities.[41]

The causal mechanisms of shorter active second stage in overweight and obese women remain unclear and difficult to determine. The shorter active second stage may be related to increased abdominal pressure with increasing BMI,[42] or perhaps increased strength when pushing.[43] One study found that adults with a history of obesity from adolescence tend to have a wider bony pelvis in adulthood,[44] which could facilitate the expulsion of the fetus. Another possible mechanism is that the increased abdominal pressure and infiltration of fat in the muscular pelvic floor may decrease its strength and resistance.[45] Yet another hypothesis could be that the presence of fat in the birth canal of obese women may delay the urge to bear down, thereby postponing active pushing until the head is lower in the maternal pelvis, which in turn may shorten the active second stage.

The information given upon overweight and obese women throughout their pregnancy often has negative connotations. The finding that they have shorter times of bearing down when they reach the active second stage may provide a small, but significant positive counterweight, both for the patient and the clinician.

Regardless of the causal mechanism, upon bearing down, the woman and her birth attendant can be motivated by evidence that her active second stage is likely to be shorter than that in normal weight women, and that the risk of emergency caesarean section in this stage is low, and similar to lower BMI groups (Tables 1 and 2). As decision making by the clinician is influenced by perceived risk,[29] disseminating the results of this study may reduce unnecessary interventions for overweight and obese women.

In conclusion, we found that increasing BMI was associated with shorter estimated median duration of the active second stage of labour.

CONFLICT OF INTERESTS

None declared. Completed disclosure of interest forms are available to view online as supporting information.

AUTHOR CONTRIBUTIONS

TBØ initiated the study and took part in writing of the protocol, statistical analyses and writing of the manuscript. RKS took part in writing of the protocol and writing of the manuscript. JK was responsible for data collection at Haukeland University Hospital and took part in writing of the manuscript. CT was responsible for data collection at Trondheim University Hospital and took part in writing of the manuscript. PvB was responsible for data collection at Stavanger University Hospital and took part in writing of the manuscript. TME took part in writing of the protocol, writing of the manuscript and the statistical analyses. All authors approved the final version and accepted responsibility for the paper as published.

ETHICAL APPROVAL

The study was carried out in accordance with the Declaration of Helsinki and was approved by the regional ethics committee in western Norway (REK 2020/109526).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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AOGS ORIGINAL RESEARCH ARTICLE

Judicious use of oxytocin augmentation for the management of prolonged labor

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Key words
Oxytocin augmentation, cesarean section, Ten group classification system, prolonged labor, estimated postpartum hemorrhage

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Conflict of interest
The authors have stated explicitly that there are no conflicts of interest in connection with this article.

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Abstract

Introduction. A protocol including judicious use of oxytocin augmentation was investigated to determine whether it would change how oxytocin was used and eventually influence labor and fetal outcomes. *Material and methods.* The population of this cohort study comprised 20 227 delivering women with singleton pregnancies ≥37 weeks, cephalic presentation, spontaneous or induced onset of labor, without previous cesarean section. Women delivering from 2009 to 2013 at Stavanger University Hospital, Norway, were included. Data were collected prospectively. Before implementing the protocol in 2010, oxytocin augmentation was used if progression of labor was perceived as slow. After implementation, oxytocin could only be started when the cervical dilation had crossed the 4-h action line in the partograph. *Results.* The overall use of oxytocin augmentation was significantly reduced from 34.9% to 23.1% ($p < 0.01$). The overall frequency of emergency cesarean sections decreased from 6.9% to 5.3% ($p < 0.05$) and the frequency of emergency cesarean sections performed due to fetal distress was reduced from 3.2% to 2.0% ($p = 0.01$). The rate of women with duration of labor over 12 h increased from 4.4% to 8.5% ($p < 0.01$) and more women experienced severe estimated postpartum hemorrhage (2.6% vs. 3.7%; $p = 0.01$). The frequency of children with pH <7.1 in the umbilical artery was reduced from 4.7% to 3.2% ($p < 0.01$). *Conclusions.* The frequency of emergency cesarean section was reduced after implementing judicious use of oxytocin augmentation. Our findings may be of interest in the ongoing discussion of how the balanced use of oxytocin for labor augmentation can best be achieved.

Abbreviations: BMI, body mass index; CS, cesarean section; TGCS, Ten group classification system; WHO, World Health Organization.

Introduction

Oxytocin augmentation has an important role in the management of labor (1). Wide variations in its use between countries and hospitals may reflect the lack of structured guidelines (2–6). Labor augmentation with oxytocin is often administered without a clinical indication and unstructured use is common (7,8). Increased uterine activity may cause fetal distress and intense surveillance is needed in laboring women stimulated with oxytocin (9,10). Incautious use of oxytocin is commonly cited in cases of obstetric malpractice and illustrates the need for further exploration (8,9,11).

Key Message

Implementation of a protocol of judicious use of oxytocin was associated with lower rates of emergency cesarean sections.

A definition of prolonged labor and explicit indications for oxytocin augmentation are warranted (1,7,12). Ideally, labor management should follow clear guidelines that are structured in an easy-to-use system (1,13). The World Health Organization (WHO) and the National Institute for Health and Clinical Excellence (NICE) recommend an active phase partograph with a 4-h action line for monitoring the progress of labor (14,15). Augmentation with oxytocin prior to confirming delay when the cervical dilation crosses the 4-h action line in labor is not recommended (14); however, the level of evidence for the recommendations is low.

The Ten group classification system (TGCS) differentiates women into 10 prospective, clinically relevant groups (13). Originally the system was designed to study cesarean section (CS) rates, but wider use is easy to implement and the differentiation also strengthens data quality when assessing other obstetrical outcomes (13,16).

To guide the use of oxytocin augmentation in our labor ward, a strict protocol was implemented using the WHO partograph. Prolonged labor was defined and augmentation with oxytocin indicated only when the cervical dilation crossed the 4-h action line. The aim of this study was to investigate whether judicious use of oxytocin augmentation would change how it was used and how it might influence labor and fetal outcomes.

Material and methods

Stavanger University Hospital has the only delivery unit in a geographical region that includes a population of 320 000 people. Information related to pregnancies and deliveries was collected prospectively and recorded in an electronic birth journal (Natus). The birth journal consists of structured variables and is continuously maintained for data entry and quality control. The study period was from January 2009 to December 2013. The study was approved by the regional ethics committee in western Norway (REK 2014/1912).

The main outcome was the frequency of emergency CS. Secondary outcomes were use of oxytocin augmentation, emergency CS due to fetal distress or dystocia, operative vaginal delivery, sphincter rupture, estimated postpartum hemorrhage >1000 mL, duration of labor >12 h, Apgar score <7 at 5 min, umbilical cord pH <7.00, and umbilical cord pH <7.10.

The study population comprised all women with singleton, term deliveries and cephalic presentations with a spontaneous onset of labor or induced labor in nulliparous and parous women without a previous CS (Figure 1; TGCS groups 1, 2a, 3, and 4a). CS was defined as a pre-labor or emergency procedure (13). Maternal body mass index (BMI) was based on pre-pregnancy weight.

Excerpt of the ten group classification system	
Group 1	Nulliparous, single, cephalic presentation, ≥37 weeks, in spontaneous labor
Group 2a	Nulliparous, single, cephalic presentation, ≥37 weeks, induced before labor
Group 3	Multiparous (excluding previous cesarean section), single, cephalic presentation, ≥37 weeks, in spontaneous labor
Group 4a	Multiparous (excluding previous cesarean section), single, cephalic presentation, ≥37 weeks, induced before labor

Figure 1. Description of the study population comprising the Ten group classification system, groups 1, 2a, 3 and 4a.

