SIMILARITIES IN MOTHER-DAUGHTER LABOUR AND BIRTH CHARACTERISTICS: A TWO-GENERATION MATCHED COHORT STUDY

by

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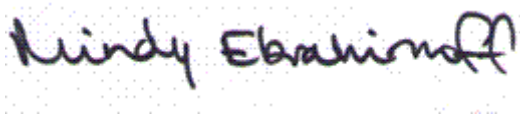

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Abstract

Physiological length of labour is highly variable and population norms have low sensitivity and specificity for individuals. Care practices for nulliparous women may be differentiated by using their mothers' first birth labour progress histories. The aim of this study was to investigate mother-daughter labour and birth characteristics and the influence of mothers' labour length on their nulliparous daughters' first births.

The aim was achieved by conducting the research in four stages: a systematic review of inter- and intragenerational influences on pregnancy and birth outcomes; a summary review of medical record-keeping and a literature review on the agreement of maternal recall of birth outcomes with hospital birth records; a prospective comparative study of agreement of maternal recall of first birth events and hospital birth records; and a matched cohort study of mother-daughter labour and birth characteristics focusing on length of labour and birth outcomes.

The systematic review of inter- and intragenerational influences on pregnancy and birth outcomes showed evidence of maternal, paternal and familial influences on pregnancy and birth outcomes in offspring. The literature review on the agreement of maternal recall of birth outcomes with hospital birth records showed that women remember important perinatal events even many years after giving birth. The empirical studies were conducted in Israel. In the first study, maternally recalled perinatal events were compared to archived hospital data. Eligible women (those who had given birth to their first child in those hospitals where the research was taking place and were willing to take part in the study) received a questionnaire, participant information sheet and consent form. Archived birth records were retrieved and compared for agreement with recalled data.

In the second study, using a matched cohort study design, nulliparous (index) women of >32 weeks' gestation attending antenatal clinics in either of two hospitals were recruited. Eligible women received a questionnaire, participant information sheet for themselves and their mothers, and an individual consent

form. Mothers' perinatal information was collected from questionnaires. Daughters' perinatal information was collected from electronic hospital records.

Findings for the maternal recall study showed that maternal recall of distant first birth events is remarkably in agreement with hospital birth records, with highest measures for mode of delivery and infant birth weight.

Univariate logistic regression analysis for the mother-daughter matched cohort study showed that daughters of mothers who had had long labours were more likely to have long labours themselves [OR 1.91 (95% CI 1.19, 3.05), $p = 0.007$]. Multivariable logistic regression analysis indicated that mothers' length of labour [OR 1.88 (95% CI 1.12, 3.17)] and daughters' age [OR 1.08 (95% CI 1.02, 1.14)], weight gain in pregnancy [OR 1.10 (95% CI 1.04, 1.16)] and non-use of anaesthesia [OR 0.27 (95% CI 0.12, 0.60)], were statistically significant factors for daughters' length of labour, with sensitivity, specificity, and positive and negative predictive values of 74%, 56%, 66%, and 64%, respectively. A linear regression model for time interval categorisations in labour (0-12 hrs, 12-18 hrs, 18+ hrs) demonstrated that daughters' length of labour is associated with mothers' length of labour in the 12-18 hour category, daughters' age, weight gain in pregnancy and use of anaesthesia. The model explained 11% ($R^2 = 0.11$) of the variance in daughters' length of labour with an F-test of overall significance indicating that the relationship is statistically significant ($F(5,285) = 6.75$, $p < 0.001$).

Length of labour in mothers' first birth reasonably predicts length of labour in their nulliparous daughters. This work presents an important endeavour using empirical data to promote an individual approach to childbirth within the hospital setting. Clinical decisions made for healthy women in labour are often driven by standardised criteria based on population norms. Practitioners could inquire about familial labour patterns as an additional heuristic to guide practice, alongside formal evidence and the signs and symptoms exhibited by the individual woman.

Key words:
Mother-daughter; length of labour; labour progression; labour duration; birth management; birth outcomes; familial.

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This research was conducted from the archives at the Sourasky Medical Center and Ma'aynei Hayeshua Hospital medical record collections. I am grateful to the staff at both locations for providing assistance with the acquisition of data.

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Glossary of Terms, Definitions and Abbreviations

Anaesthetic: A drug used to prevent pain during surgery or other procedure.

Antenatal or Antepartum: Events before birth.

Apgar score: A system used to assess the condition of the baby during the first few minutes of birth.

Artificial rupture of membranes: (AROM), also known as an amniotomy, may be performed by a midwife or obstetrician to induce or accelerate labour.

Assisted birth (instrumental birth/operative vaginal delivery): When special instruments (forceps or ventouse) are used to help deliver the baby during the pushing part of labour.

BW: Birth weight.

Caesarean section/caesarean delivery: The surgical removal of an infant from the uterus.

Cervix: The opening between the uterus and vagina that opens during labour to allow birth.

Cervical os: The opening in the lower part of the cervix between the uterus and vagina.

Clinical guidelines: Statements based on properly researched evidence which help healthcare professionals and patients to make decisions about medical care and treatments.

Contraction: When muscles tense and shorten it is called a contraction.

CS: Caesarean section (or caesarean delivery).

Dummy variable: Dummy variables are a series of dichotomous variables created in SPSS so that regression analysis can be performed using a categorical (nominal or ordinal) variable with more than two categories.

Dystocia: Means ‘difficult’. May be associated with shoulder dystocia, or labour dystocia (protracted labour).

Effacement: Thinning of the cervix that occurs in preparation for labour and delivery.

EHR: Electronic health record (system).

EFM: Electronic foetal monitoring involves the use of an electronic foetal heart rate (FHR) monitor to record the baby's heart rate.

Epidural: Used for pain control during labour and delivery.

Estimated date of delivery (EDD): This is initially based on the LMP (last menstrual period) then, usually, from a dating scan undertaken at around the 12th week of pregnancy.

Foetus (or Fetus): The developing organism in the uterus from the ninth week of pregnancy until the end of pregnancy; the unborn baby.

Forceps: See ‘assisted birth’ and ‘ventouse’.

Gestation or gestational age (GA): The completed weeks of pregnancy (not months).

Gravid: Pregnant.

Gravidity (also see parity): The number of times a woman has been pregnant, including the current pregnancy. This is regardless of the outcome of the pregnancies (for example, it includes miscarriages).

IBW: Infant birth weight.

Intrapartum: Events during labour.

Intrauterine: Within the uterus.

Induction of labour: Labour that is artificially induced by various means.

In vitro fertilisation (IVF) ***(Latin: ‘under glass’)*:** Where egg(s) harvested from the mother are fertilised in the laboratory with the father’s or a donor’s sperm.

Intrauterine growth retardation (IUGR): Foetus with an estimated weight below 10th percentile.

Labour: Childbirth is described in three stages. The first stage is when the neck of the womb (cervix) opens to 10 cm dilated. The second stage is when the baby moves down through the vagina and is born. The third stage is when the placenta (afterbirth) is delivered.

LIBW: Low infant birth weight.

LoL: Length of labour (used in tables and figures).

Midwife: A practitioner responsible for providing midwifery care to women during the antenatal, intrapartum and postnatal periods.

Miscarriage: Loss of a pregnancy that occurs before 20 weeks of pregnancy.

MR: Maternal recall.

Multigravida (or Multip): A pregnant woman who is not in her first pregnancy. A grand multip is a woman who has had a minimum of five births.

Multiple pregnancy: Pregnancy with more than one foetus.

Neonate/neonatal: The newborn baby.

Nullipara: A woman who has never delivered.

Obstetric care (maternity care): The medical care pregnant women receive throughout their pregnancy and during delivery.

Parity (see also gravidity): Refers to the number of live births plus stillbirths a woman has had.

Perinatal: Occurring at, or near the time, of birth.

Physiological first, second and third stages (see 'labour'): Natural, without the use of drugs.

Placenta: Tissue that provides nourishment to and takes waste away from the foetus.

Positive: +ve (in tables).

Negative: -ve (in tables).

PIS: Participant information sheet, given to mothers and daughters during the research phase.

Postdate pregnancy: A pregnancy that goes past the due date. The definition is two weeks past the due date (the due date is 40 weeks' gestation, postdate is 42 weeks).

Postpartum: The maternal period after delivery.

Premature or preterm (Prem): Referring to labour or delivery before 37 completed weeks of gestation.

Prenatal: Existing or occurring before birth.

Primigravida (Primip): A woman who is pregnant for the first time.

PROM: Premature rupture of membranes, the breakage of the amniotic sac before the onset of labour.

Small for gestational age (SGA): Newborns with weight below the 10th percentile for gestational age.

SiLC: Similarities in Labour and Childbirth - this study.

Spontaneous rupture of the membranes: When the 'waters break' during or after the onset of labour.

Term (gestation): When pregnancy is completed within 37-42 weeks.

Ultrasound: A scanning technique using high-frequency sound waves to provide images inside the uterus and other internal organs.

Uterus: A muscular organ located in the female pelvis that contains and nourishes the developing foetus during pregnancy.

Ventouse (also known as vacuum-assisted vaginal delivery or vacuum extraction) (see 'assisted birth'): A method to assist delivery of a baby using a vacuum device. It is used in the second stage of labour if it has not progressed adequately. It may be an alternative to a forceps delivery and caesarean section.

VIF: Variance inflation factor.

WHO: World Health Organization.

List of Oral Presentations and Posters of Work Contained in this Thesis

Ebrahimoff, M., Many, A., Downe, S. & Hall-Moran, V. (2015). “A systematic review of inter- and intra-generational influences on pregnancy and birth outcomes”. Paper presented at the Normal Labour and Birth 10th Research Conference, June 2015, Grange-over-Sands, Lake District, UK.

Ebrahimoff, M., Many, A. & Downe, S. (2016). “Length of labour in 2016. Does duration in the 2nd stage really matter?” Paper presented at the Israel Midwives Association (IMA) Second Stage of Labour – Highlights and Innovations Conference, November 2016, Jerusalem, Israel [in Hebrew].

Ebrahimoff, M., Many, A., Downe, S., Tishkovskaya, S. & Hall-Moran, V. (2017). “Agreement between maternal recall of distant first pregnancy and birth events with hospital birth records”. Paper presented at the Lis Maternity Hospital Research Conference, 30 March 2017, Tel Aviv, Israel [in Hebrew].

Ebrahimoff, M., Many, A., Downe, S., Tishkovskaya, S. & Hall-Moran, V. (2017). “Agreement between maternal recall of distant first birth events with hospital birth records: a cohort study”. Poster presented at Midwives – Making a Difference in the World. 31st ICM Triennial Congress, 18-22 June 2017, Toronto, Canada.

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Ebrahimoff, M., Downe, S. & Many, A. (2017). “Ethics, autonomy and normal childbirth in hospital: escalating technology use and medicalisation of birth in Israel”. Paper presented at the National Conference for Midwives, November 2017, Rambam Medical Center, Haifa, Israel [in Hebrew].

Ebrahimoff, M., Many, A. & Downe, S. (2017). “Length of labour in 2017. Does duration in the 2nd stage really matter?” Paper presented at the 3rd World Conference on Midwifery and Women’s Health, 13-14 November 2017, London, UK.

Ebrahimoff, M., Many, A., Downe, S. & Hall Moran, V. (2017). “A systematic review of inter- and intra-generational influences on pregnancy and birth outcomes.” Paper presented at the 3rd World conference on Midwifery and Women’s Health, 13-14 November 2017, London, UK.

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Ebrahimoff, M., Many, A., Downe, S., Tishkovskaya, S. & Hall-Moran, V. (2019). “Similarities in mother-daughter labour and birth characteristics: a two-generation matched cohort study”. To be presented at the International Maternity Expo, 12-13 November 2019, London, UK *(scheduled).*

Chapter One: Introduction to the Thesis

1.1 Introduction

This thesis explores similarities in mother-daughter first birth labour and birth characteristics. In many hospitals today, labour progress relies on time parameters and cervical dilation measurements to determine normality. When time parameters are unmet, labour is identified as pathological, justifying medical intervention which in turn may lead to increased levels of assisted and operative births. Internationally, there is evidence of a worrying increase in rates of birth by caesarean section. This thesis examines the current knowledge and theories of labour progress and explores familial mother-daughter patterns of labour and childbirth.

This first chapter presents a brief overview of the study background for the thesis. It will begin by describing the issue of risk identification in labour, and the problem of over use of interventions during childbirth, due to the application of population based evidence to individual labouring women. In addition, the effect of medicalisation and over use of risk-based management in this context is discussed. The rationale for the use of familial birth characteristics as a basis for predicting the progress and outcomes for individual women and babies is then explored. The main focus of the thesis and the research aim and objectives are described. Phases of the thesis design are portrayed and the structural framework and scope of the research are shown. Finally, the significance of the research and intended contribution to knowledge are explained.

1.2 Risk Identification in Labour and Birth

There is no dispute as to the need to offer intervention in pregnancy and labour when overt pathology occurs. The most commonly used approach to determining who needs such interventions is based on formal or informal risk assessment. However, attempts at risk scoring to discriminate between those who are and those who are not at risk have generally failed to discriminate clearly between those who do and who do not need therapeutic interventions. Generally, risk factors show low sensitivity, low specificity and unreliable predictive values (Enkin *et al*., 2000:51). In addition to composite scoring systems, researchers have noted an association amongst specific characteristics amongst subsequent pregnancies in the same woman, including prolonged gestation (Mogren *et al*., 1999), dystocia (Algovik *et al*., 2004; Berg-Lekås *et al.*, 1998), small for gestational age (La Batide-Alanore *et al*., 2002), delivery by caesarean section (Tollånes *et al*., 2008) and intrauterine growth retardation (Ghezzi *et al*., 2003) (discussed later in Chapter Two, sections 2.7.3, 2.7.4, 2.7.5 and 2.7.7 respectively). However, these observations are not relevant for women having their first baby.

Moreover, while there is consensus in guidelines and among many professionals that routine interventions should be offered to women where this could reduce the risks of, for instance, prolonged pregnancy or a slowly progressing labour, there are also concerns about iatrogenic risk for healthy women and babies exposed to such interventions on the basis of population-level evidence (Kjærgaard *et al*., 2009). While previous labour length can be a useful (but not determinative) guide to subsequent labours, nulliparous women have no such labour history and are more likely than those having subsequent babies to be inaccurately diagnosed as having atypically slow labour progress

(Neal *et al*., 2010). Exposing apparently healthy pregnant women to unnecessary medical interventions may be potentially harmful.

Non-medically indicated inductions increase the risk of delivery by caesarean section (Bailit *et al*., 2005; Clark *et al*., 2009; Laughon *et al.*, 2012b). In a study by Davey and King (2016), 42,950 nulliparous, low-risk, singleton, cephalic, 37-40 completed weeks gestations were compared for mode of delivery in induced and non-induced labour. The results showed that induction of labour in medically-uncomplicated nulliparous women at term had a more than twice as likely risk of emergency caesarean section compared with spontaneous labour (odds ratio [OR] 2.54, 95% confidence interval [CI] 2.4, 2.7, p <0.001). Conversely, in a recent study by Grobman *et al.* (2018) the opposite was found. Two groups of low-risk nulliparous women (n = >3,000 for each group) were each assigned either to labour induction or to expectant management. Induction of labour at 39 weeks resulted in a significantly lower frequency of caesarean delivery. Although randomised controlled trials tend to show that routine induction of labour at term reduces the rate of caesarean delivery, when replicated in large cohort studies of actual practice, the opposite effect may be found precluding cogent comparison or outcomes.

Skilled healthcare professionals are assumed to provide good quality care for labouring mothers and new-borns in high income countries. However, guidelines based on population evidence and applied to all women as inflexible policies may expose apparently healthy pregnant women to a routine package of care that interferes with the physiological process of childbirth and that limits the opportunity for normal birth. The point at which physiological labour becomes pathological has been a particular focus of attention.

1.3 Changing Definitions of Pathological Labour Progress

In 1954, Friedman published a seminal study on labour progress. This introduced graphic-statistical analyses for normal labour progress, based on data from 100 women. His work was the basis of the 'one centimetre an hour' rule that is standard practice in most labour wards today. This classified labour progress into timed stages, applied to all women. Based on Friedman's original work, Philpott and Castle (1972) developed the partograph in the early 1970s. This is a graphic tool which displays length of labour in hours (x-axis) and cervical dilatation in centimetres (y-axis). The key feature of this tool was the addition of alert and action lines aimed at identifying women who were likely to experience labour-related adverse outcomes. O'Driscoll *et al*. (1973) used this definition in their Active Management of Labour model, which was a package of interventions aimed at reducing the proportion of women with labour progressing at cervical dilation rates lower than one centimetre an hour.

Later research by Zhang *et al*. (2010a), based on large historical retrospective datasets, investigated 62,415 women who had a singleton term gestation, spontaneous onset of labour, vertex presentation, vaginal delivery and a normal perinatal outcome. Analysis of labour curves showed that most women enter the active phase of labour at 6cm of cervical dilation, and that progress is not linear. These data have been incorporated into an American College of Obstetrics and Gynecology (ACOG) consensus statement (ACOG, 2014). However, the partograph is still considered an essential tool for assessing labour progress, even though there is evidence to show that labour outcomes are not improved by its use (Lavender *et al*., 2013).

In a search of the Cochrane Pregnancy and Childbirth Group's Trials Register, Lavender *et al*. (2013) reviewed six trials involving comparison of partogram

with no partogram, or comparison between different partogram designs. There was no evidence of any difference between using a partogram and not using a partogram on caesarean section (risk ratio [RR] 0.64, 95% confidence interval [CI] 0.24 to 1.70); instrumental vaginal delivery [RR 1.00 (95% CI 0.85, 1.17)] or Apgar score less than seven at five minutes [RR 0.77 (95% CI 0.29, 2.06)] between the groups. More recently, Oladapo *et al*. (2015) in the 'WHO - Better Outcomes in Labour Difficulty (BOLD)' project, showed that the use of partography has not improved labour outcomes in many settings and questioned the applicability of its central feature, 'the alert line', to all women regardless of their labour characteristics. The partogram is neither reassuring nor does it deliver on the promised protection for labouring women. Today, the technology has become ubiquitous in most hospital-based childbirth settings. New research has discovered that the proposed benefits of applying a universally standardised measure of time against cervical dilation for charting labour progress in all women has been invalidated.

In recognition of this, guidelines for duration of labour and for what constitutes normal labour and birth are being updated by national and international organisations such as the World Health Organization (NICE, 2017; Abalos *et al.*, 2018; Visser *et al*., 2018; WHO, 2018). In addition, specific interventions such as external cephalic version for breech presentation, vaginal breech delivery in appropriately selected women and vaginal birth after a caesarean section are potential strategies which may impact upon maternity care decisions and reduce unnecessary caesarean sections and promote optimal physiological births (Betrán, 2018).

1.4 Rationale for the Use of Familial Birth Characteristics as a Basis for Prediction of Labour Progress

There is some evidence that characteristics of labour and birth experienced by one generation of women might also be present for the next generation of their daughters. Research has demonstrated inter and intragenerational influences on gestational age (Magnus *et al*., 1993; Hennessey & Alberman, 1998; Lie *et al*., 2006; Lunde *et al*., 2006), preterm pregnancy (Hennessey & Alberman, 1998; Selling *et al*., 2006; Plunkett *et al*., 2009) or post-term pregnancy (Mogren *et al*., 1999, Morken *et al*., 2011), dystocia (Berg-Lekås *et al*., 1998; Algovik *et al*., 2004), delivery by caesarean section (Varner *et al*., 1996; Tollånes *et al*., 2008), or birth weight that is above average (Lunde *et al*., 2006) or below average (Magnus *et al*., 1997; La Batide-Alanore *et al*., 2002; Ghezzi *et al*., 2003; Jaquet *et al*., 2005; Svensson *et al*., 2006) birth weight babies. These issues will be elaborated further within the systematic review in Chapter Two.

It has been found, for example, that there is a large variation in the length of labour among women. While there are known determinants affecting labour duration, such as anatomical factors, foetal size and uterine contractility, other possible causes remain poorly understood (Liao *et al*., 2005; Blix *et al*., 2008; Oladapo *et al.,* 2018). In addition, the application of average population progression labour curves could potentially misclassify women who are progressing slowly, but normally for them. At a fundamental level, a normal uncomplicated birth (with good clinical outcomes) may be dependent on a combination of familial genetic, social, environmental and other factors that are unique to each woman. Since women having their first baby have no labour and birth history to indicate their personal norms for physiological labour progress, intergenerational labour and birth characteristics may be a useful prediction about what good progress could look like for them.

1.5 Focus of the Thesis

This thesis investigates similarities in mother-daughter labour and birth characteristics to provide essential information that is relevant to the process of particular women in labour. The premise is that mothers' first birth characteristics and birth outcomes may provide familial markers for similar birth experiences in their daughters. Family-based studies have not yet made a major contribution to perinatal health. New personalised maternity care models, based on individual maternal birth characteristics, may provide the first example of how family-based studies may be used to understand individual variation in physiology. This thesis offers an original contribution to knowledge, since it provides the first ever analysis of paired mother-daughter associations for length of labour, and other labour and birth characteristics.

1.6 Aim of the Thesis

The aim is to explore associations between familial labour and birth characteristics of nulliparous women and the first birth of their biological mothers.

1.6.1 Objectives

The objectives of this thesis are:

1) to establish the current evidence on the familial influences on pregnancy and birth outcomes;
2) to establish the accuracy of maternal recall for cardinal labour and birth events;

3) to analyse associations between the labour and birth characteristics and outcomes of nulliparous women and the first birth of their mothers;
4) to examine variables associated with length of labour of nulliparous women, taking account of the length of labour of their mothers' first birth.

1.7 Structure of the Thesis

This research is divided into four stages. To address the first objective, a systematic review of inter- and intragenerational influences on pregnancy and birth outcomes was conducted (see Chapter Two). Current knowledge on shared or recurrent offspring/parent/sibling birth outcome characteristics was explored. A systematic review was undertaken to identify critical gaps in the evidence base on familial effects in labour and childbirth.

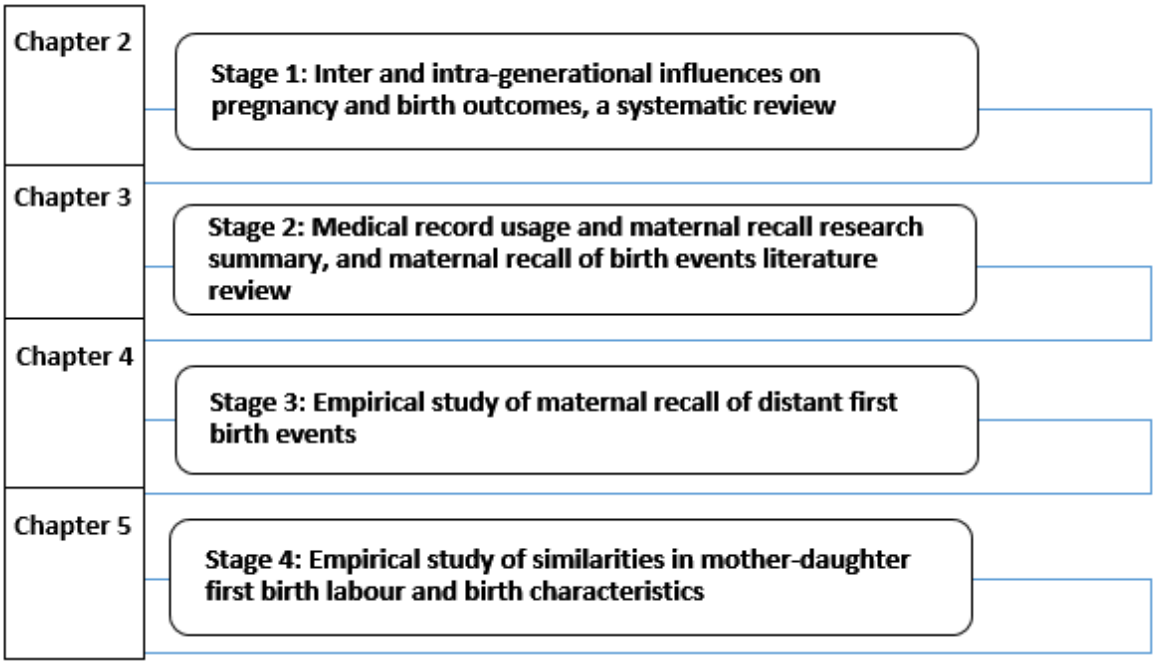
To address the second objective, a descriptive summary of research on medical record usage and maternal recall when compiling maternity information is presented (see Chapter Three). This was followed by a literature review on the agreement of maternal recall of birth outcomes with corresponding hospital birth records and an empirical study on the agreement of maternal recall of first birth outcomes with corresponding hospital birth records (see Chapter Four). This empirical study aims to assess whether maternal recall is a valid source of information even many years after delivery. Mothers' recall of details of their first birth was compared for agreement with archived birth records for use in the mother-daughter similarities in labour and birth characteristics study.

The final stage of the research addresses objectives 3 and 4. Empirical research comparing mother-daughter labour and birth characteristics and

specifically length of labour and birth outcomes was conducted (see Chapter Five). Discussion, interpretation and conclusions of the thesis are presented in the final chapter (Chapter Six). The current state of the evidence on inter- and intragenerational pregnancy and birth outcomes is reviewed, and the validity of recorded and long-term recall of birth events is discussed. Current knowledge and understanding of labour progress to birth is presented and factors influencing birth progress in nulliparous women are explored in relation to population norms for labour progress. Factors enabling or constraining normal birth in the hospital environment, advancing normal birth and achieving normal birth using a predictive model are discussed. The idea of personalised maternity care for nulliparous women is introduced and the strengths and limitations of the studies in the thesis are considered. Implications for practice, concluding observations, recommendations for future research and future research questions that could further this research are suggested.

Key focus areas of the research are presented in Figure 1.1. Here, the structure of the thesis is conveyed.

Figure 1.1: Structure of the Main Themes of the SiLC Thesis



1.8 Significance of the Research and Contribution to Knowledge

Although maternity care practices have changed dramatically within the present generation and labour curves for progress in labour show more tolerance than the original labour curves created by Friedman in the 1950s, there is still widespread concern about the over use of potentially harmful interventions for labour misdiagnosed as 'dystocic'. Once admitted to hospital, women are closely monitored for adequate progression in labour. Nulliparous women, specifically, may not progress according to expected rates for cervical dilation. Diagnosis of prolonged labour among nulliparous women is common (Kjærgaard *et al*., 2009) and constitutes the major indication for intervention by oxytocin augmentation, instrumental deliveries and delivery by emergency caesarean section (Gifford *et al*., 2000; ACOG, 2003; Ness *et al*., 2005; Boyle *et al*., 2013; Bugg *et al*., 2013; Cahill & Tuuli, 2013; Caughey, 2014). This research is motivated by the gap between the call for a global reduction of instrumental deliveries and caesarean section rates, and the continued rise of

such rates in practice. New evidence from WHO (2018) questions the use of routine obstetric interventions for ‘slow-yet-normal’ labour progress. This thesis contributes to this new debate.

To the best of my knowledge, this research is the first to focus on associations of labour and birth characteristics between mothers and daughters in a matched cohort study. Utilising familial birth histories to guide clinical decisions for nulliparous women in labour could result in the development of personalised birthing models.

1.9 Summary

Normal birth usually refers to a natural, healthy and physiological process with few or no external interventions (Drife, 1995; Enkin *et al*., 1995; Lee, 1999; Downe *et al*., 2001, Kennedy & Shannon, 2004; ICM, 2008; Downe, 2009). Every intervention presents the possibility of additional risks (Jansen *et al*., 2013). Currently, around the world, there are high rates of unnecessary medical interventions that interfere with the physiological process of childbirth. Determining appropriate intervention rates and the methods used to identify them is one of the biggest challenges today. In response to the alarming increase in caesarean section rates, there has been a strong global push to ensure that every effort should be made to provide interventions only for women who really need them (Robson, 2018; Sandall *et al*., 2018; WHO, 2018; Visser *et al*., 2018). This is because increasing caesarean section rates are associated with maternal and perinatal consequences which may compromise maternal/foetal health, with increased risks for fertility, future pregnancy and long-term childhood outcomes (Blustein & Liu, 2015; Visser, 2015; Keag *et al*., 2018). Because of the risk of repeat caesarean section in subsequent

pregnancies, reducing the rate of unnecessary caesarean section for first time mothers is a global priority (Betrán, 2018).

Every individual has unique combinations of familial factors. Familial labour and birth history may help predict and manage common or unusual recurrent familial birth trends in healthy women. Mothers' first birth histories could be of importance for improving maternity care for healthy nulliparous daughters and for supporting them to have the optimal chance of a normal birth. I hope that this thesis will offer a valuable and necessary addition to discussions about minimising intervention rates and enabling healthy women to have the maximum chance for a normal birth, specifically when they are having their first baby.

Chapter Two: A Systematic Review of Inter- and Intragenerational Influences on Pregnancy and Birth Outcomes

2.1 Background

Familial factors such as maternal health, fertility, chronological age of parents, specific birthing history and labour and birth experiences may influence pregnancy and birth outcomes (Shaw & Byers, 1998; Lisonkova *et al*., 2010; Ulfsdottir *et al*., 2014). Gene expression between parents and their offspring in specific cell lines affects genetic inheritance in offspring (Monks *et al*., 2004). Epigenetic information reveals that parental history and experiences also affect their offspring (Hochberg *et al*., 2011; Daxinger & Whitelaw, 2012), and *in utero* experiences are determinants in programming a child's development and health (Godfrey *et al*., 2010).

This chapter addresses the first objective of the thesis:

- to establish the current evidence on the familial influences on pregnancy and birth outcomes.

Based on the hypothesis that parents' birth outcomes may act as predictors for their descendants' birth outcomes, this section of the thesis reviews current knowledge on the inter- and intragenerational influences on pregnancy and birth outcomes. It is the first systematic review in the developing field of personalised or precision medicine, which is expected to become a future paradigm in healthcare (Snyder *et al*., 2010).

2.2 From Concept to Theory

Epidemiologists have used familial recurrence patterns across generations to explore maternal, paternal and in some cases sibling contributions to birth outcomes within families. Often, the association is more strongly transmitted through the maternal line, such as in the case of preterm delivery (Wilcox *et al*., 2008). Studies have reported on recurrence in specific aspects of pregnancy and delivery, such as caesarean section among relatives (Tollånes *et al*., 2008), but none of these studies have investigated mothers' birth outcomes for clinical decision support for daughters' first birth.

2.3 Methods

2.3.1 Literature Search: Design and Strategy

A search was conducted in OvidSP including: Embase, MEDLINE, ERIC, and Maternity and Infant Care resources. Search terms used (and associated truncations) were:

> (mother or woman or women or maternal) combined with (birth or deliver or reproduction or intrapartum or labo$) combined with (daughter or generation$ or familial or intergeneration$) combined with (similar$ or genetic or inherit$ or relationship$) combined with ('birth weight' or 'gestational age' or 'mode of birth' or caesarean or cesarean or 'duration of labo$').

The search was limited to 'human', 'outcomes research' and 'labour and delivery general'. No language or date restrictions were applied. The search was carried out in January 2014.

2.3.2 Inclusion and Exclusion Criteria

Included papers were empirical studies published in English which investigated inter- and intragenerational recurrence of specific pregnancy and birth variables in healthy human populations. These included gestational age, preterm birth, prolonged pregnancy, dystocia, caesarean section, birth weight, and foetal growth restriction including small for gestational age and intrauterine growth restriction. Research articles investigating pregnancy pathologies (such as hyperemesis gravidarum, pre-eclampsia and birth defects) were excluded.

2.3.3 Selection of Studies

Articles identified by the electronic search were selected based on their titles and abstracts, then initially screened by me (the research investigator). Further screening of the full text of each study was undertaken by two reviewers (myself and my university supervisor). The process was checked and any discrepancies were discussed and resolved.

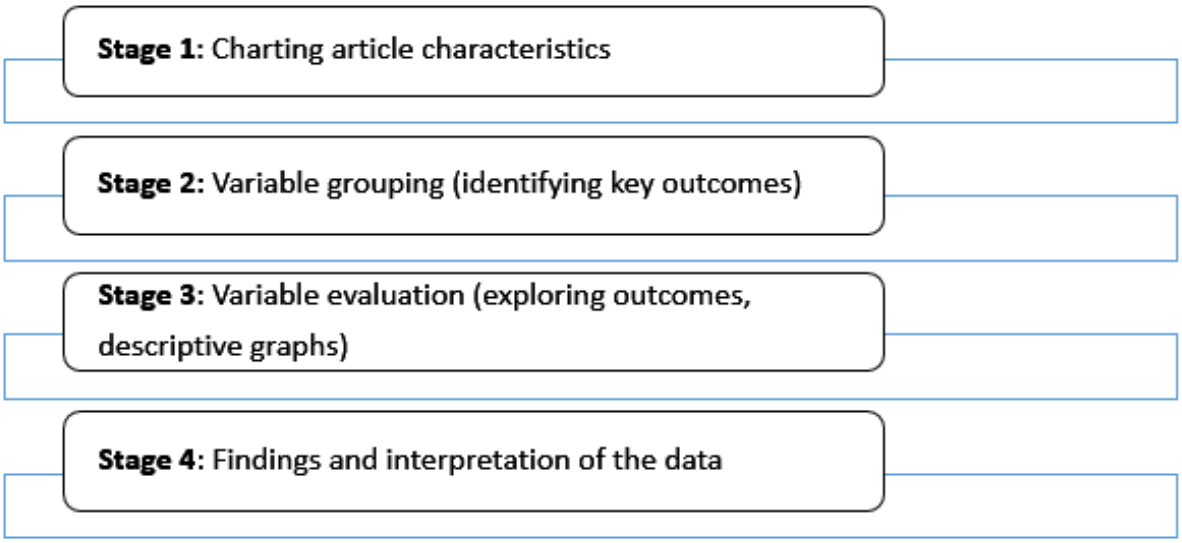
2.3.4 Quality Appraisal

Studies were checked for trustworthiness and relevance using the Critical Appraisal Skills Programme (CASP) for cohort studies (CASP, 2013) and entered into an Excel spreadsheet. Each article was assessed by myself, and 10% were rechecked by a second reviewer (my Director of Studies).

2.4 Data Synthesis

The data were synthesised using a four stage approach, as shown in Figure 2.1.

Figure 2.1: Diagrammatic Representation of the Stages Undertaken to Explore the Data



Variables were grouped according to birth outcomes. Key outcomes were categorised and, wherever possible, presented graphically. Descriptive graphs were prepared for those studies with individual summary statistics (CI, OR and RR). Due to the heterogeneity of the outcome data in the studies, a meta-analysis could not be performed. Tabulated data and forest plots summarised the data to show the overall effect of the findings. The horizontal points on the forest plots (diamonds) showed the limits of the 95% confidence interval (CI) with the summary measure of each individual study.

2.5 Results

The initial search of the key terms generated 723 hits. After the predetermined limits of ‘human’, ‘outcomes research’ and ‘labour and delivery general’, 278 hits remained. Duplicate articles (71 entries) were deleted. The abstracts and full texts of the remaining 207 articles were screened and 184 were eliminated because they focused on pregnancy conditions outside the scope of this review. Two additional relevant articles were added from reference lists resulting in the

final inclusion of 25 papers (see Figure 2.2). The articles were classified by birth outcomes (see Table 2.1).