Estimated date of delivery was determined by a second trimester ultrasound scan (eSnurra) (17) or from menstrual data when no ultrasound examination was performed.

Start of labor was determined when the woman experienced regular and painful contractions. In 2009, the WHO partograph was introduced for routine use and start of the active phase of labor was defined when the woman had regular contractions and the cervix was dilated 4 cm and effaced. A clear definition of prolonged labor did not exist in the Department and the midwives and obstetricians individually used oxytocin for augmentation if they felt that labor was progressing slowly. The new protocol with judicious use of oxytocin was implemented 1 January 2010. Prolonged labor was defined when the cervical dilation crossed the 4-h action line, and only then could augmentation with oxytocin be administered. The protocol did not contain new guidelines for the use of oxytocin in the second stage of labor.

In labors with a spontaneous onset in nulliparous and parous women (groups 1 and 3), oxytocin augmentation was defined as oxytocin used to stimulate contractions after prolonged labor during the first stage of labor. Routine amniotomy was not performed during the active phase of labor, but always prior to oxytocin augmentation. The second stage of labor was defined as when the cervix was fully dilated, and the active phase of the second stage was defined as when maternal effort was added. An operative vaginal delivery was considered if the active second stage of labor exceeded 60 min. Malmström metal cup was the preferred device for operative vaginal delivery. Duration of labor was defined from the start of the active phase of labor until delivery.

Misoprostol 25 μg vaginally every 4 h up to a maximum dose of 100 μg/day over 2 days was used as an induction agent in women with Bishop score <6. In women with Bishop score ≥6, amniotomy was performed and oxytocin added if contractions were not established after 1–3 h. Oxytocin was never used as a primary induction agent. The use of oxytocin in induced labors of

nulliparous and parous women (groups 2a and 4a) included use of oxytocin to stimulate contractions before start of the active phase and/or after prolonged labor was defined in the first stage of labor.

An intravenous infusion of 5 IU (0.01 mg) oxytocin in 500 mL saline was administered. The infusion rate started at 6 mIU/min (30 mL/h), with a dose increment of 3 mIU/min (15 mL/h) every 15 min to a maximum of 40 mIU/min (180 mL/h) until progression in labor or regular contractions at a rate of three to five every 10 min was achieved. A combination of low-dose ropivicaine/fentanyl was used for epidural analgesia. Routinely, active management of the third stage of labor included intramuscular administration of 5 IU of oxytocin. Blood loss was visually estimated, and blood-soaked compresses were collected and measured when possible. Estimated blood loss exceeding 1000 mL was defined as severe postpartum hemorrhage. Sphincter rupture was defined as partial or complete tears of the anal sphincter muscles (grade 3–4 perineal tears).

The linear-by-linear association trend test was used in categorical data analyses, and continuous variables were compared using one-way analysis of variance with Bonferroni correction. Data were analyzed with the statistical software package SPSS statistics version 22.0 (IBM SPSS, Armonk, NY, USA) and *p*-values <0.05 were considered significant.

Results

In total, 24 134 women delivered at the hospital during the study period. The overall CS rate was 13.8%, of which 8.8% were emergency CS and 5.0% pre-labor CS. The study population comprised 20 227 (83.8%) deliveries: 6897 (28.6%) were nulliparous with spontaneous onset (group 1); 2144 (8.9%) were nulliparous induced (group 2a); 8967 (37.2%) were parous with spontaneous onset (group 3); and 2219 (9.2%) were parous induced (group 4a). The characteristics of the study population are presented in Table 1.

The mean maternal age was higher in 2013 than in 2009 or 2011 ($p < 0.01$) and the mean gestational age was younger in 2012 and 2013 than in 2009, 2010 or 2011 ($p < 0.05$). The frequency of induced labor increased significantly over this period. We did not observe any changes in maternal BMI or infant birthweight.

Changes in the use of oxytocin augmentation during the study period are presented in Table 2 for the total study population and subgroups. The use of oxytocin augmentation was significantly reduced in all groups over the study period.

The overall frequency of emergency CS declined from 6.9% to 5.3% ($p < 0.05$) and emergency CS performed due to fetal distress from 3.2% to 2.0% ($p = 0.01$). In subgroup analyses, the rate of emergency CS among nulliparous women with induced labor (group 2a) declined from 26.5% to 15.7% ($p < 0.01$). Furthermore, there was a trend toward a reduced frequency of CS performed due to fetal distress in all groups, which reached statistical significance among nulliparous women only (groups 1 and 2a). The frequency of CS due to prolonged labor did not change.

Table 2. Use of oxytocin in the study population of singleton, term deliveries and cephalic presentation in each of the four subgroups (Ten group classification system groups 1, 2a, 3 and 4a) from 2009 to 2013.

	%					
Years	2009	2010	2011	2012	2013	*p*-value[a]
Total study population	35.5	25.9	26.5	23.6	23.6	<0.01
Nulliparous, spontaneous (Group 1)	45.9	30.7	35.8	31.2	34.4	<0.01
Nulliparous, induced (Group 2a)	79.1	73.7	64.1	59.0	55.2	<0.01
Parous, spontaneous (Group 3)	12.3	5.8	7.6	5.6	6.7	<0.01
Parous, induced (Group 4a)	62.3	57.6	37.6	34.5	24.0	<0.01

[a]Linear trend analyses.

Table 1. Characteristics of the study population ($n = 20\ 227$) from 2009 to 2013.

Years	2009 ($n = 3926$)	2010 ($n = 4144$)	2011 ($n = 4113$)	2012 ($n = 4091$)	2013 ($n = 3953$)	*p*-value
Nulliparous women (%)	46.1	44.7	45.0	43.8	44.0	0.04[a]
Maternal age (years)	29.6	29.8	29.6	29.9	30.0	<0.01[b]
Gestational age (days)	282.0	281. 9	281.5	281.4	281.3	<0.01[b]
BMI (kg/m^2)	23.9	24.0	23.8	23.8	23.7	0.07[b]
Infant birthweight (g)	3567	3572	3569	3557	3578	0.30[b]
Induction of labor (%)	18.6	18.9	21.4	24.0	24.9	<0.01[a]

[a]Linear trend analyses.
[b]One-way ANOVA.

The frequency of sphincter rupture decreased among induced nulliparous women (group 2a) from 5.6% to 1.2% ($p < 0.01$). The frequency of women spending more than 12 h in active labor increased from 4.4 to 8.5% ($p < 0.01$). In subgroup analyses, the increase was statistically significant among nulliparous women (groups 1 and 2a). An increase in estimated severe postpartum hemorrhage from 2.6 to 3.7% ($p = 0.01$) was observed in the overall study population. Among women with a vaginal delivery, the frequencies of estimated severe postpartum hemorrhage were 2.2, 2.7, 2.6, 2.8, and 3.2% during each of the 5 years, respectively ($p = 0.1$). The increase in mean estimated hemorrhage was not significant: 354, 352, 352, 359 and 371 mL, respectively. Among women with a CS, the respective frequencies of estimated severe postpartum hemorrhage each year were 8.9, 11.8, 11.4, 9.4, and 13.2% ($p = 0.4$). In women with a CS, the increase in mean estimated hemorrhage was not significant: 625, 651, 630, 621 and 655 mL during each year, respectively. Blood transfusion rates among all deliveries in the delivery unit decreased by 3.4, 3.2, 2.1, 2.4, and 2.7% ($p < 0.01$), respectively, during each year of the study.