2.5.1 Appraisal of Articles

The assessment of risk of bias is shown in Table 2.2. All the selected studies addressed a clearly focused study question. Twenty-four of the included studies were cohort studies and one was a review (Ramakrishnan *et al*., 1999). In all cases the study design was appropriate. There was variability in how gestational age at delivery was assessed, with some studies relying on self-reporting from participants, and some using a combination of the date of last menstrual period with ultra-sound measurements if available. Twenty-one of the twenty-five studies documented possible confounding factors although there was variation in the adjustment for these. All studies provided a statistical summary measure and all of the studies were published in peer reviewed journals.

Figure 2.2: Flow Chart of Search Strategy

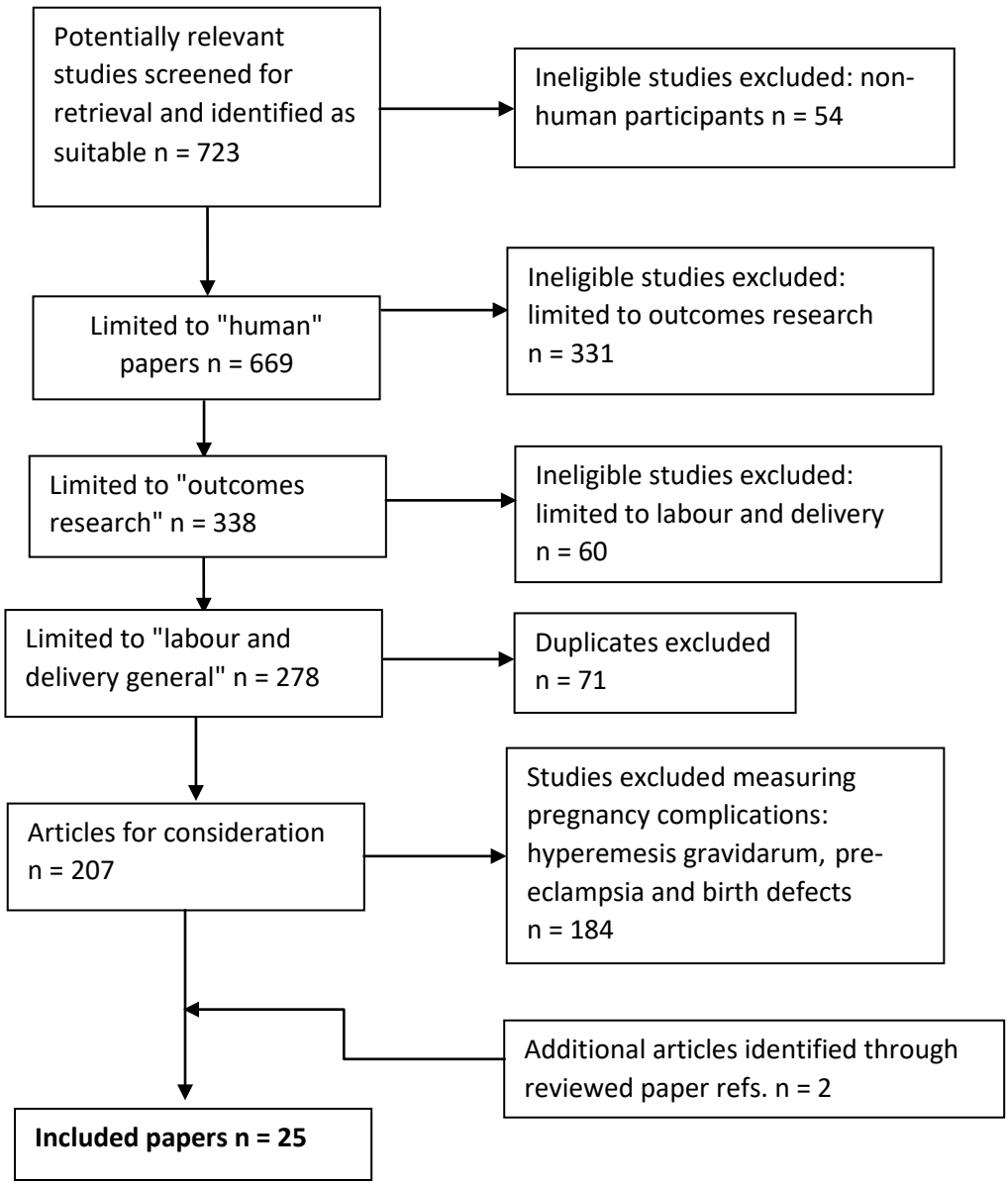


Table 2.1: Articles Grouped by Birth Outcomes

Birth outcome	**Gestational age** (4 articles)	**Preterm birth** (3 articles)	**Post-term pregnancy** (2 articles)	**Dystocia** (2 articles)	**Caesarean section** (2 articles)	**Birth Weight** (9 articles)	**Small for gestational age & intrauterine growth retardation** (6 articles)
Author, Year, Title.	**Magnus *et al.* (1993).** Correlations of birth weight and gestational age across generations. **Hennessey & Alberman (1998).** Intergenerational influences affecting birth outcome. Preterm delivery and gestational age in the children of the 1958 British birth cohort. **Lie *et al.* (2006).** Maternal and paternal influences on length of pregnancy. **Lunde *et al.* (2006).** Genetic and environmental influences on birth weight, birth length, head circumference and gestational age by	**Hennessey & Alberman (1998).** Intergenerational influences affecting birth outcome. Preterm delivery and gestational age in the children of the 1958 British birth cohort. **Selling *et al.* (2006).** Intergenerational effects of preterm birth and reduced intrauterine growth: a population-based study of Swedish mother-offspring pairs. **Plunkett *et al.* (2009).** Mother's genome or maternally-inherited genes acting in the foetus influence gestational age in familial preterm birth.	**Mogren *et al.* (1999).** Recurrence of prolonged pregnancy. **Morken *et al.* (2011).** Recurrence of prolonged and post-term gestational age across generations: maternal and paternal contribution.	**Berg-Lekås *et al.* (1998).** Familial occurrence of dystocia. **Algovik *et al.* (2004).** Genetic influence on dystocia.	**Varner *et al.* (1996).** The intergenerational predisposition to operative delivery. **Tollånes *et al.* (2008).** Caesarean section among relatives.	**Klebanoff *et al.* (1984).** Low birth weight across generations. **Carr-Hill *et al.* (1987).** Is birth weight determined genetically? **Magnus *et al.* (1993).** Correlations of birth weight and gestational age across generations. **Ramakrishnan *et al.* (1999).** Role of intergenerational effects on linear growth. **Collins *et al.* (2003).** Low birth weight across generations. **HyppÖnen *et al.* (2004).** Parental growth at different life stages and offspring birth weight: an intergenerational study.	**Magnus *et al.* (1997).** Birth weight of relatives by maternal tendency to repeat small for gestational age births in successive pregnancies. **La Batide-Alanore *et al.* (2002).** Familial aggregation of foetal growth restriction in a French cohort of 7,822 term births between 1971 and 1985. **Ghezzi *et al.* (2003).** Idiopathic foetal intrauterine growth restriction: a possible inheritance pattern.

	use of population-based parent-descendant data.					**Agnihotri *et al.* (2008).** Intergenerational study of trends in human birth weight across two successive generations. **Nordtveit *et al.* (2009).** Intergenerational birth weight associations by mother's birth order - the mechanisms behind the paradox: A population-based cohort study. **Kuzawa and Eisenberg (2012).** Intergenerational predictors of birth weight in the Philippines: correlations with mother's and father's birth weight and test of maternal constraint.	**Jaquet *et al.* (2005).** Significant paternal contribution to the risk of small for gestational age. **Svensson *et al.* (2006).** Familial aggregation of small for gestational age births: the importance of foetal genetic effects. **Selling *et al.* (2006).** Intergenerational effects of preterm birth and reduced intrauterine growth: a population-based study of Swedish mother-offspring pairs.

Table 2.2: Assessment of Risk Bias

Author & year	Peer reviewed?	Clearly focused study question?	Study design	Cohort recruitment acceptable?	Case control appropriate study method (Case control studies)	Exposure (Familial variable measurement) accurately measured?	Outcome (Offspring predisposition) accurately measured?	Confounding factors identified?	Confounding factors accounted for?	Statistical summary measure given?
Agnihotri *et al*., 2008	Yes	Yes	Cohort	Yes	N/A	Records by trained health workers	Hospital records	Yes	Yes	Yes
Algovik *et al*., 2004	Yes	Yes	Cohort	Yes	N/A	Birth registry	Yes	Yes	Yes	Yes
Berg-Lekås *et al*., 1998	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	No	No	Yes
Carr-Hill *et al.*, 1987	Yes	Yes	Cohort	Yes	N/A	Obstetric data bank	Obstetric data bank	No	No	Yes
Collins *et al*., 2003	Yes	Yes	Cohort	Yes	N/A	Maternal birth records	Infant birth records	Yes	Yes	Yes
Ghezzi *et al*., 2003	Yes	Yes	Cohort	Yes	Yes	Out-patient clinic enrolment (index)	Self-report for previous birth	Yes	Yes	Yes
Hennessy & Alberman, 1998	Yes	Yes	Cohort	Yes	N/A	British National Child Development Study	British National Child Development Study	Yes	Yes	Yes

Hyppönen *et al*., 2004	Yes	Yes	Cohort	Yes	N/A	Self-report	Self-report individual interview	Yes	Yes	Yes
Jaquet *et al*., 2005	Yes	Yes	Cohort	Yes	N/A	Maternity registry	Maternity registry	Yes	Yes	Yes
Klebanoff *et al.*, 1984	Yes	Yes	Cohort	Yes	N/A	Maternal report/ Interview by trained interviewer	Maternal report (validated)	Yes	Yes	Yes
Kuzawa & Eisenberg, 2012	Yes	Yes	Cohort	Yes	N/A	Health & Nutrition Survey	Maternal recall & foetal birth weight records	Yes	Yes	Yes
La Batide-Alanore *et al*., 2002	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Yes	Yes
Lie *et al*., 2006	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	No	No	Yes
Lunde *et al.*, 2006	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Partial	Yes
Magnus *et al.,* 1993	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	No	No	Yes
Magnus *et al.,* 1997	Yes	Yes	Cohort	Yes	N/A	National Institute of Child health and Human Development Survey	Survey	Yes	Yes	Yes
Mogren *et al*., 1999	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Partial	Yes

Morken *et al*., 2011	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Partial	Yes
Nordtveit *et al.*, 2009	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Yes	Yes
Plunkett *et al.,* 2009	Yes	Yes	Cohort	Yes	N/A	Birth records /self-report	Birth records	Yes	No	Yes
Ramakrishnan *et al.,* 1999	Yes	Yes	Review	Yes	N/A	Birth registry	Hospital records	Yes	Yes	Yes
Selling *et al.,* 2006	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Yes	Yes
Svensson *et al*., 2006	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Yes	Yes
Tollånes *et al.,* 2008	Yes	Yes	Cohort	Yes	N/A	Birth registry	Birth registry	Yes	Yes	Yes
Varner *et al*., 1996	Yes	Yes	Cohort	Yes	N/A	Birth records	Birth certificates	Yes	Yes	Yes

2.6 Stages 1 & 2: Characteristics of Included Studies and Variables Identified for Analysis

All but one of the included articles were quantitative cohort studies spanning almost three decades (from 1984 to 2012) and three continents. Only Ramakrishnan *et al.* (1999) conducted a review, which included 14 studies. All except two studies on dystocia with twins (Berg-Lekås *et al.*, 1998; Algovik *et al*., 2004) included singleton birth data. The search of inter- and intragenerational influences identified seven pregnancy and birth outcomes: gestational age, preterm birth, prolonged pregnancy, dystocia, caesarean section, birth weight, and foetal growth restriction including small for gestational age and intrauterine growth restriction.

2.7 Stage 3: Variable Analysis

2.7.1 Gestational Age

Four studies investigated familial influences on gestational age (Magnus *et al*., 1993; Hennessey & Alberman, 1998; Lie *et al*., 2006; Lunde *et al.,* 2006). The sample sizes were 1,092, 7,501, 77,452 and 91,617 respectively. Two studies found a relationship between mothers' gestational age and the gestational age of their offspring (Hennessey & Alberman, 1998; Lie *et al*., 2006). Hennessey and Alberman (1998) found that the strongest and only likely independent intergenerational effect on gestational age is parental gestational age (adjusted regression coefficient = 0.067 weeks per week in mothers and 0.045 in fathers). Furthermore, a mother born at 37 weeks or more had a greater likelihood of her first born offspring being delivered at >37 weeks (p = 0.008). Lie *et al*. (2006) found that offspring gestational age increased by 1.22 days for each additional week in their mother's gestational age at the time they were born, which was twice the effect of their father's gestational age (0.58 days). One interpretation

of this finding suggests that mother-offspring recurrence is determined by the sum of foetal and maternal influences, while the father-offspring recurrence is determined only by foetal influences. Magnus *et al*. (1993) investigated familial correlation with gestational age and infant birth weight, which involved measuring concordance rates for both outcomes. Although they found that both the mother's gestational age and infant birth weight affect her firstborn's gestational age, especially if her firstborn is female (Magnus *et al*., 1993), offspring gestational age from maternal birth weights could not be predicted with confidence. This finding may be explained by the fact that foetal genes contribute to the correlation. Lunde *et al.* (2006) found three major contributing factors (maternal, paternal and environmental) affecting offspring's gestational age. Maternal genetic effects and the full sibling environment were found to be most important (14% and 13% of the variation respectively). Paternal influences on gestational age in offspring were found to a lesser degree. This suggests that there are factors associated with the mother that are more important than the foetal genes for the normal duration of pregnancy.

2.7.2 Preterm Birth

Three articles explored the intergenerational effects on preterm delivery (Hennessey & Alberman, 1998; Selling *et al*., 2006; Plunkett *et al*., 2009). The sample sizes for the studies were 10,248, 38,720 and 1,130 respectively. Two of the studies tested maternal and paternal influences on preterm birth and found evidence to support parental genetic influences (Hennessey & Alberman, 1998; Plunkett *et al*., 2009). In addition to genetic influences, Hennessey and Alberman (1998) found that mothers' age may have a strong influence on preterm births, with mothers younger than 16 or over 30 having an increased proportion of preterm births. After performing segregation analysis, Plunkett *et*

al. (2009) found preterm births seem more influenced by maternally inherited genes acting on the foetus than paternally inherited genes.

Although Selling *et al*. (2006) found intergenerational effects on preterm births [OR 1.24 (95% CI 0.95, 1.62)] when comparing mothers who had been born at term to mothers born preterm, the odds ratio for delivering a preterm child was higher among small for gestational age mothers [OR 1.30 (95% CI 1.05, 1.61)]. Women whose intrauterine growth was moderately reduced (but who did not meet the criterion of being born small for gestational age) were also predisposed to preterm births.

Although familial recurrence of preterm birth contributes to a notable proportion of all preterm births, the nature of its genetic component is complex and has not been identified (Plunkett *et al.*, 2009).

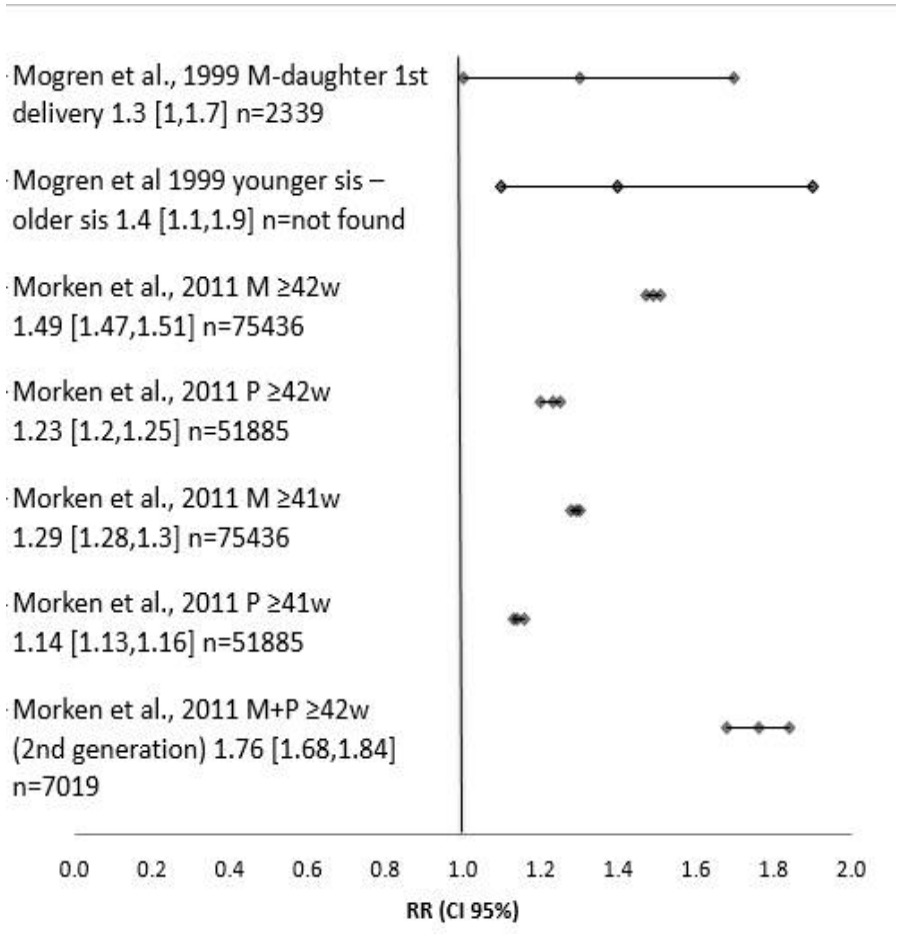
2.7.3 Prolonged or Post-Term Pregnancy

A prolonged pregnancy or post-term birth is defined as a pregnancy or birth which continues two weeks or more past the expected delivery date, and was the subject of two papers identified by the search (Mogren *et al.*, 1999; Morken *et al*., 2011). The sample sizes for the studies were 48,076 (Mogren *et al.*, 1999); and 478,627 (mother-child units), 353,164 (father-child units) and 295,455 (trios) (Morken *et al*., 2011) respectively.