Blood samples from the umbilical cord were collected in 60.4, 57.9, 67.8, 65.8 and 73.6% of the study population from 2009 to 2013, respectively. The frequency of infants with pH <7.1 in the umbilical artery was reduced from 4.7% to 3.2% ($p < 0.01$), but the reduction in infants with pH <7.0 did not reach statistical significance ($p = 0.10$). There was a trend toward a reduced frequency of children with umbilical artery pH <7.1 in the pooled group that reached statistical significance in spontaneous, nulliparous women (group 1; $p < 0.05$). Changes in labor and fetal outcomes in the total study population are presented in Table 3. Subgroup analyses are available in Tables S1 and S2.

Table 3. Labor and fetal outcomes in the study population from 2009 to 2013.

	%					
Years	2009	2010	2011	2012	2013	*p*-value[a]
Emergency CS	6.9	5.9	6.0	6.7	5.3	<0.05
CS due to fetal distress	3.2	2.7	2.8	2.4	2.0	0.01
CS due to dystocia	2.2	1.8	2.1	2.5	1.7	0.75
Epidural analgesia	34.3	34.8	36.5	35.2	36.4	0.06
Duration of labor >12 h	4.4	5.8	7.0	8.0	8.5	<0.01
Operative vaginal delivery	14.8	14.0	13.5	14.0	15.5	0.42
Sphincter rupture	2.3	1.4	1.7	2.0	1.5	0.10
PPH >1000 mL	2.6	3.2	3.2	3.3	3.7	0.01
Apgar score after 5 min <7	0.8	0.7	0.8	1.0	1.0	0.17
pH umbilical cord <7.00	0.7	0.8	0.5	0.6	0.4	0.10
pH umbilical cord <7.10	4.7	4.8	4.2	3.5	3.2	<0.01

Duration of labor: from start of active phase of labor until delivery.
CS, cesarean section; PPH, estimated postpartum hemorrhage.
[a]Linear trend analyses.

Discussion

The frequency of labors augmented with oxytocin decreased significantly after implementation of judicious use of oxytocin in the obstetrical department. This change was associated with a reduced overall emergency CS rate and fewer CSs performed due to fetal distress.

Oxytocin is a drug with potential side effects and recent statements have focused on stricter protocols, recommending a medical indication for its use (8,18,19). The increased use of oxytocin is not only due to the rise in induced labor; rates above 50% among nulliparous women in spontaneous labor are reported (7,18). Several delivery units have tried to implement active management of labor with the intention of stopping the observed increase in CS rates and reducing the rate of prolonged labors (20). Importantly, active management of labor includes several elements in addition to active use of oxytocin: one-to-one care during the active stage of labor, routine amniotomy, and restricting the duration of the active stage of labor to 12 h (20). The rising and, at times, incautious use of oxytocin may be caused by too much focus on implementing the active use of oxytocin in obstetrical departments while overlooking the other aspects of active management of labor. Our finding that reduced use of oxytocin augmentation was not associated with an increase in the CS rate differs from earlier findings (2,21,22). This may reflect the complexity of designing and implementing a uniform guideline for the use of oxytocin augmentation during labor (1,3,14).

Changes in both the characteristics of the population, such as higher BMI and older maternal age, and obstetrical practice, such as more use of epidural and more induction of labor, may influence the risk of prolonged labor and CS (23). Our observed decrease in gestational age is probably associated with increased induction rates. More liberal use of induction in high risk women and more women with post-term pregnancies were induced because these guidelines changed during the study period. This implies a change over time in the population of the four TGCS groups studied, which might have biased our results. The role of oxytocin in the management of labor is essential. Still, after 40 years of administration of the drug, its optimal timing and use is yet to be revealed (24).

The importance of precise definitions of labor progression should be stressed (1). Prolonged labor depends on when the start of the active phase of labor is determined. By choosing the definition suggested by WHO, we proceeded to implement a common indication for the use of oxytocin and, subsequently, oxytocin augmentation was administered only when indicated. In advance, we arranged audits for all staff discussing the pros and cons, realizing that implementation of new routines in daily practice is challenging (25). Efforts were made before the protocol was accepted and approved. One midwife was responsible for the follow up of routines and the use of oxytocin was monitored monthly for quality assurance. A reduction in the frequency of women with stimulated labors was observed beginning in the first years after introduction of the new routines. The consistent use of the WHO partograph might have influenced the overall CS rate but would not explain the decreasing trend of CSs performed due to fetal distress. The declining trend in newborns with low umbilical artery pH was not observed until 2012 and 2013. This may be due to an increased vigilance concerning the maximum dose of oxytocin used and reduced overall use of oxytocin, particularly in the second stage of labor (26).

Previous studies have documented that oxytocin augmentation is associated with a shorter duration of labor, which is in accordance with our findings (5,21,24). Childbirth satisfaction is an important health outcome and it may be desirable to avoid long labors (27). However, a systematic review on women's satisfaction with childbirth did not find labor length to be an influencing factor (28). Another study concluded that early oxytocin augmentation for slow labor progression did not appear to be more beneficial than expectant management regarding women's perceptions of childbirth (29). To address this issue further, knowledge of the women′s experiences of childbirth before and after our study would have been of major interest and should be a focus of new studies. Long duration of labor and lower maximal dosing of oxytocin are both associated with an increased risk of postpartum hemorrhage (30). These findings are consistent with our observations and need further attention. However, in subgroup analyses the rate of prolonged labors increased, the difference being significant only among nulliparous women (groups 1 and 2a). The rates of estimated severe postpartum hemorrhage increased significantly only among parous woman (groups 3 and 4a) (data shown in Tables S1 and S2) and the overall transfusion rates in the delivery unit decreased.

Our study design has limitations. We cannot prove causality between oxytocin augmentation and labor outcomes in an observational study. In addition, the use of oxytocin was only recorded as a dichotomized variable; the duration of the augmentation or the maximum doses used were not available for analyses. The use of oxytocin in induced labor (groups 2a and 4a) includes both oxytocin used to stimulate contractions before the start of the active phase and/or after prolonged labor in the first stage of labor. The differentiation between oxytocin used as an induction agent or as an augmentation agent is difficult. Still, the overall decrease in the use of oxytocin was significant in women with induced labor, and we believe that this is a valuable observation. Prolonged labors may affect the frequency of chorioamnionitis, but this information was not recorded. Visual estimates of blood loss are crude, and we realize the inaccuracy of this method. Unfortunately, due to different databases, the blood transfusion rates were not available for subgroup presentation in the TGCS. Arterial blood sampling from the umbilical cord was performed in 67% of the delivering women, with an increased frequency later in the study period. This may have biased our results. Our findings should be generalized with caution because the data were collected from only one hospital. However, the data were checked regularly for quality control. The major strengths of the study were the high number of patients included and the differentiation of the population into subgroups according to the TGCS classification. The hospital serves a nonselected population and this strengthens the credibility of our observations. Continuous monitoring of the new procedure resulted in successful implementation. In this way, we introduced a clearly defined indication for the use of oxytocin augmentation.

In summary, implementation of a protocol clearly defining the start of active labor, prolonged labor, and indications for oxytocin use, was associated with decreased use of oxytocin augmentation. The rate of emergency CS and CS performed due to fetal distress decreased. More women experienced prolonged labor and estimated severe postpartum hemorrhage. Our findings may be of interest in the ongoing discussion of how balanced use of oxytocin for labor augmentation can best be achieved.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Table S1. Use of oxytocin (%) and labor characteristics in singleton, term deliveries and cephalic presentation among nulliparous women with spontaneous onset of labor (n = 6897; group 1) and induced labor (n = 2144; group 2a) from 2009 to 2013.

Table S2. Use of oxytocin (%) and labor characteristics in singleton, term deliveries and cephalic presentation among parous women with spontaneous onset of labor group 3 (n = 8967; group 3) and induced labor (n = 2199; group 4a) from 2009 to 2013.

OBSTETRICS

Sonographic prediction of outcome of vacuum deliveries: a multicenter, prospective cohort study

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BACKGROUND: Safe management of the second stage of labor is of great importance. Unnecessary interventions should be avoided and correct timing of interventions should be focused. Ultrasound assessment of fetal position and station has a potential to improve the precision in diagnosing and managing prolonged or arrested labors. The decision to perform vacuum delivery is traditionally based on subjective assessment by digital vaginal examination and clinical expertise and there is currently no method of objectively quantifying the likelihood of successful delivery. Prolonged attempts at vacuum delivery are associated with neonatal morbidity and maternal trauma, especially so if the procedure is unsuccessful and a cesarean is performed.

OBJECTIVE: The aim of the study was to assess if ultrasound measurements of fetal position and station can predict duration of vacuum extractions, mode of delivery, and fetal outcome in nulliparous women with prolonged second stage of labor.

STUDY DESIGN: We performed a prospective cohort study in nulliparous women at term with prolonged second stage of labor in 7 European maternity units from 2013 through 2016. Fetal head position and station were determined using transabdominal and transperineal ultrasound, respectively. Our preliminary clinical experience assessing head-perineum distance prior to vacuum delivery suggested that we should set 25 mm for the power calculation, a level corresponding roughly to +2 below the ischial spines. The main outcome was duration of vacuum extraction in relation to ultrasound measured head-perineum distance with a predefined cut-off of 25 mm, and 220 women were needed to discriminate between groups using a hazard ratio of 1.5 with 80% power and alpha 5%. Secondary outcomes were delivery mode and umbilical artery cord blood samples after birth. The time interval was evaluated using survival analyses, and the outcomes of delivery were evaluated using receiver operating characteristic curves and descriptive statistics. Results were analyzed according to intention to treat.

RESULTS: The study population comprised 222 women. The duration of vacuum extraction was shorter in women with head-perineum distance ≤25 mm (log rank test <0.01). The estimated median duration in women with head-perineum distance ≤25 mm was 6.0 (95% confidence interval, 5.2–6.8) minutes vs 8.0 (95% confidence interval, 7.1–8.9) minutes in women with head-perineum distance >25 mm. The head-perineum distance was associated with spontaneous delivery with area under the curve 83% (95% confidence interval, 77–89%) and associated with cesarean with area under the curve 83% (95% confidence interval, 74–92%). In women with head-perineum distance ≤35 mm, 7/181 (3.9%) were delivered by cesarean vs 9/41 (22.0%) in women with head-perineum distance >35 mm ($P < .01$). Ultrasound-assessed position was occiput anterior in 73%. Only 3/138 (2.2%) fetuses in occiput anterior position and head-perineum distance ≤35 mm vs 6/17 (35.3%) with nonoccput anterior position and head-perineum distance >35 mm were delivered by cesarean. Umbilical cord arterial pH <7.10 occurred in 2/144 (1.4%) women with head-perineum distance ≤35 mm compared to 8/40 (20.0%) with head-perineum distance >35 mm ($P < .01$).

CONCLUSION: Ultrasound has the potential to predict labor outcome in women with prolonged second stage of labor. The information obtained could guide whether vacuum delivery should be attempted or if cesarean is preferable, whether senior staff should be in attendance, and if the vacuum attempt should be performed in the operating theater.

Key words: cesarean delivery, labor, sonography, transabdominal ultrasound, transperineal ultrasound, umbilical artery blood samples, vacuum extraction

Introduction

The tension between optimizing neonatal outcome while promoting vaginal delivery is nowhere more pertinent than in the management of the second stage of labor. Prolonging the upper limit of what is acceptable for duration of the second stage of labor is found to reduce the frequency of cesarean delivery in nulliparous women.[1] While a higher likelihood of vaginal delivery represents a beneficial maternal outcome, this may not be without risk for the fetus and hence led to concerns from obstetricians.[2] Furthermore, equating vaginal delivery with optimal outcome is simplistic, as complicated vaginal deliveries are associated to damage to the pelvic floor and anal sphincter ruptures.[3,4] No choice is risk neutral and cesarean deliveries at low fetal head station are also associated with risk of maternal and fetal complications.[5-7] So, the goal of obstetric care in the second stage of labor must be to avoid cesarean deliveries where assisted or spontaneous vaginal delivery is likely to be safe and achievable. Unnecessary cesarean delivery has a cumulative effect as it is widely accepted that prevention of the primary cesarean delivery will have an important influence on subsequent deliveries.[8] Sonography has the potential to be helpful in deciscion-making.[9]

There are 130 million births worldwide every year, and 3-14% are operative vaginal deliveries with highest rates in high-resource countries.[10,11] Failed

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operative deliveries are reported to occur in 6.5% of vacuum extractions.[12] The determinants to achieve successful delivery and avoid fetal and maternal complications rely on both accurate assessments of fetal position and station, and on operator skill.[12] A consensus of current guidance is that operative vaginal delivery is not recommended above station 0 in relation to the ischial spines and that the duration of an operative vaginal delivery should not exceed 20 minutes.[13,14] Obstetrics, however, remains a largely subjective art. In clinical obstetrics the fetal head is considered engaged in the mother's pelvis when the leading part has reached the level of maternal ischial spine (station 0) based on digital examination.[15] Such clinical assessment is subjective, poorly reproducible, and unreliable.[16]

Fetal head position is more precisely examined with ultrasound than with clinical examinations.[17,18] In a transabdominal scan the fetal head is considered engaged when the biparietal diameter is below the maternal pelvic inlet.[19] Using transperineal ultrasound, fetal station can be assessed as head-perineum distance[20-22] or angle of progression.[23] The ischial spines cannot be seen on ultrasound, but station 0 was found to broadly correspond with head-perineum distance around 35 mm and angle of progression around 120 degrees.[24,25]

Prolonged attempts at vaginal delivery and failed operative vaginal deliveries are associated with increased risk of fetal and maternal complications.[26,27] Hence, greater diagnostic precision of fetal position,[18] descent,[28] and attitude[29] is warranted, and the recently described techniques of intrapartum ultrasound have the potential to improve accuracy of assessments[30] and to predict delivery mode.[31] The aim of this study was to assess if ultrasound measurements of fetal position and station can predict duration of vacuum extractions, mode of delivery, and fetal outcome in nulliparous women with prolonged second stage of labor.