Mogren *et al.* (1999) calculated a baby's gestational age from the date of its mother's last menstrual period, and daughter's baby's gestational age by both her last menstrual period and by ultrasound, adjusting the calculations for 62.7% of the daughters from their ultrasound data. Morken *et al.* (2011) assigned a baby's gestational age by its mother's last menstrual period, but the daughters' generation relied solely on ultrasound data. In both studies, mothers

who had a prolonged pregnancy were more likely to have daughters who had prolonged pregnancies, being RR 1.3, 95% CI 1.0, 1.7 (Mogren *et al.*, 1999) and RR 1.49, 95% CI 1.47, 1.51 (Morken *et al*., 2011). A younger sister's incidence of having a prolonged pregnancy increased if an older sister had a prolonged pregnancy [RR 1.4 (95% CI 1.1, 1.9)] (Mogren *et al.*, 1999). A post-term father also contributed to post-maturity in offspring, albeit to a weaker extent than a post-term mother [RR 1.23 (95% CI 1.20, 1.25)] (Morken *et al*., 2011). However, post-maturity in both parents greatly increases the recurrence incidence of post-maturity in their offspring [RR 1.76 (95% CI 1.68, 1.84)] (Morken *et al*., 2011) (see Figure 2.3).

Figure 2.3: Odds Ratio (OR) and Confidence Intervals (CI) for Maternal (M) and Paternal (P) Influences on Prolonged Pregnancy in Offspring



Legend: M = maternal; P = paternal; sis = sister; w = weeks.

A potential limitation of these studies may be the use of last menstrual period as a method for calculating gestational age. Research has shown that women with either irregular menstrual cycles or delayed ovulation may be inaccurately assessed (Waldenstrom *et al*., 1991; Tunon *et al*., 1996). Yet Morken *et al.* (2011:1633) contend that “relative risk estimates were not influenced by using ultrasound based gestational age determination for the ... second generation”.

Moreover, confounding effects such as nulliparity, maternal age, and maternal and paternal birth weights were not found to influence outcomes (Morken *et al*., 2011). Both attributed post-term birth to genetic effects (Mogren *et al.*, 1999; Morken *et al*., 2011).

2.7.4 Dystocia

Dystocia describes a difficult or abnormal labour. Assisted deliveries, including delivery by vacuum extraction, forceps or caesarean section are often the result of dystocia. However, dystocia has become a term sometimes used to describe a labour that is longer than the population norm. Furthermore, an inherent genetic predisposition to reduced capacity of the pelvis, and differing mechanisms in initiating labour, or protocols for augmenting labour and treating labour abnormalities or any combination of these, may add to the susceptibility of experiencing dystocia. Two papers explored the intergenerational effects on length of labour and dystocia.

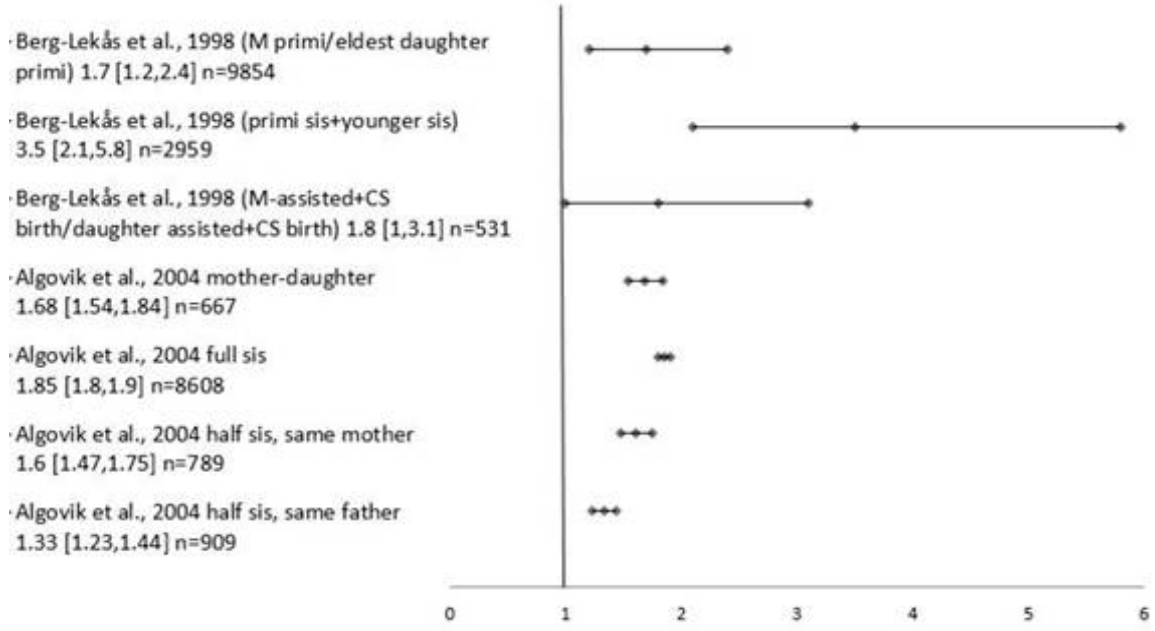
Parametric linkage analysis, a method which defines explicit relationships between phenotypic and genetic similarity, was used by Berg-Lekås *et al*. (1998) and Algovik *et al*. (2004) to assess the relative incidence of dystocia. Berg-Lekås *et al*. (1998) made the diagnosis of dystocia more reliable by including all deliveries requiring instrumental intervention (forceps or vacuum

extraction) or caesarean section. Algovik *et al*. (2004) used the diagnosis of dystocia according to the International Classification of Diseases (ICD-8, 9 & 10).

Daughters of mothers who had an assisted delivery have a higher risk (not quantified) of having an assisted delivery (vacuum extraction, forceps or caesarean section). Between siblings, a monozygotic twin whose co-twin had dystocia showed an almost four-fold increase in the risk of dystocia [OR 3.82 (95% CI 2.47, 5.91)] (Algovik *et al*., 2004). Full sisters (i.e., same father and same mother) (Berg-Lekås *et al*., 1998) and sisters (related through one parent only) or half-sisters from the same mother (Algovik *et al*., 2004) also have an increased risk of having a dystocic birth in their first pregnancy [OR 1.85 (95% CI 1.80, 1.90)] compared with women whose mother or sister had not been diagnosed with dystocia. However, half-sisters who share a father (not a mother) are relatively less likely to suffer from dystocia, but still show an increased risk [OR 1.33 (95% CI 1.23, 1.44)] (Algovik *et al*., 2004) compared with a woman whose sister had not been diagnosed with dystocia (see Figure 2.4).

Both studies concluded that dystocia is probably influenced by maternal genes which affect the ripening of the cervix, a malfunction of the myometrium, or both.

Figure 2.4: Odds Ratios (OR) and Confidence Intervals (CI) for Recurrent Dystocia in Offspring (only Studies with OR and CI Results)



Legend: M = mother; primi = primipara; sis = sister.

2.7.5 Caesarean Section

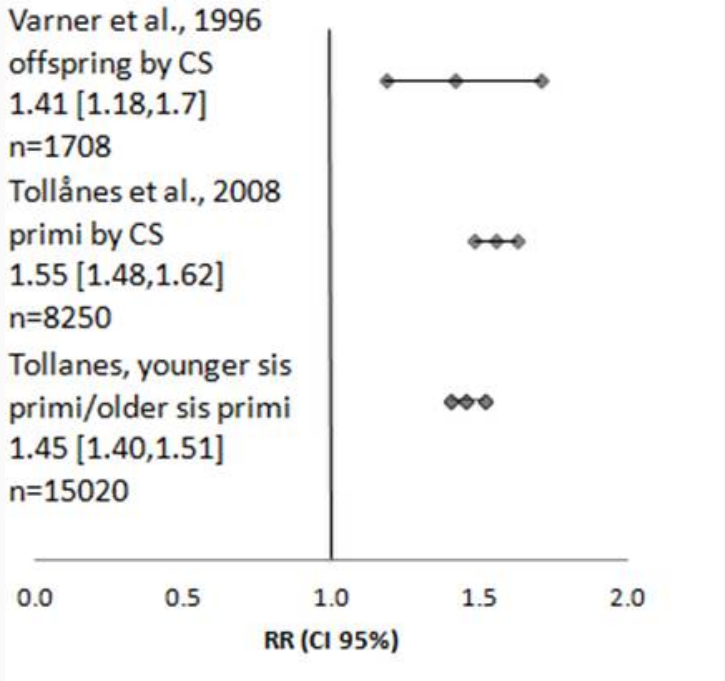
Caesarean sections are performed for various reasons, which range from overt pathologies of mother and/or baby to maternal request and doctor preference. This paper focuses on the maternal and foetal indications which may be affected by familial effects.

Two studies investigated familial predisposition to caesarean section (Varner *et al.,* 1996; Tollånes *et al*., 2008). Both found that women (mothers) who themselves were born by caesarean section have an increased incidence of having their first child by caesarean section. Results from the Varner *et al*. study (1996) show an odds ratio [OR 1.41 (95% CI 1.18, 1.70), p <0.001] while the study by Tollånes *et al*. (2008) showed a 55% increased incidence [adjusted RR 1.5 (95% CI 1.48, 1.62)]. The same was not found for fathers born by caesarean section [RR 1.02 (95% CI 0.96, 1.10)] (Tollånes *et al*., 2008). A

woman whose older sister's first child was delivered by caesarean section has a 45% increased incidence of having her first child by caesarean section (Tollånes *et al*., 2008) (see Figure 2.5).

In both studies, reasons for caesarean section delivery were prolonged or dysfunctional labour, or cephalopelvic disproportion (dystocia). Maternal caesarean without dystocia were also included in the studies. However, changes in practice management over the two generations may have led to increased frequency of diagnosis of labour and delivery complications in daughters.

Figure 2.5: Relative Risk (RR) and Confidence Intervals (CI) for Women who were Delivered by Caesarean Section and the Risk of Subsequently Delivering their Children by Caesarean Section



Legend: CS = caesarean section; primi = primipara; sis = sister.

2.7.6 Infant Birth Weight

Infant birth weight was the most widely researched topic of the seven variables (9/24 = 37% of the studies). The articles indicate that parents' infant birth weights affected their offspring's' infant birth weight (see Figure 2.6). Six studies were conducted in high-income countries, while three studies were conducted in low/middle-income countries.

The studies conducted in high-income Western populations (Klebanoff *et al.,* 1984; Carr-Hill *et al.,* 1987; Magnus *et al*., 1993; Collins *et al*., 2003; Hyppönen *et al*., 2004; Nordtveit *et al*., 2009) reported a stronger maternal than paternal effect on offspring infant birth weight. Klebanoff *et al*. (1984), who speculated on a possible role of familial factors in infant birth weights between mothers and their daughters, relied on recall data for maternal birth weights. Findings show an over one and a half times increased likelihood of maternal birth weight determining infant offspring birth weight [OR 1.66 (95% CI 0.82, 3.39)]. However, the confidence interval includes 1 suggesting that in a larger population this finding may gain significance. Other studies in high income countries using prospective record-linkage found maternal effects on offspring birth weights. Hyppönen *et al*. (2004) found mothers' birth weight was the strongest determinant of offspring's birth weight [effect size per SD 112 g (95% CI 97, 128)]. Nordtveit *et al*. (2009) confirmed intergenerational birth weight associations between maternal and offspring birth weight by mothers' and offspring's' birth order (first born, second born, third born, fourth or later born [p <0.001]). Magnus *et al*. (1993) found the mother's birth weight a stronger predictor of daughter's birth weight than son's birth weight (correlation coefficient 0.240 for mother-daughter pairs and 0.246 for mother-son pairs), with a stronger maternal-offspring effect than paternal-offspring effect. Collins *et al*. (2003) found no disparity between white mothers and African-American mothers and maternal-infant low birth weight, corroborating that maternal-infant

low birth weight is independent of race and socioeconomic factors and probably based upon familial effects (see Figure 2.7). Only Carr-Hill *et al*. (1987) found a small maternal effect on offspring birth weight correlations. After analysing 505 intergenerational pairs of first births all giving birth in one city (Aberdeen), mother-daughter correlations (n = 266) were found to be higher than mother-son correlations (n = 239) (correlation of residuals 0.178 and 0.138 respectively). They found that a mother who was herself of low birth weight had a 2.4-fold increased likelihood of having a low birth weight baby than a mother who was of normal birth weight.

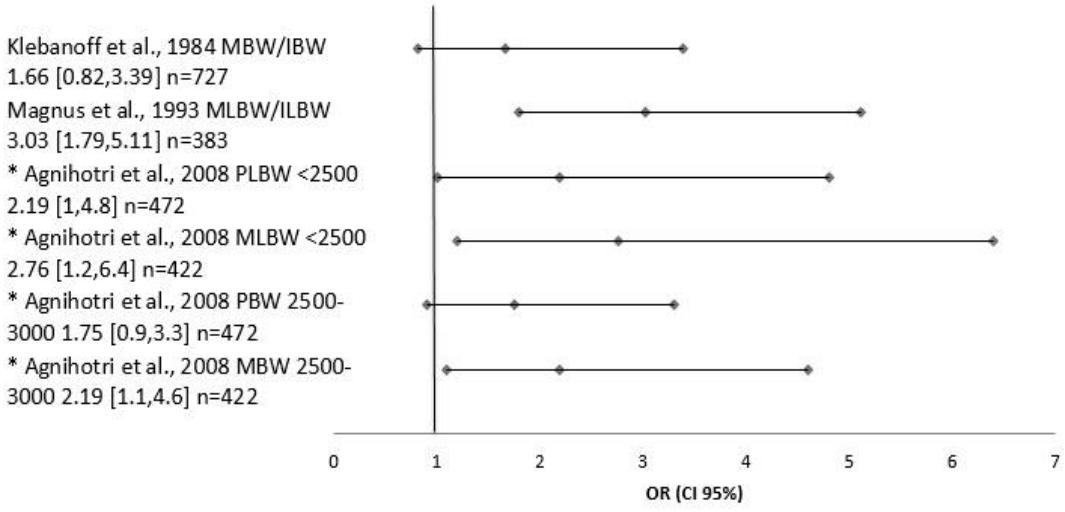
Those studies conducted in low-income populations also found maternal-infant birth weight a significant predictor of offspring's infant birth weight. Kuzawa and Eisenberg (2012) found the mother's birth weight a strong predictor of her daughter's birth weight (p 0.0001), with a stronger maternal-offspring effect than paternal-offspring effect (paternal $p = 0.014$).

A Guatemalan study (Ramakrishnan *et al*., 1999) found that the mother's birth weight was a significant predictor of her child's infant birth weight ($p < 0.05$). In addition, a 10-20g increase in infant birth weight for every 100g increase in maternal birth weight was found ($p < 0.001$). This relationship is interesting and may be explained by the fact that women living in low income countries typically 'inherit' both similar genes and inadequate environments across generations.

Agnihotri *et al.* (2008) investigated parental and offspring infant birth weights in India, finding that parents' infant birth weights were a strong determinant of their offspring's' infant birth weights. Low infant birth weight mothers' effect on low infant birth weight offspring [OR 2.8 (95% CI 1.2, 6.4) $p = 0.02$] was stronger than that of fathers' [OR 2.2 (95% CI 1.0, 4.8) $p = 0.05$]. However, every 100g increase in maternal birth weight was associated with an increase in offspring

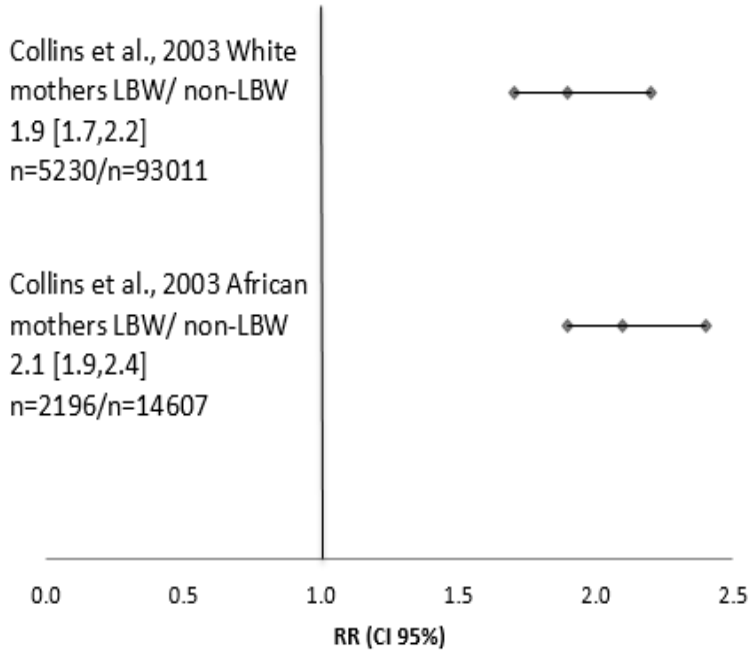
birth weight of 14g, with the equivalent figure for paternal birth weight 18.1g (*p* = <0.001 for both). Paternal infant birth weight was found to be a stronger genetic predictor in India than in high income countries. A possible explanation for this trend in India is that the father, providing food and financial security, is often the major contributor to the (non-genetic) environment (Agnihotri *et al.,* 2008). Another explanation is that poor growth of female foetuses in India may lead to poor growth of reproductive organs and intrauterine constraint which, in turn, leads to another generation of growth failure. However, research in the Philippines presents alternative conclusions. Kuzawa and Eisenberg (2012) found that each additional kilogram in the mother's infant birth weight (271±53g, *p* = 0.00001) had twice the effect of each additional kilogram in the father's infant birth weight (132 ±55g, *p* = 0.017) on their offspring's' infant birth weights. The researchers suggest that false paternity rates may explain these differences.

Figure 2.6: Odds Ratios (OR) and Confidence Intervals (CI) for Recurrent Infant Birth Weight in Offspring (only Studies with OR and CI Results)



Legend: M = maternal; I = infant; P = paternal; IBW = infant birth weight; LBW = low birth weight
* low-income country.

Figure 2.7: Relative Risk (RR) and Confidence Intervals (CI) for White Mothers and African Mothers Maternal-infant Low Birth Weight



Legend: LBW = low birth weight

2.7.7 Foetal Growth Restriction (Small for Gestational Age and Intrauterine Growth Retardation)

Familial associations with foetal growth restriction, as expressed by small for gestational age and intrauterine growth retardation, were investigated within six selected studies (Magnus *et al*., 1997; La Batide-Alanore *et al*., 2002; Ghezzi *et al*., 2003; Jaquet *et al*., 2005; Selling *et al*., 2006; Svensson *et al*., 2006). Although the terms 'small for gestational age' and 'intrauterine growth retardation' are often used interchangeably, they are not synonymous. Small for gestational age studies refer to newborns whose birth weight is below the 10th percentile for the appropriate gestational age, whilst intrauterine growth retardation refers to foetuses with a declining growth rate delivered before they have actually achieved a weight that would make them small for gestational age.

The incidence of small for gestational age was investigated in parent-offspring (Magnus *et al*., 1997; Jaquet *et al*., 2005; Selling *et al*., 2006), parental brothers and sisters (Svensson *et al*., 2006) and sibling-sibling (La Batide-Alanore *et al*., 2002) recurrence. Within the 25 articles selected for consideration in this study, only one study investigated familial inheritance patterns for intrauterine growth retardation (Ghezzi *et al*., 2003).

Selling *et al*. (2006) found the odds ratio for giving birth to small for gestational age children was higher among small for gestational age mothers [OR 2.68 (95% CI 2.11, 3.41)] compared with the average for gestational age mothers. Similarly, Jaquet *et al*. (2005) reported a higher incidence (4.7 times greater) of small for gestational age infants being born to mothers who were small for gestational age compared with the average for gestational age mothers [OR 4.7 (95% CI 2.27, 9.73)]. They also reported a higher incidence (3.5 times greater) of small for gestational age infants born to fathers who were small for gestational age [OR 3.48 (95% CI 0.86, 14.07)]. When both parents were small for gestational age, the incidence was 16.3 times greater compared to non-small for gestational age parents [OR 16.33 (95% CI 3.16, 84.35)]. Magnus *et al*. (1997) compared reduced foetal growth outcome in successive sibling births and found that the correlation between the mother's infant birth weight and the small for gestational age child's infant birth weight was 0.205 (p <0.001, n = 996); between the father and the child it was 0.117 (p <0.001, n = 913). However, they also report that in sibships where both parents were small for gestational age, the odds ratio of the father having been small for gestational age was higher than the mother being small for gestational age (OR 2.49 and 1.74, respectively). Although the larger paternal effect may argue for an inherited factor, the sample size was too small (87 families) to be considered definitive.

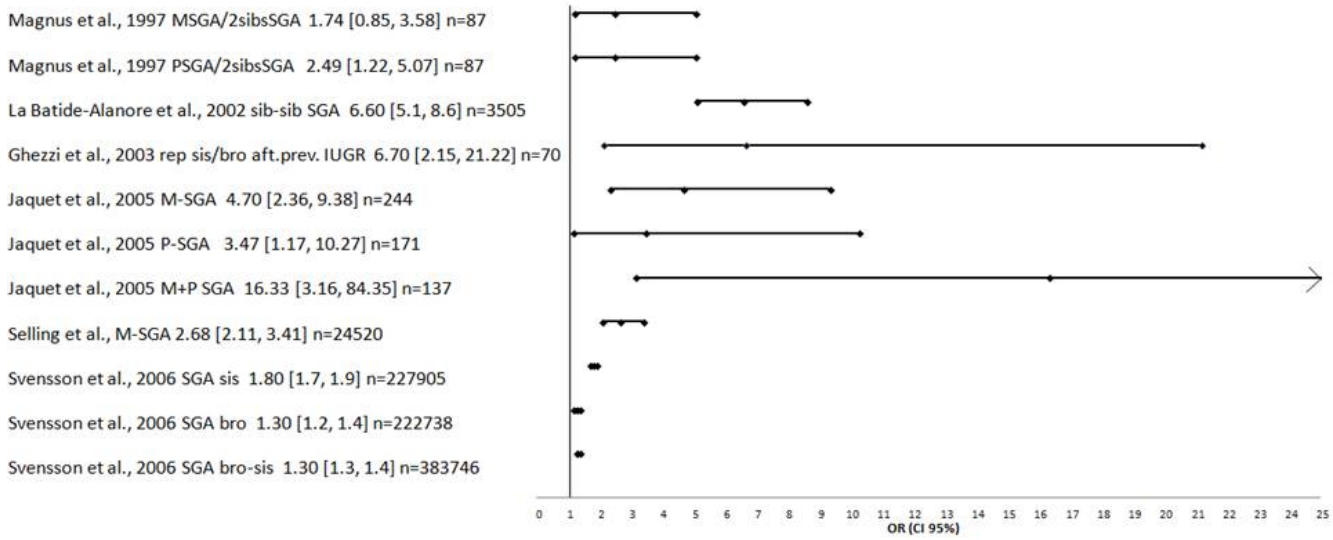
Having an older small for gestational age sibling may increase the incidence of being born small for gestational age more than fourfold. This small for gestational age incidence further increases (to a relative risk of six) when the child born small for gestational age was not the first born (i.e., the older sibling was small for gestational age) (La Batide-Alanore *et al*., 2002).

In a very large sample (>2,000,000), Svensson *et al*. (2006) compared the incidence of a small for gestational age birth when a mother's full sibling had a small for gestational age birth. Women whose full sisters had offspring born small for gestational age had a significantly increased risk of having a small for gestational age child themselves [OR 1.8 (95% CI 1.7, 1.9)] The corresponding risk for brothers was lower [OR 1.3 (95% CI 1.2, 1.4)] and for mixed sibling pairs (brother-sister, OR 1.3); however, the incidence is lower than for sisters. These results corroborate findings that familial factors influence the risk of small for gestational age, with variability among relationships in families. The statistically significant increased ORs between brothers and mixed sibling-pairs also suggest that the familial component of small for gestational age might be heritable also through the father, yet to a lesser degree.

A foetus that has not reached its growth potential because of genetic or environmental factors is termed 'intrauterine growth retardation'. Idiopathic foetal intrauterine growth retardation was specifically investigated by Ghezzi *et al*. (2003), who analysed families with women who had more than one intrauterine growth-retarded child. Seventy families who had intrauterine growth-retarded infants and seventy controls with similar demographic characteristics were enrolled in the study. The delivery of a previous intrauterine growth retarded infant was found to be an almost seven-fold increased risk factor for having a subsequent intrauterine growth retarded infant [OR 6.7 (95% CI 2.15, 21.22), p <0.01]. Fifteen of the families with women who had delivered

a previous intrauterine growth retarded infant agreed to be investigated for genetic counselling. Analysis revealed a familial relationship of intrauterine growth retarded children in all 15 families that were investigated. In nine out of the cases, the condition was observed in first-degree relatives down the generational line in two and three generations, suggesting a dominant inheritance pattern through both the father and the mother. The second group of families (6/15) showed a horizontal distribution of intrauterine growth retardation (across siblings), suggesting a recessive pattern of inheritance. These data, although taken from a very small study (only 15 families), suggest that a woman's tendency to have successive intrauterine growth-retarded births may be genetic but further studies are needed (see Figure 2.8).

Figure 2.8: Odds Ratios (OR) and Confidence Intervals (CI) for Recurrence of Small for Gestational Age and Intrauterine Growth Retardation in Offspring (only Studies with OR and CI Results)



Legend: M = maternal; P = paternal; sis = sister; bro = brother; sib-sib = siblings
SGA = Small for gestational age; IUGR = Intrauterine growth retardation

2.8 Stage 4: Summary of Findings

Five pregnancy and two neonatal recurrent familial variables were identified from the literature review: gestational age, preterm birth, prolonged pregnancy (post-term pregnancy), dystocia, caesarean section, infant birth weight, and foetal growth restriction including small for gestational age and intrauterine growth retardation. The published data shows that a mother's maternity history is a strong predictor of future incidence for her daughter's pregnancies and birth outcomes. A sister's maternity history and birth outcomes may also predict recurrent factors in sisters, with mother, mother and father, parents' siblings and siblings all potentially influencing birth outcomes of offspring. The current weight of the evidence for familial recurrence of birth outcomes in this review confirms the importance of taking a familial birth history for birthing women, especially in the perinatal period. Preterm birth and low birth weight are two examples of problems that may lead to mortality or birth diseases, and can affect the future health of an infant. Although these hazards are known, the familial relationship with these hazards has not yet been recognised as a potential source to avoid adverse birth outcomes.

Maternal associations for gestational age, preterm birth, prolonged pregnancy (post-term pregnancy), dystocia, caesarean section, infant birth weight, and small for gestational age suggest there are specific mechanisms through which mothers can transmit certain perinatal outcomes to children. Moreover, combined maternal, paternal, and brother and sister recurrence associations were observed for preterm birth, prolonged pregnancy, dystocia, infant birth weight and small for gestational age. Empirical research shows that there may be up to three intergenerational effects (Ghezzi *et al*., 2003).

Pregnancy and birth risk factors may lead to both spontaneous and provider-initiated complications. Identification of risk factors in early pregnancy (such as a familial incidence of preterm birth, or a familial propensity for dystocia) may prompt appropriate maternity care that can help prevent these complications.

Familial associations with preterm and post-term births may help identify women in need of preventive interventions. Dystocia, especially in nulliparous women, is a high risk indicator for augmentation of labour and caesarean delivery. This review found that mothers who themselves had dystocia in labour predict dystocia in their daughters. The finding that half-sisters from the same mother are more likely to experience dystocia than half-sisters from the same father is particularly relevant and contributes further to evidence of the importance of maternal history for nulliparous women.

Intragenerational (within family) influences include sisters' effects on prolonged pregnancy and caesarean section, especially for a first birth in the latter category. In addition, a maternal predisposition to repeat intrauterine growth retardation in successive pregnancies suggests that children of the same mother may repeat intrauterine growth retardation. However, consecutive birth outcomes for the same mother may be partially dependent on the mother's factors which remain fixed throughout all her pregnancies, such as her own intrauterine development, her childhood growth and attained adult height. With recent advances in molecular biology and genetics, other causes for intrauterine growth retardation have been identified. As well as the maternal factor, intrauterine growth retardation can be the result of foetal, placental or genetic causes, or can be the result of a combination of these factors (Sharma *et al*., 2016).

2.9 Discussion

The literature review identified positive parental influences and sibling influences on pregnancy and birth outcomes. Above-average gestational age and birth weight babies may have an association with prolonged pregnancy factors, dystocia, and caesarean section. Below-average gestational age and birth weight babies may have an association with preterm births, and intrauterine growth retardation factors. Familial maternal and paternal traits influence offspring birth weight and gestational age. The influence of the mother on birth weight is more influential than that of the father. In some families, larger or smaller than average babies may represent constitutionally large or small babies suggesting a familial variation in foetal size which is not necessarily pathological.

Familial history may provide opportunities for prevention and intervention during the perinatal period. Clinical and non-clinical influences profoundly affect medical decisions. Non-clinical influences include women's expectations and wishes (such as caesarean delivery on maternal request), physician-related factors such as unnecessary medical interventions that interfere with the physiological process of childbirth (discussed in section 1.9), and local management policies. In addition, within the non-clinical spectrum, a familial tendency for a dystocic labour (a longer more protracted labour than the norm) may be a positive independent predictor for a long normal birth. Yet nulliparous women with no reported family birthing history who fail to meet time limits and progress milestones in labour may be misdiagnosed with labour dystocia, experience long pushing phases, a higher rate of forceps or vacuum use, and even a caesarean section (Altman & Lydon-Rochelle, 2006; Boyle *et al*., 2013). Furthermore, since various factors (including women's choice) contribute to an

increased caesarean delivery rate, interest in familial predisposition rather than clinical considerations for caesarean section has become less relevant.

Both clinical and non-clinical factors may result in adverse outcomes and may be sensitive and specific markers for pathology. Awareness of iatrogenic results of over-treatment (such as misuse of oxytocin) may improve management of these women. Although clinical criteria such as post-term pregnancy are screened for potential risk of an adverse outcome, after 41 weeks' gestation 76% of post-term mothers and babies who have a subsequent normal long labour are likely to have a healthy outcome (Stock *et al*., 2012). Yet, post-term foetuses are often larger in size and weight (foetal macrosomia), leading to higher induction rates, which in turn may cause complications such as prolonged labour, dystocia, foetal distress and caesarean section delivery (Berg-Lekås *et al*., 1998; Mogren *et al*., 1999; Algovik *et al*., 2004; Lie *et al*., 2006). Although having large babies may be hereditary, there is no independent predictive hereditary effect for delivery by caesarean section for cephalopelvic disproportion in a family (Varner *et al*., 1996).

Identifying low birth weight babies presenting with intrauterine growth retardation or a short gestational period places small babies similarly at risk of expected adverse outcomes when compared with population foetal growth norms. Adjustments made for small for gestational age-born mothers delivering small for gestational age infants (Klebanoff *et al*., 1984; Magnus *et al*., 1997) and the multiplicative effect seen on small for gestational age offspring when both parents were born small for gestational age (Jaquet *et al*., 2005) may distinguish between babies requiring intervention for impaired uterine growth and constitutional physiological smallness unrelated to established criteria for detection of risk.

2.9.1 Strengths and Limitations

This systematic review synthesised available literature on inter- and intragenerational influences on pregnancy and birth outcomes. Major datasets of women with familial, transmitted or recurrent birth outcome variables were included. Evaluating more than 2,000,000 women from different ethnic and demographic backgrounds represented many regions and socioeconomic settings, permitting a more global view towards trends. Different study designs and statistical methods made comparison of these studies' outcomes difficult. The considerable heterogeneity in the way authors defined reference points for perinatal variables and how they measured and reported their findings could potentially have affected the results.

In those studies that examined the relative contribution of maternal and paternal influences on offspring birth outcomes, some variability in findings was likely associated with whether familial dynamics or genetic effects were at the root of these relationships. Few studies have been able to separate these different influences. Moreover, differential maternal aetiologies of the same variable are also inconsistent across the literature. For instance, the results of one study suggests that maternal low infant birth weight influenced preterm delivery (Klebanoff *et al*., 1984); yet another study found that mothers who themselves had been born preterm were not more likely to deliver their own offspring preterm (Selling *et al*., 2006). Other studies report a substantial sibling influence of being born small for gestational age (La Batide-Alanore *et al*., 2002), yet Magnus *et al.* (1997) found that successive small siblings were associated with the mother's infant birth weight.

Finally, many studies show evidence of maternal contributions to infant birth weight. By comparing the offspring of Indian unions versus European unions, only Agnihotri *et al.* (2008) found that Indian fathers' infant birth weights are a

stronger predictor than the infant birth weights of fathers from Western countries. Given that familial characteristics may be affected by a wide range of conditions, other variables, such as maternal diet, may play a significant role in infant birth weight outcome (Crume *et al*., 2016). Influential factors on the spontaneous onset of preterm labour may include infection or a medically expedited labour for maternal or foetal indications (Goldenberg *et al*., 2008). Other important factors that should not be overlooked include genetic and psychosocial factors, and pathogenic variants which may typify one, or more than one individual in a family.

The studies included in this review used heterogeneous populations, different study designs and different statistical methods, making objective comparisons between the studies complex. Descriptive graphs could only be prepared for those studies with individual summary statistics (CI, OR and RR), increasing the difficulty in making inter-study comparisons. Notwithstanding these above limitations, the review provided useful supporting information and a starting point for examining the primary hypothesis of this thesis. Characteristics of labour and birth in one generation of women may predict these characteristics in the next generation of their daughters.

This thesis explores similarities in mother-daughter first birth labour and birth characteristics. One of the key areas of this research is to investigate the relationship between mother-daughter patterns of labour and childbirth with a particular focus on length of labour. Normal labour progression for nulliparous women is highly variable between women and is often slower than in multiparous women (Zhang *et al*., 2010a). This is of importance because the rate of cervical dilation (cm/hr) may influence the course of action for clinicians and midwives providing care to labouring women. Moreover, common expectations of cervical dilation may be unrealistically fast for nulliparous

women leading to high intervention rates which in turn may impose unnecessary risks on the mother and foetus.

Utilising mothers' birth histories may temper rigid time limits currently applied to labour progress in clinical practice. A longer than normal labour should not be measured on the basis of duration alone. The mother's birth history may help maternity carers make clinical decisions responsive to the familial circumstances of individual women.

2.10 Conclusions

Pregnancy and birth characteristics and outcomes have been attributed to genetic, physiological, sociological, and possibly epigenetic effects. Findings from the systematic literature review confirm the existence of familial influences on pregnancy and birth outcomes. Mothers' birthing history may explain and account for irregular but non-pathological variations to population based norms that are the basis for hospital protocols. Routine assessment of intergenerational family (and particularly maternal) birthing history may be useful to identify individuals with apparent variants from the population norm, but who nonetheless fall within the norm of their family context. Assessing women for individual variation of pregnancy and birth outcomes based on familial physiological characteristics may reduce or eliminate unnecessary interventions which disrupt normal physiologic birth. A personalised and focused ante- and intrapartum care plan may allow greater understanding of an individual's birth potential, offer a more accurate prediction of what constitutes a physiological pregnancy and birth outcome within the family context, and prevent unnecessary interventions for women birthing under institutional constraints. Furthermore, strategies incorporating familial risk-reduction,

counselling and increased monitoring of familial risk markers are needed to understand how family history influences mother-daughter recurrence.