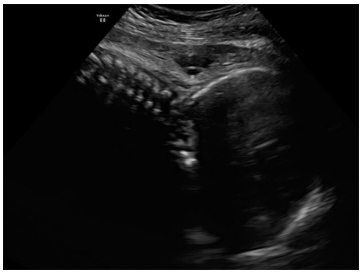
Materials and Methods

We conducted a prospective cohort study in nulliparous women with prolonged second stage of labor. Eligible for inclusion were those with a live singleton fetus in cephalic presentation and gestational age ≥37 weeks and <42 weeks. The second stage of labor was differentiated into a passive phase (<2 hours) and an active phase with pushing. Women were included and examined with ultrasound when the birth attendant diagnosed prolonged second stage of labor after at least 45 minutes of active pushing and vacuum extraction was considered. Repeated ultrasound examinations were not performed. Women were not eligible when fetal compromise was suspected due to abnormal or nonreassuring cardiotocography.

From November 2013 through July 2016, 223 women were recruited at Stavanger University Hospital, Norway (n = 135); University Hospital of Bologna, Italy (n = 34); Trondheim University Hospital, Norway (n = 16); Queen Charlotte's and Chelsea Hospital, Imperial College Healthcare National Health Service Trust, London, United Kingdom (n = 14); Lund University Hospital, Sweden (n = 9); Hvidovre University Hospital, Copenhagen, Denmark (n = 9); and University Hospital of Parma, Italy (n = 6). All participating centers had experience in transperineal scanning, and the ultrasound examiners were trained before the start of the study. The ethics committees approved the study with reference numbers Regional Ethics Committee 2012/1865 in Norway; 3348/2013 in Italy; Research Ethics Committee 15/LO/1341, ID project identification 169478 in the United Kingdom; Diarie Number 2012/808 in Sweden; and H-4-2014-038 in Denmark. All women gave informed written consent and the study was registered in Clinical Trials with identifier NCT01878591.

First a transabdominal scan was performed. Fetal head position was defined using a transabdominal or transperineal scan and categorized into occiput anterior (OA) position (Figure 1 and video clip 1) or non-OA position (posterior or transverse position) (Figures 2 and 3 and video clips 2 to 4). The position was described as a clock face with 12 hourly divisions; positions ≥10 o'clock and ≤2 o'clock were classified as OA.[32] Fetal station was assessed from the transperineal scan. The woman was placed in a semirecumbent position with the legs flexed at the hips and knees at 45-degree and 90-degree angles, respectively, and a transperineal scan performed after ensuring the bladder was empty (Figure 4). Angle of progression was measured in the sagittal plane as the angle between the longitudinal axis of the pubic bone and a line joining the lowest edge of the pubis to the lowest convexity of the fetal skull (Figure 5 and video clip 5).[23] Head-perineum distance was measured in a transverse transperineal scan (in the axial plane) as the shortest distance from the outer bony limit of the

FIGURE 1
Fetus in occiput anterior position



Sagittal transabdominal image with transducer in midline and occiput at 12 o'clock.

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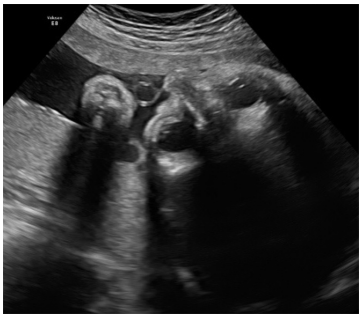
FIGURE 2
Fetus in occiput posterior position



Transverse transabdominal image with fetal nose at 10 o'clock and occiput at 4 o'clock.

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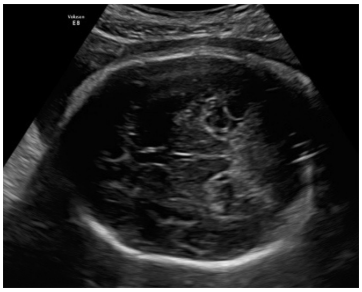
FIGURE 3
Fetus in left occiput transverse position



Transverse transabdominal image with occiput at 3 o'clock.

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fetal skull to perineum (Figure 6 and video clips 6 and 7). The transducer was placed between the labia majora (in the posterior fourchette), and the soft tissue compressed with firm pressure against the pubic bone without creating discomfort for the woman.[20,22,33,34] The transducer was angled until the skull contour was as clear as possible, indicating that the ultrasound beam was perpendicular to the fetal skull. A cineloop was stored and used to identify the shortest distance possible between the transducer (perineum) and the fetal skull. This distance represents the remaining part of the birth canal for the fetus to pass. The transperineal measurements were done between contractions, and all ultrasound measurements were done online 2-dimensionally in the labor room. Neither the women nor the birth attendant were informed about the ultrasound results. The ultrasound operator was not involved in clinical decisions or management of labor. Both obstetricians and midwives performed ultrasound examinations.

The ultrasound devices used were GE Voluson i (GE Medical Systems, Zipf, Austria) or GE Voluson S6 in Stavanger (GE Medical Systems), Norway, and GE Voluson i in Trondheim, Norway; Lund, Sweden; Copenhagen, Denmark; and Bologna, Italy (GE Medical Systems). In London, United Kingdom, Samsung PT60A and Samsung HM70 were used, and in Parma, Italy, a Samsung WS70 was used (Samsung, Seoul, Republic of Korea). The Malmstrom vacuum cup was the preferred device used in Stavanger and Trondheim, Norway; Lund, Sweden; London, United Kingdom; and Copenhagen, Denmark. In Bologna and Parma, Italy, the Kiwi cup was used. Body mass index was calculated from maternal height and prepregnant weight.

Cord blood was obtained by direct puncture of the umbilical artery without clamping of the cord, and acid-base analysis was performed immediately after collecting the samples. Umbilical artery pH <7.10, known to be associated with adverse neonatal outcome, was used as the cut-off level.[35,36]

The main outcome measure was duration of vacuum extractions. Secondary outcomes were frequencies of spontaneous deliveries, vacuum extractions, cesarean deliveries, and umbilical artery blood samples after birth (pH and base excess).

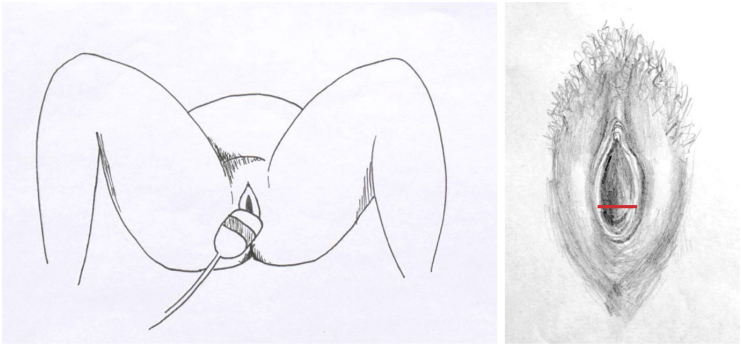
Power analysis

Our preliminary clinical experience assessing head-perineum distance prior to vacuum delivery suggested that we should set 25 mm for the power calculation, a level corresponding approximately to +2 below the ischial spines. The main outcome of the study was duration of vacuum extraction analyzed using survival analyses. The main predictor variable was head-perineum distance with a predefined cut-off at 25 mm to discriminate between the groups. To identify a hazard ratio (HR) as low as 1.5 with 80% power, 2-sided test, with alpha 5%, one third of the women with distance >25 mm and two thirds with distance ≤ 25 mm, we determined that 220 women should be included when expecting 10% censoring. The calculations were based on log rank test using the Freedman method and performed in a statistical program (Stata for Windows, Version 12; StataCorp, College Station, TX).

Statistical analyses

Variables were compared using χ^2 test and linear regression. To evaluate differences in the time interval from start of vacuum extraction to complete delivery according to head-perineum distance and angle of progression, we used Kaplan-Meier methods and Cox[37] regression analyses. The Kaplan-Meier method was used to generate survival plots, and we used head-perineum distance 25 mm as cut-off value in accordance with the power analysis. Cox regression was used to calculate HR as an

FIGURE 4
Placement of transducer measuring head-perineum distance



Woman is placed in semirecumbent position with legs flexed at hips and knees at 45-degree and 90-degree angles, respectively. Transducer placed transverse in posterior fourchette (red line) when head-perineum distance measured and rotated to sagittal plane when angle of progression measured.

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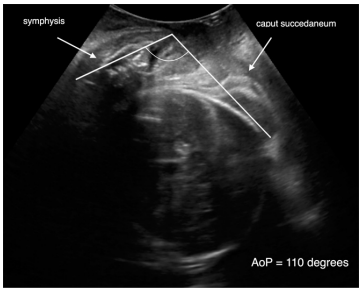
FIGURE 5
Measurement of angle of progression



Sagittal transperineal image illustrating measurement of angle of progression (AoP).

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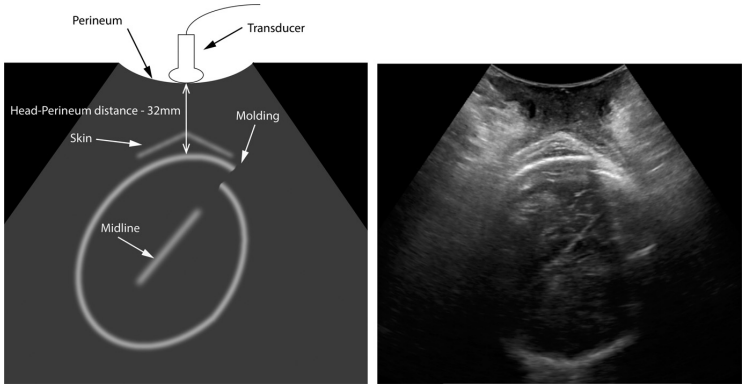
estimate for relative risk of delivery. In the Cox regression analysis we controlled for fetal position, prepregnancy body mass index, maternal age, induction of labor, epidural analgesia, and augmentation with oxytocin, and in an additional analysis we included institution as a covariate. Women with a spontaneous vaginal delivery were not included in the survival analyses and cesarean deliveries were right censored at the time of the decision to perform a cesarean delivery. Cox regression assumes proportional hazards, and this was evaluated by log minus log plots and tests of Schoenfeld residuals using the global and detailed ph test in Stata software. The assumption was satisfied ($P = .66$).

The association between head-perineum distance and delivery mode was analyzed at 5 different cut-off levels: ≤20, 21-25, 26-30, 31-35, >35. In a previous study 35 mm was found to correspond to station <0 by clinical examinations,[24] therefore, we focused on 35 mm as cut-off level and presented test characteristics related to this level. The association between angle of progression and delivery mode was analyzed at cut-off levels: <120, 120-129, 130-139, 140-149, ≥150 degrees. The associations between spontaneous and cesarean delivery related to head-perineum distance and angle of progression as continuous variables were evaluated using receiver operating characteristic (ROC) curves. These analyses were first performed as intention to treat because cesarean deliveries done without a vacuum attempt were included. Thereafter, we did separate analyses that only included cesarean deliveries performed after a vacuum attempt. The area under the curve was considered to have discriminatory potential if the lower limit of the confidence interval (CI) was >0.5. $P < .05$ was considered statistically significant.[38] Data were analyzed with the statistical software package SPSS Statistics, Version 23.0 (IBM Corp, Armonk, NY) and Stata for Windows, Version IC 13.

FIGURE 6
Measurement of head-perineum distance



Transverse transperineal image (frontal plane related to woman) illustrating measurement of head-perineum distance (double arrow). Head midline and molding are seen.

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Results

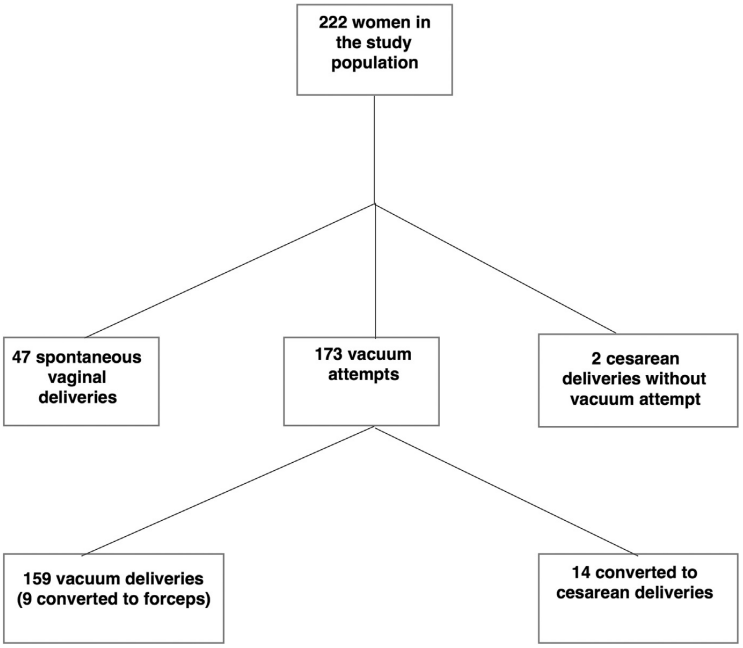
Study population

A total of 223 women were included and 1 woman was excluded because information about the main outcome was missing, leaving 222 women in the study population. Figure 7 is a flow chart illustrating delivery methods. Head-perineum distance was successfully measured in all women and angle of progression was successfully measured in 182/222 (82%). Characteristics of the study population differentiated between women with head-perineum distance ≤25 mm vs >25 mm are presented in Table 1.

Duration of vacuum extraction

Survival analyses were performed in women with a vacuum attempt. The duration of operative delivery was significantly shorter in women with head-perineum distance ≤25 mm (log rank test <0.01) (Figure 8). The estimated median duration (Kaplan-Meier analyses) in women with head-perineum distance ≤25 mm was 6.0 (95% CI, 5.2−6.8) minutes vs 8.0 (95% CI, 7.1−8.9) minutes in women with head-perineum distance >25 mm. The HR in Cox regression analyses was 0.56 (95% CI, 0.41−0.78) and adjusted value 0.58 (95% CI, 0.41−0.82). Head-perineum distance and angle of progression were analyzed as continuous variables in separate analyses. They were both significantly associated with the duration of operative vaginal deliveries after adjusting for covariates. Adjusted HR was 0.96 (95% CI, 0.94−0.98) for increasing head-perineum distance (Table 2) and 0.98 (95% CI, 0.97−0.996) for decreasing angle of progression. The center-adjusted HR estimate for increasing head-perineum distance was 0.93 (95% CI, 0.91−0.96) when the centers were included in the analysis. Duration was >20 minutes in 3 women and 3 women had >2 cup detachments. The median duration from the

FIGURE 7
Study population



Flow chart of study population.

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ultrasound examination to delivery was 25 (interquartile range 15-38) minutes.