Familial influences on pregnancy and birth outcomes have taken on renewed significance as a consequence of the development of personalised medicine in healthcare. Tailoring a birth plan to an individual woman's requirements may have new etiologic significance for ante-, intra- and postpartum care. Although the genetic make-up of the foetus differs from that of the mother, this chapter has described inter- and intragenerational data to show that mothers (and other family members) may play a role in the recurrence of certain familial birth outcomes.

Chapter Three: Maternal Recall of Birth Events

3.1 Introduction

The previous chapter established the rationale for focusing on inter- and intragenerational pregnancy and birth outcomes. However, studies in this area are constrained by the lack of good quality and comprehensive records of childbirth, particularly for previous generations of women. Data collection, therefore, relies to a greater or lesser extent on maternal recall.

The second objective of the thesis is designed to address this issue:

- To establish the accuracy of maternal recall for cardinal labour and birth events.

Chapter three addresses this question and provides evidence on the accuracy of maternal recall many years after giving birth. After summarising the limitations of paper/microfiche medical records, I present the design and findings of a literature review on agreement between maternal recall of birth events and hospital birth records for specific birth variables. I identify a research gap in the surveyed literature and make recommendations for future research.

3.2 Medical Record Usage

The systematic documentation of a woman's perinatal history, including ante-, intra- and postpartum information, is commonly referred to as either the ‘administrative medical records’, ‘administrative birth records’, ‘medical birth records’, ‘hospital birth records’ or ‘birth records’. These interchangeable terms for maternity data include prescriptions for the administration of medication

(such as an iron supplement), laboratory tests, ultrasound scans and screening tests, as well as details on admission and discharge, maternal history, complications of pregnancy and childbirth, and birth outcome. Record holders are usually under a legal and ethical obligation to maintain records safely and securely for minimum retention periods. In the United Kingdom, the National Health Service medical records belong to the Secretary of State for Health and are subject to policies and procedures for record retention and disposal (Mersey Care NHS Trust, 2016). In most countries, medical birth records are confidential documents and are only released when permitted by law or with written authorisation of the woman.

The records of each woman's perinatal history are primarily compiled, maintained, dated and signed by healthcare providers. These administrative records collate mothers' self-reported health information and maternal lifestyle factors that are discussed during healthcare visits. Maternity records, used to monitor and assess health, should be shared with relevant healthcare providers and should track progress at every stage of ante-, intra- and postpartum care. An informative and accurate reproductive history is assumed to facilitate effective management of maternal foetal clinical information crucial for the routine care of healthy birthing women and their babies (in line with recommendations by the National Institute for Health and Care Excellence (NICE) (NICE guidelines [CG190], 2014).

Today, many countries use electronic health record systems. Electronic health record adoption rates vary widely. For example, Greg (2013) lists the top ten countries for electronic health record adoption: Norway (98%), Netherlands (98%), United Kingdom (97%), New Zealand (97%), Australia (92%), Germany (82%), United States (69%), France (67%), Canada (56%) and Switzerland (41%).

Originally designed to compile statistical information, generate patient care forms and support insurance and billing activities, contemporary information technology healthcare systems hold targeted information recording a mother's personal health status, clinical visits, familial maternity history, routine information on extended family health, family members contact information, and socioeconomic status. With the development of electronic health record systems comes the ability to improve the quality of patient care. Acknowledging this potential, the World Health Organization (WHO, 2007) has published a manual on implementing electronic health record systems for developing countries. However, electronic health record systems are still highly varied across healthcare systems, with providers in each country struggling with how to ensure that clinical information follows patients seamlessly between care settings.

Women with an itinerant lifestyle may, despite electronic record-keeping, have missing or incomplete maternity histories which might directly affect maternal and newborn medical management. Despite the well documented reports on the benefits of electronic health, adoption remains low in developing countries such as Tanzania and Kenya (Omary *et al.,* 2010; Juma *et al*., 2012).

3.3 Limitations of Paper and Microfiche Medical Records

Any analysis of historical hospital records should factor in poor charting, limited record retention and the pitfalls of storage and accessibility. Physical records need to be stored. Location and retrieval of archived material can be complex.

Although transference of medical records to microfiche has created a more reliable and concise format, some information may be lost when paper records

are converted to roll microfilm. In addition, although more durable than paper records, microfiche records are also subject to deterioration and damage, and are especially sensitive to environmental factors such as humidity and temperature. Thus, even when retrieved, the data in paper birth records and microfiche may be limited by a combination of illegible handwriting and poor preservation (Hewson & Bennett, 1987). Moreover, all hospital records include errors, inconsistencies and missing data (Maresh *et al*., 1983; Joffe & Grisso, 1985; Hewson & Bennett, 1987). In addition, information decay in old datasets may contribute to the loss of important clinical information and historical record formats may no longer be readable (Kemp *et al.,* 1997). Some records (paper or electronic) may have been lost or misfiled, and so are no longer available (Joffe & Grisso, 1985; Hewson & Bennett, 1987; Troude *et al*., 2008; Elliot *et al*., 2010).

3.3.1 Empirical Maternal Recall Research and Data Sources

Microfiche birth records were used for the maternal recall empirical study described in the next chapter. As explained above, microfiche records created by converting paper records suffer similar limitations as paper records. Furthermore, clinical information stored in birth records may be limited in their scope. Although having the advantage of being composed and compiled by maternity staff, including nurses, midwives, hospital doctors and consultants, birth records are limited to the actual information recorded. Note keeping and record documentation may be affected by nurse/physician variances in writing style. Nurses and midwives tend to focus on the ‘big picture’ using ‘narrative’ to describe a clinical situation, whereas physicians tend to use bullet points of critical information (Leonard *et al*., 2004). In addition, institutional requirements for item inclusion in medical records are not uniform (Joffe and Grisso, 1985; Hewson & Bennett, 1987). For example, some hospital birth records may only

document a particular pregnancy and birth at a specific hospital, thereby ignoring a mother's entire history of prior pregnancies and birth outcomes. In some cases, women who have been referred between hospitals may arrive without notes (Landry *et al*., 2014).

Particular issues relevant to this thesis include imprecise charting of progress in labour resulting from vaginal examinations performed by different examiners (Tufnell *et al*., 1989; Robson, 1991; Clement, 1994; Buchmann & Libhaber, 2007), and irregular logging of exact durations of labour by overburdened or understaffed hospital midwives (Landry *et al*., 2014). Overwork may also result in insufficient evaluation of labour progress and poor documentation of clinical information. Thus, data obtained from hospital records may not be accurate and complete (Tilley *et al*., 1985; Hewson & Bennett, 1987; Laurell *et al*., 1994; Harris *et al*., 1997).

3.3.2 Summary of Medical Record Usage for Clinical Information

Combining maternal self-report and hospital maternal record data may be the best method for accruing a complete obstetric history. Evidence on general health (such as for diabetes, hypertension, cardiovascular disease and ambulatory care) shows that combining data from patient self-report interviews and medical record documentation may provide the most valid and complete assessment of a patient's health (Okura *et al*., 2004; St Sauver *et al*., 2005; Tisnado *et al*., 2006; Goulet *et al*., 2007; Corser *et al*., 2008; Hure *et al*., 2015). To determine whether maternal self-reports of events during pregnancy and childbirth are similarly salient, studies on the agreement between maternal recall of birth events and hospital records are reviewed in the next section. Factors affecting reporting bias were also investigated.

3.4 Association Between Maternal Recall of Birth Events and Hospital Birth Records: a Literature Review

3.4.1 Background

Perinatal information on a mother's history and wellbeing may be obtained through hospital birth records and maternally recalled birth events. The accuracy of this information is important, since pregnancy outcomes often recur in subsequent pregnancies or within families. Patient demographics, past medical history, reproductive and prenatal history, pregnancy, labour and birth outcomes, and postpartum and neonatal information may all be significant factors or predictors for birth outcomes for the specific mother and her offspring.

When access to medical records is limited or administrative records are found lacking, physicians and midwives often rely on maternal reporting of perinatal history. However, self-reported maternity histories may be inadequate as a sole data source. A mother's age (Gayle *et al*., 1988), recall timeframe since birth (Tomeo *et al*., 1999), perinatal events and birth outcome (Yawn *et al*., 1998), memory lapses, ethnicity, verbal competence, education (Elkadry *et al*., 2003) and socioeconomic status (Elkadry *et al*., 2003; Adegboye and Heitman, 2008) may all affect the quality of maternal reporting. Furthermore, mothers may ignore, under-represent or exaggerate obstetric complications that required intervention, such as low birth weight (Tilley *et al*., 1985; Seidman *et al*., 1987; Casey *et al*., 1992). This may be the result of various forms of information accrual or reporting bias resulting in repeated, but false, birth history information.

The first systematic review on the agreement of maternal recall and hospital birth records was conducted by Wenar in the US in 1963, who reviewed five studies on infant birth weight and gestational age (Macfarlane, 1938; Haggard *et al*., 1960; Goddard *et al*., 1961; Robbins, 1961; Wenar & Coulter, 1962).

Wenar concluded that infant birth weight and gestational age were reliably recalled up to eight years post-delivery, although no statistical analysis was conducted due to methodological inconsistencies between the studies.

Since Wenar's review, studies on the agreement between maternally recalled perinatal outcome and hospital birth records have been conducted on a range of birth variables in a number of countries. Maternal recall of birth events over time is a key variable in women's health research.

3.5 Aim

To review published literature on the agreement between maternally recalled perinatal outcomes and hospital birth records over time.

The reviewed studies were also examined for their assessment of the influences of demographic and socioeconomic factors, and maternal/infant outcomes on the accuracy of maternal recall.

3.6 Methods

3.6.1 Literature Search Methods, Data Sources and Selection Criteria

First, a search was conducted (from 1980 to August 2015) accessing Ovid SP including Embase, MEDLINE, ERIC, HMIC, and Maternity and Infant Care resources. No language restrictions were applied. Second, a Google internet search was launched to identify unpublished studies not yet included in these electronic databases. Third, a manual search of reference lists of included and/or relevant articles was performed.

The following key terms (and associated truncation) were used: (mother$ or maternal or women$) and (memory or recall$ or remember$ or recol$) and (delivery or birth or childbirth or labor or labour$ or pregnan$) and (agree$ or valid$ or accura$).

For the purposes of this thesis and pertinent study aims, the following were selected for inclusion criteria:

(a) studies that compared questionnaire or interview data collection methods vs. medical records, and;
(b) maternal recall of at least one of the following birth outcomes: gravidity, parity, onset of labour, length of labour, use of pain relief in labour, mode of delivery (vaginal, assisted or caesarean), gestational age at delivery, and infant birth weight.

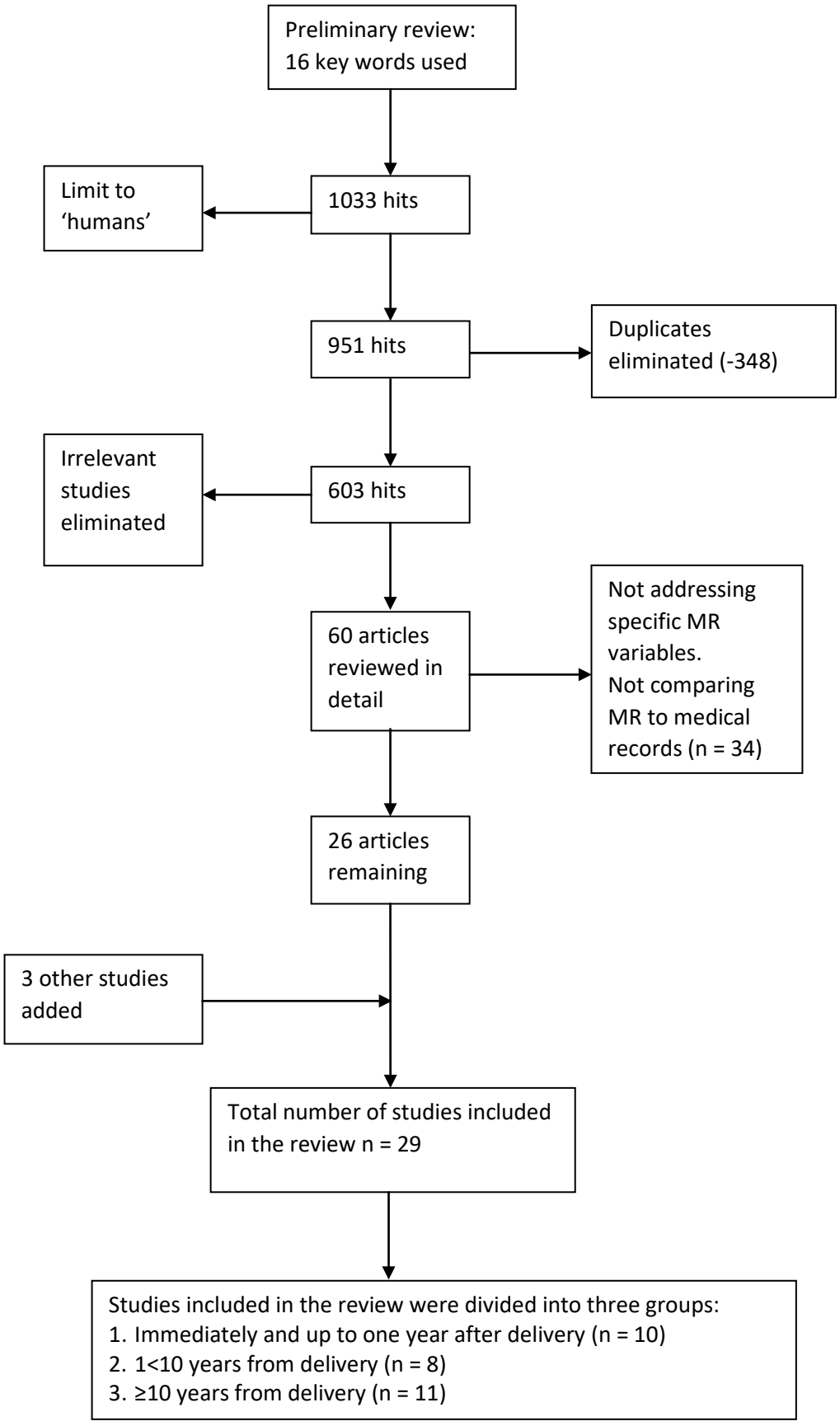
The search strategy was formulated conjointly with my Director of Studies and University Supervisor. I, as the research investigator, selected articles for review based on title then, based upon abstract and full text, eligible studies for final study selection were chosen by the reviewer team (my Director of Studies, my university supervisor and myself). Relevant studies included in the review were summarised for sample size, year and country of publication, methodology, statistical procedures, elapsed time from birth event to recall, recalled variable(s) and source of medical records.

3.7 Results

The electronic database search identified 1,033 citations, of which 82 were excluded when limiting to ‘humans’ (n = 951). Eliminating duplicates left 603 citations. A further 543 citations were excluded because they did not focus on

maternal recall of pregnancy and birth events. The remaining 60 articles were screened for maternal recall of predefined variables relevant to the investigation. Some 29 articles were included in the review; 26 from electronic databases and an additional 2 from references and 1 from the Google internet search. Figure 3.1 presents a flow chart of the search strategy utilised.

Figure 3.1: The Article Elimination Process



3.8 Data Synthesis

The data were synthesised using a four-stage approach:

Stage 1 Charting article characteristics in this literature review (study population, design, variable identification, statistical analyses, results, discussion and potential confounders) and identifying maternally recalled perinatal variables for agreement analysis with hospital records.

Stage 2 Review of time elapsed since the birth event and agreement analysis. Birth data from maternal recall by questionnaire interview and hospital records were compared for agreement for the following time intervals: 1) immediately and up to one year after delivery, 2) 1<10 years from delivery, and 3) ≥10 years from delivery.

Stage 3 Assessment of maternal recall and hospital record data of perinatal variables for influence by sociodemographic factors.

Stage 4 Analysis, interpretation and discussion of the data.

3.8.1 Stage 1: Characteristics of Studies Included in this Review

The 29 articles for review were all published in English and spanned almost three decades (from 1984 to 2013) (see Table 3.1 for a summary of included papers).

A total of 95,399 women were recruited from nine countries on four continents: Asia (China and Israel), Australia and Oceania (Australia), Europe (Denmark, France, Netherlands and the UK), and North America (Canada and the USA). Studies were heterogeneous, with sample sizes ranging from 47 (Oates & Forrest, 1984) to 12,391 mothers (Quigley *et al*., 2006). The time to recall for report varied from 3 weeks to 70 years, and for self-report ages from teens to

80 years. The majority of these studies explored maternal recall of singleton birth data. The exceptions were a twin study by Liu *et al*. (2013) and a study by Troude *et al*. (2008) who analysed the firstborns of twin or triplet pregnancies. Methods of data collection included maternal interviews or questionnaires on labour and delivery at various timespans following birth. Only fifteen studies collected sociodemographic details.

Recorded data were from hospital records and were used for agreement with maternal recall. Twenty-eight studies compared maternal report of perinatal events to paper medical records. One study (Bat-Erdene *et al*., 2013) compared maternal report of perinatal events with electronic health records.

Various methods were used for agreement analysis in the studies. Almost half of the authors (n = 13) used the kappa coefficient correlation (Cohen, 1960) which corrects for agreement based on chance alone. Values of 0.81 to 1.0 represent almost perfect agreement, values of 0.61 to 0.8 represent substantial agreement, values of 0.41 to 0.6 represent moderate agreement, values of 0.21 to 0.4 represent fair agreement, while levels of 0 to 0.2 represent slight agreement and 0 represents poor agreement (Landis & Koch, 1977). Four studies used simple percent agreement, which does not eliminate agreements resulting from chance alone and thus may yield an inflated estimate of agreement. Additional methods used were levels of sensitivity and specificity, *p*-values, Bland Altman plots, Chi-square, Fisher, Kruskal-Wallis and Mann-Whitney tests, Intraclass Correlation Coefficient, and Pearson's and Spearman's Correlation Coefficients. Regression analyses were used to assess the influence of ethnicity, education and social circumstance.

All studies reported metric measures (g) for birth weight except for Gayle *et al*. (1988) who reported ounces. All included articles reported on at least one or a

combination of the following maternity variables: gravidity, parity, length of labour, pain relief, mode of delivery (vaginal, forceps/vacuum, caesarean section), gestational age and birth weight.

3.8.2 Stage 2: Time Elapsed Since the Birth Event and Agreement Analysis

Studies were divided into three intervals, based on the time elapsed since birth:

1. Immediately and up to one year after delivery n = 10 (overall mean recall period since the birth event = 20.66 weeks).
2. 1<10 years from delivery n = 8 (overall mean recall period since the birth event = 6 years).
3. ≥10 years from delivery n = 11 (overall mean recall period since the birth event = 22.59 years).

Results are presented in Table 3.1. For the nine studies in this review that used only percentage agreement or percentage agreement for certain variables (Oates & Forrest, 1984; Gayle *et al*., 1988; O'Sullivan *et al*., 2000; Walton *et al*., 2000; Elkadry *et al*., 2003; Tate *et al*., 2005; Li *et al*., 2006; Quigley *et al*., 2006; Poulsen *et al.,* 2011), percentage agreement together with the terms cited in the article's texts (excellent/high/good, moderate or low agreement) were used to depict results. Percentage agreement was classified similarly to kappa scores, whereby 80-100% depicts almost perfect agreement; 60-80% depicts substantial agreement, 40-60% depicts moderate agreement, 20-40% depicts fair agreement, and levels of 0-20% depicts slight agreement. Statistical analyses used to test agreement are listed below in Table 3.1.

Table 3.1: Agreement Between Maternally Recalled and Recorded Birth Outcomes in all Three Time Intervals

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
Gravidity and parity			Liu *et al.* (2013) (n = 611, twin cohort)	Perfect agreement for maternal history of previous live births †(k = 1.0)	Buka *et al.* (2004) (n = 96)	Excellent agreement for parity = 0 and parity >4 †(k = 0.98 and k = 0.93 respectively) and number of prior pregnancies ‡§ ICC = 0.94.
					Tilley *et al.* (1985) (n = 1,421)	Good agreement for number of prior pregnancies †(k = 0.84). Substantial agreement for number of miscarriages prior to participants' births (k = 0.74).
					Tomeo *et al.* (1999) (n = 154)	High agreement for history of previous spontaneous or induced abortions §(Spearman Correlation r = 0.88)
Length of labour (LoL)	Elkadry *et al*. (2003) (n = 277)	Length of first stage events accurately recalled "Most women accurately recalled 1st stage events" (p.197). 71% accurately recalled 2nd stage LoL within 15 mins.	Rice *et al*. (2006) (n = 126)	Fair agreement for very short (<3 h) and very long (>36 h) labours †(k = 0.26 and 0.21, respectively)	Hopkins *et al*. (2007)* (n = 178 mothers / 401 births)	Women slightly underestimated the length of the second stage of labour with median length 18 minutes by MR and 20 minutes from chart abstraction. ¥Sensitivity (95% CI) 0.62 (0.28-0.87); specificity (95% CI) 0.84 (0.76-0.89).
					Tomeo *et al.* (1999) (n = 154)	Moderate correlation: §Spearman Correlation Coefficient r = 0.53

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
	Troude *et al*. (2008) (n = 580 twin/triplet cohorts)	1st stage events good agreement †k = 0.83. 2nd stage events excellent agreement k = 0.99			Buka *et al.* (2004) (n = 96)	Moderate agreement for prolonged labour †(k = 0.43)
Pain relief	Bat-Erdene *et al*. (2013) (n = 2,552)	Epidural anaesthesia moderate agreement †(k = 0.73)	Githens *et al.* (1993) (n = 102)	Moderate agreement for anaesthesia as a categorical variable 4-6 years postpartum †(kappa coefficients 0.58, 65% agreement)	Hopkins *et al*. (2007) (n = 178 mothers / 401 births)	Anaesthesia in labour very accurately recalled ¥(sensitivity 0.83)
	Hewson & Bennett (1987) (n = 397 primiparae)	General anaesthetic 100% agreement. Pethidine near perfect agreement †(k = 0.85).			Buka *et al*. (2004) (n = 96)	Anaesthesia in labour very accurately recalled ¥(sensitivity 87%). 8% of women who reported taking pain relief had no record of it (specificity = 30%).
Mode of birth	Bat-Erdene *et al*. (2013) (n = 2,552)	Caesarean section excellent agreement †k = 0.99 ¥(99.7% sensitivity & 99.8% specificity)	Githens *et al.* (1993) (n = 102)	Moderate agreement †(k = 0.79) for mode of delivery in 3 categories (vaginal births, assisted deliveries and caesarean sections).	Buka *et al.* (2004) (n = 96)	Excellent agreement ¥(0.98% sensitivity). Perfect recall of caesarean section, breech delivery and multiple birth †k = 1, k = 1, k = 1.
	Casey *et al.* (1992) (n = 69)	Excellent agreement for type of birth - caesarean section or vaginal (100% agreement)	Liu *et al*. (2013) (n = 611, twin cohort)	†k = 0.97 for both twins.	Hopkins *et al*. (2007) (n = 178 mothers/401 births)	Excellent agreement †(k = 0.98) For caesarean section ¥sensitivity (0.98), specificity (1.00).

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
	Elkadry *et al.* (2003) (n = 277)	Perfect agreement for caesarean section. Substantial agreement for instrumental birth †k = 0.66.	Oates & Forrest (1984) (n = 47)	45% recalled normal birth - labour <24hrs, non-instrumental, compared with 62% normal births recorded. 22 mothers recalled prolonged labour + forceps birth, whereas 14 cases were recorded.	Yawn *et al.* (1998) (n = 281)	Excellent agreement †(k = 1.0)
	Hewson & Bennett (1987) (n = 397)	100% agreement on CS, vaginal birth and only 1 disagreement on use of forceps. CS †k = 1, Forceps k = 0.95.	Rice *et al.* (2006) (n = 126)	Agreement perfect for CS †k = 1.0. Use of forceps or vacuum k = 0.9. Emergency CS k = 0.7.		
	Lederman & Paxton (1998) (n = 144)	Perfect agreement for mode of birth: vaginal, primary and secondary CS (no stats given).	Sou *et al.* (2006) (n = 208)	Caesarean section delivery ¥ 100% sensitivity, 100% specificity.		

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
	Quigley *et al.* (2006) (n = 12,391)	94% agreement using 6 categories (normal, forceps, ventouse, assisted breech, elective CS, emergency CS). 98% agreement using 3 categories (normal, assisted, CS). >99% agreement for CS vs. not CS. Of women who reported having CS, 10.7% discrepancies between elective and emergency CS.				
	Troude *et al.* (2008) (n = 580 twin/triplet cohorts)	Elective CS excellent agreement †k = 0.83. CS emergency excellent agreement k = 0.99.				

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
Gestation-al age	Bat-Erdene *et al.* (2013) (n = 2,677)	Exact agreement in 71.5%. 98.3% within 2 weeks. Excellent LIBW agreement †k = 0.82	Adegboye & Heitman (2008) (n = 1,271)	Overall there was a tendency to overestimate GA. Good general agreement ‡ICC = 0.76, correlation coefficient r = 0.85. Markedly lower agreement for post-date >41w §r = 0.37; ‡ICC = 0.42. Significant underestimation among mothers of non-white children and single mothers. Mothers who gave birth to SGA underestimated GA compared with AGA & LGA.	Buka *et al*. (2004) (n = 96)	Pre/post-term delivery fair agreement †k = 0.36, k = 0.31. GA term ‡ICC = 0.64 shows moderate agreement.
	Casey *et al.* (1992) (n = 69)	Moderate agreement for preterm delivery. Q: "Baby born more than 2 weeks early?"	Liu *et al*. (2013) (n = 611, twin cohort)	Poor agreement for recall of GA for both twins †(k = 0.17 & k = 0.21).	Hopkins *et al.* (2007) (n = 178 mothers/ 401 births)	Agreement with a mean variance of 3 days. ¥Specificity for preterm birth (<37 wk) (0.98).
	Gayle *et al.* (1988) (n = 46,637)	67.2% agreement <37 71.4% agreement >37	Oates & Forrest (1984) (n = 47)	51% agreement, GA being defined as 2 weeks before or 1 week after the expected date of delivery. 36% overestimated the length of gestation.	Seidman *et al*. (1987) (n = 97 mothers of 662 children)	100% agreement in 39% of sample (mothers n = 97/children n = 880) 74% agreement to within 1 week GA 94% agreement to within 2 weeks GA

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
	Poulsen *et al*. (2011) (n = 8,058)	‡ICC almost perfect for exact agreement 0.86. 72.2% agreement for GA. 94.5% agreement ±1wk. 98% agreement for 3 groups (<32; 32-36; 37+wks).	Olson *et al*. (1997) (n = 302)	High agreement §(r = 0.86) with mean difference between the two sources -0.35 weeks. When categorised as <38w, 38-41w, and ≥42 w agreement was moderate †(k = 0.6).	Tomeo *et al.* (1999) (n = 154)	Preterm delivery high agreement §(Spearman Correlation r = 0.82)
	Troude *et al.* (2008) (n = 580 twin/triplet cohorts)	Categorical GA excellent agreement †k = 0.85.	Sou *et al*. (2006) (n = 208)	§r = 0.83 for term. r = 0.93 for preterm. 62.6% of term deliveries and 66.3% of preterm deliveries had exact agreement. 93.4% of term deliveries and 91.1% of preterm deliveries had agreement of within 1 week.	Yawn *et al*. (1998) (n = 281)	Just under half of all women in sample could recall GA. 45% of those women showed moderate to substantial agreement ‡(ICC = 0.62). For women who gave a recalled due date (86%), GA was calculated & agreement was substantial (ICC = 0.9).Recall was better for women delivering preterm infants.
Infant birth weight	Bat-Erdene *et al.* (2013) (n = 2,552)	Exact agreement in 11.6%. 91.7% agreement IBW within 200g.	Adegboye & Heitman (2008) (n = 1,271)	High agreement ‡ICC = 0.93, r = 0.97 with high reliability across subgroups.	Buka *et al*. (2004) (n = 96)	Good recall for low IBW (<5lbs) †(k = 0.88)

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
	Casey *et al.* (1992) (n = 69)	Excellent agreement (100%) for IBW (less than or greater than 2,500g)	Gofin *et al.* (2000) (n = 259)	99% of mothers of normal IBWs recalled birth weight of >2,500g. 73% of LIBW infants recalled birth weights <2,500g. Near perfect agreement †k = 0.71.	Catov *et al.* (2005) (n = 120)	High agreement for first births ‡ICC = 0.96. Moderate for subsequent births ICC = 0.59. MR highly reliable for first births §r = 0.95 and subsequent births r = 0.87.
	Gayle *et al.* (1988) (n = 46,637)	89% reported within 1 ounce agreement of recorded IBWs.	Liu *et al*. (2013) (n = 611, twin cohort)	Near perfect agreement both twins †(k = 0.84, k = 0.82).	Hopkins *et al.* (2007) (n = 178 mothers/401 births)	¥Sensitivity IBW ≥4,000g (0.86); specificity IBW ≥4,000g (0.91).
	Lederman & Paxton (1998) (n = 144)	Very good agreement for IBW. Records slightly higher (3,452 ± 450g, mean ± SD) than MR.	Oates & Forrest (1984) (n = 47)	Only 50% of mothers had accurate agreement.	Li *et al.* (2006) (n = 1,432)	¥Low sensitivity (52.4%) with consistent over-reporting of IBW by Taiwanese mothers.
	Tate *et al.* (2005) (n = 11,890)	Overall 92% accuracy within 100g. Range: 94% among British/Irish white mothers to 69-89% for other ethnic groups.	Olson *et al*. (1997) (n = 302)	High agreement (§r = 0.98, †k = 0.9)	Lumey *et al.* (1994) (n = 626)	Recalled and recorded IBWs identical for 35% of sample, and symmetric around the mean for the remainder. No significant difference between recalled and recorded IBWs (paired t-test, p >0.5).
	Troude *et al.* (2008) (n = 580 twin/triplet cohorts)	Categorical IBW, 3 groups excellent agreement †k = 0.99	Rice *et al*. (2006) (n = 126)	LIBW infant (<2,500g) †k = 0.8; Very LIBW infant (<1,500g) k = 1.0; IBW continuous measure §r = 0.991	O'Sullivan *et al.* (2000) (n = 649)	75% of recalled IBW were within 50g of hospital records.

Birth outcomes	Immediately and up to one year after birth, n = 10 articles		1<10 years from birth, n = 8 articles		≥10 years from birth, n = 11 articles	
	Authors	**Findings**	**Authors**	**Findings**	**Authors**	**Findings**
			Sou *et al*. (2006) (n = 208)	High agreement for term §r = 0.89 and higher for preterm group r = 0.95. 80.4% of mothers with term delivery and 96% of mothers with preterm delivery recalled IBW within 100g.	Seidman *et al*. (1987) (n = 97 mothers of 662 children)	MR highly accurate: 41% within 10g; 75% within 100g; 87% within 200g. Recall of IBW was best for birth order 1 and 10-12. Mothers of LIBW (≤2,500g) and high IBW (>4,000g) were more accurate. First births best recalled.
					Tilley *et al*. (1985) (n = 1,421)	Excellent agreement recruited group †k = 0.95. Excellent agreement walk-in group k = 0.96.
					Tomeo *et al.* (1999) (n = 154)	Excellent agreement §r = 0.94.
					Walton *et al*. (2000) (n = 1,015)	84.4% accurately recalled IBW to within 227g. Parents of high and LIBW infants recalled IBW less accurately than parents of normal IBW infants.
					Yawn *et al.* (1998) (n = 281)	Excellent agreement ‡ICC = 0.99

*Defined as >120 minutes for nulliparous women or >60 minutes for multiparous women who did not receive regional anaesthesia; or defined as >180 minutes for nulliparous women or >120 minutes for multiparous women who did receive regional anaesthesia.

† Kappa coefficients (k) for agreement analysis values: 0.81 to 1.0 represent almost perfect to perfect agreement, 0.61 to 0.8 represent substantial agreement, 0.41 to 0.6 represent moderate agreement, 0.21 to 0.4 represent fair agreement, 0 to 0.2 represent slight agreement, and 0 represents poor agreement (Landis & Koch, 1977).

‡ Intraclass Correlation Coefficient (ICC) for agreement analysis values: >0.8 indicates almost perfect agreement, 0.7-0.8 indicates strong agreement, 0.5-0.6 indicates moderate agreement, 0.3-0.4 indicates fair agreement, 0-0.2 indicates poor agreement.

§ Spearman's Correlation Coefficient (for continuous variables) is shown as an r-estimate (robust estimation based on a rank test) measuring the strength of association between maternal recall and hospital records. Strength of correlation: 0.80-1.0 indicates very strong, 0.60-0.79 indicates strong, 0.40-0.59 indicates moderate, 0.20-0.39 indicates weak, 0.00-0.19 very weak.

¥ Sensitivity and specificity for categorical variables:
Sensitivity of maternal recall shows the proportion of women who recalled the event when it had actually occurred.
Specificity of maternal recall shows the proportion of women who did not report events which had not occurred.

3.8.3 Stage 3: Agreement of Maternal Recall and Hospital Record Data of Perinatal Variables Across all Time Intervals and the Influence of Demographic Factors

Stage 3 is divided into two sections. The first section summarises agreement/disagreement of maternal recall with hospital birth records across all time intervals since birth. The second section reports on other independent factors (using logistic regression) associated with agreement/disagreement of maternal recall with hospital records. These included ethnic, social and birth characteristics.

Clinical factors such as previous reproductive history (gravidity and parity) were only investigated in the ≥*10 years from delivery* timeframe. Two studies (Tilley *et al*., 1985; Buka *et al*., 2004) reported that women were highly accurate in their recall of personal maternity history even up to 30 years postpartum (k = 0.74-0.98).

Six studies reported on agreement with hospital birth records for maternally recalled length of first and second stages of labour and was found to be excellent in one study (Troude *et al*., 2008), accurate for the first stage in another study (Elkadry *et al*., 2003), and showed fair accuracy in every time interval category since birth in the remaining studies (Tomeo *et al*., 1999; Buka *et al*., 2004; Rice *et al*., 2006; Hopkins *et al*., 2007). Only one study (Elkadry *et al*., 2003), reported on lower recall in mothers in the second stages of labour with discrepancies of up to 15 minutes between agreement with medical records. Since labour onset is often self-diagnosed and women vary in their response to assessing painful contractions (Gross *et al*., 2003), there is no research-based information on measuring labour length. Length of labour in clinical notes is based on maternal reports, is dependent on when a vaginal exam took place and the vaginal exam itself is an imprecise measure of labour

progress when performed by different examiners (Buchmann & Libhaber, 2007). Thus, a 15-minute discrepancy becomes rather irrelevant and cannot be counted within the averages when measuring length of labour.

Four studies across all timeframes recalled pain relief in labour with a high degree of accuracy when compared with hospital records (Hewson & Bennett, 1987; Buka *et al*., 2004; Hopkins *et al*., 2007; Bat-Erdene *et al*., 2013). Results for pethidine use, epidural use and general anaesthetic showed sensitivity 83-87%; pethidine use with near perfect agreement k = 0.85, and 100% agreement for general anaesthetic. In contrast, only Githens *et al*. (1993) reported on moderate agreement for anaesthesia (k = 0.58 and 65% agreement) four to six years after delivery.