Fetal station

Median head-perineum distance in women with fetal head station of 0 from clinical examination was 36 mm, mean 34 mm, range 15-49 mm, and interquartile range 7 mm. Median angle of progression in women with palpated station 0 was 132 degrees, mean 133 degrees, range 112-164 degrees, and interquartile range 24 degrees.

Delivery mode

Head-perineum distance and angle of progression were correlated (r = 0.48). The associations between delivery mode and head-perineum distance and angle of progression were categorized into 5 different groups as presented in Figures 9 and 10. The frequency of cesarean deliveries was 1% (1/99) in women with head perineum distance ≤25 mm vs 12% (15/122) in women with distance >25 mm ($P < .01$). Using head-perineum distance >35 mm as cut-off level, the sensitivity in predicting cesarean delivery was 56% (95% CI, 33−77%), false-positive rate was 16% (95% CI, 11−21%), positive predictive value was 22% (95% CI, 12−33%), and negative predictive value was 96% (95% CI, 92−98%). Head-perineum distance and angle of progression were significantly associated with a spontaneous delivery with area under the ROC curve 83% (95% CI, 77−89%) (Figure 11) and 75% (95% CI, 66−85%), respectively, but only head-perineum distance was significantly associated with cesarean delivery; area under the ROC curve was 83% (95% CI, 74−92%) for head-perineum distance (Figure 12) vs 56% (95% CI, 42−69%) for angle of progression.

We separately analyzed the association of cesarean delivery with head-perineum distance after a vacuum attempt. This occurred in 14/173 (8%) vacuum extractions and the results were similar to the intention-to-treat analyses. Head-perineum distance was associated with a cesarean with 83% (95% CI, 73−93%) vs angle of progression with 52% (95% CI, 38−66%).

Ultrasound-assessed position was OA in 73% and non-OA in 23% with missing information in 4%. In women with head-perineum distance ≤35 mm 7/181 (3.9%) were delivered by cesarean delivery vs 9/41 (22.0%) in women with head-perineum distance >35 mm ($P < .01$). In fetuses with OA position 6/162 (3.7%) were delivered by cesarean compared to 10/50 (20.0%) in non-OA position ($P < .01$). Only 3/138 (2.2%) of fetuses in OA position in combination with head-perineum distance ≤35 mm were delivered by cesarean and 6/17 (35.3%) with non-OA position in combination with head-perineum distance >35 mm were delivered by cesarean.

Umbilical artery blood samples

pH in the umbilical artery were measured in 184/222 (83%) cases. Only 1 newborn had pH <7.0 (pH 6.90 and base excess 18). This baby was delivered by vacuum and head-perineum distance before start of vacuum was 38 mm. pH <7.10 occurred in 10 newborns, and head-perineum distance was >35 mm in 8/40 (20.0%) compared to 2/144 (1.4%) in cases with head-perineum distance ≤35 mm ($P < .01$). Base excess was >12 in 3 cases in which head-perineum distance was >35 mm in 2.

Comment

Principal findings

The main finding in our study was a significant association between ultrasound-assessed fetal station and duration of vacuum extraction. Fetal station assessed with head-perineum distance and angle of progression predicted the probability of a spontaneous delivery, but only head-perineum distance predicted cesarean delivery. We observed significant association between low umbilical cord pH and head-perineum distance >35 mm.

The importance of these findings differs in high and low resource countries.

TABLE 1
Characteristics of study population

	Head-perineum distance ≤25 n = 99		Head-perineum distance >25 n = 123	
Maternal characteristics				
Maternal age, y	29	20–43	30	17–41
Prepregnant body mass index	23	18–39	24	18–39
Gestational age, wk	40	38–42	40	37–42
Labor characteristics				
Induction of labor	30 (30)	–	43 (35)	–
Epidural analgesia	80 (81)	–	95 (77)	–
Oxytocin augmentation	72 (73)	–	98 (80)	–
Characteristics of newborn				
Birthweight, g	3660	2570–4665	3650	2152–4930
5-min Apgar score	10	7–10	10	5–10
pH in umbilical artery, n = 184	7.24	7.09–7.43	7.24	6.90–7.40
Birth characteristics				
Bleeding, mL	400	100–2000	400	100–3400
Third- and fourth-degree anal sphincter tears	8 (8)		6 (5)	

Values are median, n (%), or range.
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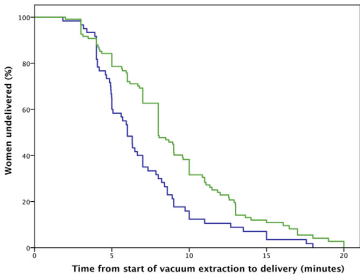
Firstly, the transperineal scan requires little training and can be undertaken with the type of ultrasound equipment frequently found in many delivery units worldwide. Thus, the technique is generalizable. In high-income countries, the benefit of the technique is 3-fold: (1) a previously subjective and unreproducible measurement is converted into an objective and recordable measure; (2) knowledge of the likely difficulty and duration of labor will determine the seniority of the operator and the setting of the delivery; and (3) the likelihood of cesarean delivery can be discussed with the woman and a decision made in advance not to proceed with a potentially futile attempt at vacuum delivery.

In many low- and mid-resource countries there is an increase in cesarean rates and declining use of operative vaginal deliveries, including vacuum.[10,39] In the United States a declining trend is also observed.[40] In low-resource countries cesarean delivery is associated with increased risk of maternal complications and high risk of uterine rupture in subsequent pregnancies.[41] Training of clinicians in vacuum deliveries might reduce the frequency of late-stage cesarean deliveries[40,42] and use of intrapartum ultrasound might add important information and reassure clinicians that a vacuum attempt at low stations has low risk of failure. New studies in low-resource settings are necessary.

FIGURE 8
Duration of vacuum extractions



Kaplan-Meier plot of time from start of vacuum extraction to delivery within 20 minutes differentiated into those with head-perineum distance ≤25 mm (blue) and >25 mm (green). Women who were delivered by cesarean were censored at time when decision to convert to cesarean was done ($P < .01$; log rank test).

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Clinical significance

We found that head-perineum distance ≤20 mm was associated with a high probability of a spontaneous delivery (Figure 9), and birth attendants might be patient in these situations as long as the fetal heart rate is normal. In a previous study head-perineum distance >35 mm corresponded to station ≥0,[24] and this finding agreed well with our new study (mean head-perineum distance 34 mm and median head-perineum distance 36 mm at clinically assessed station 0). It is usually not recommended to perform an operative vaginal delivery at levels above this station.[13] We found that the probability of cesarean in women with head-perineum distance >35 mm was 22% and 35% if it was combined with a non-OA position. A failed operative vaginal delivery is associated with risks for the mother and the fetus and a fearful experience for the woman. Our study

TABLE 2
Cox regression analysis for predicting duration of vacuum extraction in nulliparous women with slow progress in second stage of labor

	Unadjusted HR	95% CI	Adjusted HR	95% CI
Head-perineum distance[a]	0.96	0.94–0.98	0.96	0.94–0.98
Body mass index[a]	1.05	1.004–1.09	1.05	1.01–1.10
Maternal age[a]	0.99	0.97–1.03	1.00	0.96–1.03
Fetal position (n = 212)				
Occiput anterior (reference)	1.00	—	1.00	—
Nonoccput anterior	0.46	0.32–0.68	0.56	0.38–0.84
Induction of labor				
No (reference)	1.00	—	1.00	—
Yes	0.97	0.69–1.36	1.10	0.76–1.60
Epidural analgesia				
No (reference)	1.00	—	1.00	—
Yes	0.69	0.47–1.03	0.73	0.49–1.10
Augmentation with oxytocin				
No (reference)	1.00	—	1.00	—
Yes	0.75	0.52–1.09	0.87	0.59–1.29

HR with CI not crossing 1.0 were assumed significant.

CI, confidence interval; *HR*, hazard ratio.

[a] Analyzed as continuous variable.

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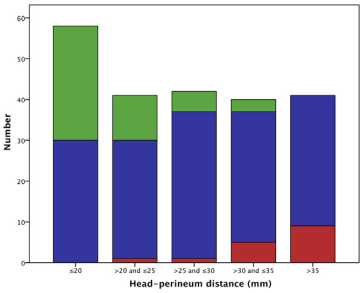
FIGURE 9
Delivery mode related to head-perineum distance



Distribution of spontaneous (green), operative vaginal (blue), and cesarean (red) deliveries in relation to head-perineum distance in nulliparous women with prolonged second stage of labor.

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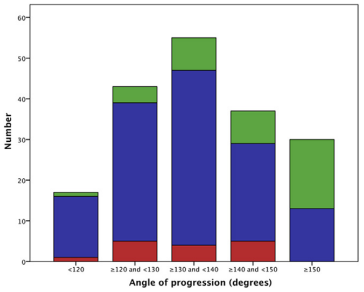
confirms that vacuum deliveries at high station are associated with a high failure risk, but at head-perineum distance levels <35 mm there is very good chance (96%) of a vaginal delivery. Another important finding is that pH <7.10 was more commonly observed among cases with head-perineum distance >35 mm. Although our study did not include fetuses with suspected compromise before start of vacuum, a significantly lower pH in cases with greater head-perineum distance might be explained by the longer duration of vacuum extractions at higher levels.

Research implications

Labor progress in the second stage of labor is evaluated by fetal descent and traditionally assessed by clinical assessment of station.[43] In 1977 Lewin et al[44] assessed fetal head station by ultrasound. They measured the distance from the fetal head to the sacral tip. Barbera et al[23] suggested angle of progression as a measure of head descent and found that an angle of >120 degrees was associated with subsequent spontaneous vaginal deliveries. Sonographically assessed head station has already been shown to be associated with duration of labor and delivery mode in nulliparous women with prolonged first stage.[33,34] Kalache et al[45] evaluated 41 women with prolonged second stage of labor, but included only the 26 women with OA position in the final analyses. They found that angle of progression >120 degrees was associated with a spontaneous delivery or an easy vacuum extraction.[45] Henrich et al[46] studied 20 women and found that head direction with respect to the long axis of the symphysis was associated with a successful operative vaginal delivery. Sainz et al[47] found that angle of progression <105 degrees and "head-down" direction before vacuum extraction was very unfavorable. Bultez et al[14] measured angle of progression in 235 women immediately before vacuum extraction. Duration of extraction exceeding 20 minutes or detaching of the vacuum cup >3 times were defined as failed vacuum extraction. The area under the ROC curve for predicting failure of vacuum extraction was 67% (95% CI, 57–77%) with optimal cut-off at 146 degrees. Our results cannot be directly compared with this study

FIGURE 10
Delivery mode related to angle of progression



Distribution of spontaneous (green), operative vaginal (blue), and cesarean (red) deliveries in relation to angle of progression in nulliparous women with prolonged second stage of labor.

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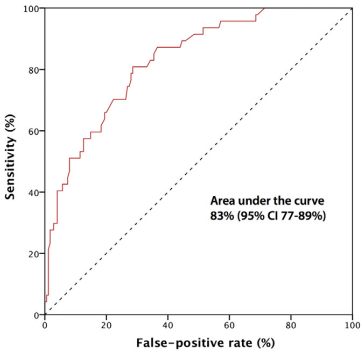
FIGURE 11
ROC-curve illustrating prediction of spontaneous deliveries



Receiver operating characteristic curves for head-perineum distance in prediction of spontaneous deliveries in women with prolonged second stage of labor.

CI, confidence interval.

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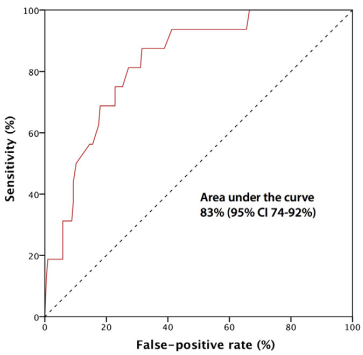
because our prespecified outcome was different. We found that head-perineum distance predicted cesarean delivery with area 83% (95% CI, 74−92%) under the ROC curve. It should be noted that in our study the duration of vacuum extraction exceeded 20 minutes in only 3 women, 3 women experienced >2 detachments, and that the frequency of cesarean after a vacuum attempt was 8%. In the original studies angle of progression was only used in OA fetuses. In our study, all positions were included. The third cardinal movement is different in occiput posterior positions[48,49] and this might explain why angle of progression did not predict cesarean. Because varying cut-off levels for the angle of progression in predicting cesarean deliveries are suggested in previous studies (from 120-146 degrees),[14,45] we decided to investigate angle of progression as a continuous variable.

FIGURE 12
ROC curve illustrating prediction of cesarean deliveries



Receiver operating characteristic curves for head-perineum distance in prediction of cesarean deliveries in women with prolonged second stage of labor.

CI, confidence interval.

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Head-perineum distance is easy to measure and can be used at all stations. The transabdominal transducer should be placed in the posterior fourchette and pressed until resistance against the pubic arches is achieved. Repeatability has been investigated in a previous study. The intraobserver variation was within 3 mm in 87%, and the interobserver variation was within 3 mm in 61%. The limits of agreement for intraobserver variation were −3.0 to 5.3 mm, and for interobserver agreement −8.5 to 12.3 mm.[20] A randomized study is warranted, but it might be difficult to perform because adverse fetal outcomes are fortunately rare. It is shown that women prefer ultrasound examinations before vaginal examination,[50,51] and maternal experiences of fear and pain might be used as outcomes in a future randomized study.

Strengths and limitations

Strengths of this study are the multicenter design, inclusion of only nulliparous women with prolonged second stage in the active phase of labor, and that the ultrasound examiners and the birth attendants were blinded to each other's findings. Limitations of the study were that some centers had few inclusions and that different vacuum devices were used. The study period was long with relatively few inclusions/months because it was often difficult to find ultrasound examiners not involved in the clinical care, and the integrity of the study relied on study examinations not biasing clinical decisions.

In measuring angle of progression, the complete length of the symphysis and the skull contour should be visualized on the same image; this failed in 18% of the cases. Women could be included after 45 minutes of active pushing. In the Norwegian guidelines operative delivery is recommended after 1 hour of active pushing.[52] This period differs from recommendations in many other countries and might affect the external validity of the study since the majority of participants were Norwegian women. The final decision of delivery method was based on subjective considerations of the responsible physician, and difficult to standardize. The study design was observational, and local guidelines should be followed.

Conclusion

In summary, ultrasound measurement in women with prolonged second stage of labor might predict duration of assisted vaginal delivery and the likelihood of cesarean delivery, and was associated with fetal acid-base status. We did not examine the clinical impact of this information nor did we attempt to change clinical decision-making. This work sets the scene for further studies of management in prolonged second stage of labor.

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