Twelve studies reported excellent agreement for mode of birth across all timeframes (Hewson & Bennett, 1987; Casey *et al*., 1992; Lederman & Paxton, 1998; Yawn *et al*., 1998; Buka *et al*., 2004; Quigley *et al*., 2006; Rice *et al*., 2006; Sou *et al*., 2006; Hopkins *et al*., 2007; Troude *et al*., 2008; Bat-Erdene *et al*., 2013; Liu *et al*., 2013). Kappa coefficients ranged from 0.80-1.00 and 98-100% agreement, with caesarean section deliveries exceptionally well recalled. Two studies reported substantial and moderate agreement for mode of delivery in the *immediately and up to one year after delivery* and *one to ten years from delivery* timeframes respectively (Githens *et al*., 1993; Elkadry *et al*., 2003). One study (Oates & Forrest, 1984) in the *one to ten years from delivery* timeframe found only 72% agreement. However, the researchers concluded that their small sample size of 47 Kenyan women consisting of poorly educated mothers of low socioeconomic status may have biased results.

Eleven studies reported moderate to very high agreement for gestational age as a categorical variable across all timeframes (Seidman *et al*., 1987; Casey *et al*.,

1992; Olson *et al*., 1997; Yawn *et al*., 1998; Buka *et al*., 2004; Sou *et al*., 2006; Hopkins *et al*., 2007; Adegboye & Heitman, 2008; Troude *et al*., 2008; Poulsen *et al*., 2011; Bat-Erdene *et al*., 2013) summary range k = 0.6 to k = 0.85.

Two studies (Oates & Forrest, 1984; Liu *et al*., 2013) in the *one to ten years from delivery* timeframe found poor to fair agreement for gestational age (k = 0.17 and k = 0.21 and 51% respectively). The first was a small sample (n = 47) of poorly educated mothers of low socioeconomic status (as pointed out by the researchers), and the second study was a twin study.

Birth weight was the most commonly examined variable across all timeframes with substantial to excellent agreement of maternal recall of infant birth weight with hospital birth records (summary range k = 0.71 to k = 1). Catov *et al*., (2005) explored women's recalled infant birth weight among older women 35-70 years after birth. With an average of 57 years recall, agreement with hospital records was found to be particularly precise for first births. Studies by Gofin *et al*. (2000), O'Sullivan *et al*. (2000), Walton *et al*. (2000), Tate *et al*. (2005) and Rice *et al*. (2006) reported no mean difference between mothers' recalled birth weight of term babies and infant birth weight recorded in hospital birth records. When infant birth weight was analysed as a categorical variable (some studies estimated infant birth weight to within the nearest 50g-200g to account for small differences in recalled and recorded birth weights), excellent agreement was reported in 18 studies (Oates & Forrest, 1984; Tilley *et al*., 1985; Seidman *et al*., 1987; Gayle *et al*., 1988; Casey *et al*., 1992; Lumey *et al*., 1994; Olson *et al*., 1997; Yawn *et al*., 1998; Lederman & Paxton, 1998; Tomeo *et al*., 1999; Buka *et al*., 2004; Catov *et al*., 2005; Sou *et al*., 2006; Hopkins *et al*., 2007; Adegboye and Heitman, 2008; Troude *et al*., 2008; Bat-Erdene *et al*., 2013; Liu *et al*., 2013), with a summary range of 87-91.7% within 200g, 75-96% within 100g and 75-89% within 50g. These small discrepancies in birth weights may in part be

attributed to infant size at birth. Mothers of low or high birth weight infants tended to recall birth weight less accurately than mothers of normal birth weight infants (Tilley *et al*., 1985; Seidman *et al*., 1987; Gayle *et al*., 1988; Lumey *et al*., 1994; Walton *et al*., 2000; Sou *et al.,* 2006).

Other factors contributing to discrepancies in infant birth weight were rounding off birth weights to the nearest half or full kilogram or pound, confusion when transposing or converting birth weights from pounds and ounces to kilograms in records, missing decimal points or missing a leading zero when recording weights, and incorrect linkage of two children of multiple births due to misreporting of birth order (Walton *et al*., 2000; Tate *et al*., 2005).

Cultural practices may be responsible for Taiwanese mothers' consistent over-reporting of infant birth weight in two Chinese studies (Li *et al*., 2006; Sou *et al*., 2006). High value is placed by this group on a fatter child (Bolton *et al*., 2016). Thus, Li *et al*. (2006) found exact agreement as low as 15.9% but this increased to 67.7% if maternal reports of infant weight were increased by 500g. Sou *et al*. (2006) observed a smaller discrepancy of over-reporting of birth weights with 80.4% of mothers recalling their child's birth weight within 100g. Finally, maternally recalled infant birth weights of multiple births were found to be more accurate than singleton births, possibly because events surrounding a multiple birth may be more memorable to mothers than for those expecting a single child (Liu *et al*., 2013).

The accuracy of maternal reporting of infant birth weight has received more attention than any other birth outcome, probably because gender and infant birth weight is usually the first information awaited by parents and extended family members after delivery. Overall, women had excellent recall of infant birth weight with no significant differences in mean discrepancies between

maternal recall and recorded infant birth weights across subgroups. For those mothers who had inaccurate recall of birth weight, their tendency was to underestimate by an average margin of 25-200 grams.

3.8.4 Sociodemographic and Birth Characteristics Related to Accuracy of Maternal Recall

Logistic regression models were used in 24 studies to assess the influence of demographic and birth characteristics on maternal recall agreement with hospital birth records. The variables considered were ethnicity, education, socioeconomic characteristics, marital status, maternal age at birth, number of years elapsed since delivery, birth order (first vs. subsequent), anaesthesia, labour events, type of delivery (caesarean section vs. vaginal and complicated labours), infant birth weight, gestational age, preterm delivery, post-term birth and multiparity.

In this review of the literature, six of 11 articles examining the influence of ethnicity on agreement of maternal recall with hospital birth records found lower levels of agreement in non-Caucasian mothers' self-report when compared with hospital birth records (Gayle *et al*., 1988; Walton *et al*., 2000; Elkadry *et al*., 2003; Tate *et al*., 2005; Quigley *et al*., 2006; Adegboye & Heitman, 2008). Five studies, however, found no association between ethnicity and maternal recall agreement with records (Tilley *et al*., 1985; Lumey *et al*., 1994; Olson *et al*., 1997; Gofin *et al*., 2000; Catov *et al*., 2005).

Maternal education was adjusted for in 14 out of the 29 studies. Four studies showed that women with higher education levels had more reliable recall than women with lower education levels of the following birth events: labour induction (Elkadry *et al*., 2003; Bat-Erdene *et al*., 2013), epidural use (Bat-Erdene *et al*., 2013), length of labour (Rice *et al*., 2006), mode of delivery (Elkadry *et al*.,

2003) and infant birth weight (Gayle *et al*., 1988). Three other studies showed that women with higher education levels had significantly more reliable recall of birth events in general than women with lower levels of education (Githens *et al*., 1993; Buka *et al*., 2004; Poulsen *et al*., 2011). However, Catov *et al*. (2005) observed that women with less than a high school education had reliable recall of first birth events, although having less consistent recall of subsequent births. Moreover, seven studies found no association between maternal education and maternal recall agreement with hospital birth records (Seidman *et al*., 1987; Gofin *et al*., 2000; Catov *et al*., 2005; Tate *et al*., 2005; Quigley *et al*., 2006; Rice *et al*., 2006; Troude *et al*., 2008). Conversely, women with less than a high school education showed better agreement with hospital records when recalling having no prior pregnancies (parity = 0) and having received anaesthesia during delivery than did women with at least a high school education (Buka *et al*., 2004). In addition, Adegboye and Heitman (2008) observed that mothers with a higher education provided a higher estimate of gestational age than that recorded in the notes when compared with less educated mothers.

Thirteen studies using questionnaire data explored other socio-demographic factors such as low socioeconomic status, unemployment and marital status. Four studies found low socioeconomic status to be significantly associated with lower levels of agreement for mothers' self-reports compared with hospital birth records. Findings by Tate *et al*. (2005) and Poulsen *et al*. (2011) included adjustment for maternal unemployment. Gayle *et al*. (1988) and Adegboye and Heitman (2008) found low agreement was influenced by single marital status. However, eight other studies found no association between maternal recall agreement with hospital birth records and low socioeconomic status (Tilley *et al*., 1985; Lumey *et al*., 1994; Olson *et al*., 1997; Catov *et al*., 2005; Quigley *et al*., 2006; Rice *et al*., 2006; O'Sullivan *et al*., 2000; Bat-Erdene *et al*., 2013),

even after adjustment for marital status, maternal occupation (Quigley *et al*., 2006) and maternal income (Catov *et al*., 2005).

Only one study found that older age at delivery was associated with higher levels of maternal recall agreement with hospital birth records (Elkadry *et al*., 2003), whereas Tate *et al*. (2005) found no evidence that older age at delivery had better agreement with hospital birth records.

Seven studies reported no influence by maternal age at recall on maternally recalled birth weight data when compared with birth records (Seidman *et al*., 1987; Gofin *et al*., 2000; O'Sullivan *et al*., 2000; Catov *et al*., 2005; Quigley *et al*., 2006; Troude *et al*., 2008; Bat-Erdene *et al*., 2013). However, Gayle *et al*. (1988) and Poulsen *et al.* (2011) found lower agreement for birth weight and gestational age, and gestational age respectively in women who gave birth under the age of 18. In addition, although Taiwanese mothers were found to have a general tendency to overestimate the birth weight compared to hospital records, Li *et al*. (2006) found that teen mothers were less likely to report higher infant birth weight than that recorded. Finally, Tomeo *et al*. (1999) observed that maternal recall of labour duration was more in agreement with records for women who were high school graduates at the time of delivery.

One out of three studies observed lower maternal recall agreement with increasing number of years elapsed since delivery (Elkadry *et al*., 2003), yet two other studies found that the time elapsed since birth had no influence on maternal recall agreement with birth records (Li *et al*., 2006; Rice *et al*., 2006).

Seven studies showed that agreement of mothers' self-reports compared with hospital birth records was influenced by parity and birth-order. Higher levels of agreement were observed for lower total parity (Sou *et al*., 2006), higher birth

order (Seidman *et al*., 1987; Li *et al*., 2006; Hopkins *et al*., 2007), more recent delivery (Seidman *et al*., 1987; Elkadry *et al*., 2003) and first delivery (Seidman *et al*., 1987; Catov *et al*., 2005; Sou *et al*., 2006; Hopkins *et al*., 2007; Poulsen *et al*., 2011). In six other studies, however, birth order was found to cause discordance between maternally recalled and recorded birth information (Olson *et al*., 1997; Elkadry *et al*., 2003; Tate *et al*., 2005; Sou *et al*., 2006; Adegboye & Heitman, 2008; Poulsen *et al*., 2011). Buka *et al.* (2004), however, found that parity had no influence on maternal recall agreement.

Of the 24 studies examining maternal recall agreement of infant birth weight, ten studies from the US (Tilley *et al.,* 1985; Casey *et al*., 1992; Olson *et al*., 1997; Lederman & Paxton, 1998; Yawn *et al*., 1998; Tomeo *et al*., 1999; Buka *et al.,* 2004; Catov *et al.,* 2005; Hopkins *et al.,* 2007; Liu *et al.,* 2013), three studies from the UK (O'Sullivan *et al*., 2000; Walton *et al*. 2000; Rice *et al.,* 2006), two studies from China (Li *et al*., 2006; Sou *et al.,* 2006), one study each from Denmark (Adegboye & Heitman, 2008) France (Troude *et al*., 2008) and Canada (Bat-Erdene *et al*., 2013), and two studies from Israel (Seidman *et al*., 1987; Gofin *et al*., 2000) found a range of good to perfect agreement between maternal recall of infant birth weight and hospital birth records irrespective of sociodemographic and maternal characteristics. Tate *et al*. (2005), however, found higher agreement (94%) among British/Irish white mothers than in other ethnic groups (69-89%).

Gayle *et al*. (1988) and Adegboye and Heitman (2008) observed that multiparous mothers confused offspring birth weight, however, Seidman *et al*. (1987) found that 75% of multiparas recalled birth weights were in agreement with records to within 100g.

Lastly, the study reporting the lowest level of agreement between maternal recall of birth weight and that recorded in the notes (50%) included 47 women noted as poorly educated and of low economic status by the researchers (Oates and Forrest, 1984).

Two studies found lower agreement of maternal recall for mode of delivery (forceps and vacuum) in women who had received anaesthesia during labour than women who had not received anaesthesia during labour (Hewson & Bennett, 1987; Tomeo *et al*., 1999). In addition, Elkadry *et al*. (2003) observed lower agreement for complicated labours; however, women who were induced or who had had caesarean sections had substantially higher maternal recall agreement with records (typically >90%). Hopkins *et al*. (2007) also observed that mothers had better recall of induction in subsequent births than in first births.

Preterm delivery was found to have both positive and negative effects on maternal recall agreement with hospital birth records. Yawn *et al*. (1998), Sou *et al*. (2006) and Hopkins *et al*. (2007) found preterm birth associated with higher levels of maternal recall agreement with hospital records. On the other hand, Gayle *et al*. (1988) found preterm delivery associated with lower levels of maternal recall agreement with hospital records.

Lastly, one study examined maternal recall of post-term birth for concordance with hospital records and found poor agreement (Poulsen *et al*., 2011).

3.8.5 Summary of Results

In summary, this review of 29 studies showed that agreement between maternal recall and birth records for mode of delivery, gestational age and infant birth

weight was excellent. Other variables such as labour induction and length of labour showed good agreement. There was little evidence for an effect of time elapsed since birth event on the levels of agreement of the recalled variables. Sociodemographic factors showed only small differences, with some studies suggesting that recall may be more or less accurate within some ethnic, socioeconomic or clinical subgroups. Childbirth appears to be a salient enough event that maternal recall of several factors are reliably remembered many years after the birth.

3.8.6 Stage 4: Interpretation of the Data and Discussion

Comparing self-reported perinatal data with hospital birth records suggests that maternal recall of events occurring around the time of labour and delivery are accurate for most events, even when recalled many years after delivery. Findings suggest that maternal recall does not deteriorate over time, although some studies have shown that ethnic, social and delivery factors may influence levels of maternal reporting agreement with hospital birth records. In addition, some studies found that the level of agreement may vary according to the types of information women were asked to recall. High agreement between maternal recall and hospital birth records for infant birth weight, in particular, may be because birth weight is repeated to family and friends after the birth of the child, which might aid memory.

The perinatal variables considered in this review (gravidity, parity, length of labour, pain relief, mode of delivery [vaginal, forceps/vacuum, caesarean section], gestational age and infant birth weight) showed generally strong to excellent agreement between maternally recalled and recorded birth data (>85% specificity), with the exception being findings by Oates and Forrest (1984) for gestational age and birth weight (the sample was small, n = 47, and

women were noted as being poorly educated and of low economic status), and Liu *et al*. (2013) for gestational age in twins. In addition, Chinese mothers were likely to exaggerate their infant's birth weight (Li *et al*., 2006; Sou *et al*., 2006) since they place a high social value on the fatter child (discussed in section 3.9.4).

Associations between maternally recalled and recorded events were highest for mode of delivery, gestational age and infant birth weight (100%, 98% and 85% respectively). Five studies, from the shortest to the longest time intervals, showed that 90% of mothers have excellent recall and are in agreement within 200g of their infant's recorded birth weight (Tilley *et al*., 1985; Gayle *et al*., 1988; Casey *et al*., 1992; O'Sullivan *et al*., 2000; Walton *et al*., 2000). Even in the groups with lowest agreement, birth weight agreement was still ≥78.5% (except for Oates & Forrest, 1984; see discussion in section 3.8.6). Gestational age across all time intervals showed higher agreement than birth weight, with ≥88% agreement within two weeks of the hospital records.

By comparing women's recalled birth events to hospital birth records, it was found that maternal self-report of perinatal events has high agreement with recorded birth events. The literature is conflicting as to whether women with higher education have more agreement with hospital records, with some studies showing that more educated women have better agreement with records and other studies showing no effect of education on agreement. It is plausible that women with higher educational attainment ask more questions during labour and delivery and, as such, are more aware of events during labour and delivery.

Subsequent to the completion of this research, a systematic review has been published with a focus on agreement between maternal recall *'at any time after birth'* and hospital recorded birth weight (Shenkin *et al*., 2017). Strong

correlation was found between recalled and recorded infant birth weight, estimated as 0.90 (95% CI 0.86-0.93).

3.9 Strengths and Limitations

The strength of this literature review is based upon the inclusion of studies from all parts of the world with a wide range of nationalities and populations. However, participant sample sizes, heterogeneity of populations and methods, varied outcome definitions, and wide-ranging statistical models did not allow use of the data for meta-analysis. In addition, variations in study design made study comparisons difficult. For example, some studies assessed mode of delivery as binary data (i.e. vaginal or non-vaginal birth) (Liu *et al*., 2013), whereas other studies divided mode of delivery into categorical variables such as vaginal, assisted or caesarean section (Githens *et al*., 1993; Quigley *et al*., 2006). Furthermore, some studies estimated infant birth weight and gestational age agreement within narrow categories (Lumey *et al*., 1994 and Sou *et al*., 2006 respectively), while other studies left a wider response range (Adegboye & Heitmann, 2008). Consequently, sensitivity and specificity of the same birth outcomes in different studies and different countries may differ depending on classification or individual interpretation of clinical references, such as ‘small’ or ‘large’ birth weight infants, or ‘early’ or ‘late’ gestation age of infants.

Maternal recall agreement may also vary according to context. Rice *et al*. (2006) included a large proportion of primigravidae women (i.e., women who are pregnant for the first time) following IVF treatment, while Seidman *et al*. (1987) included a large proportion of multiparae women (i.e., women who have given birth two or more times) and grand multiparae women (i.e., women who have given birth five or more times), although this was accounted for in the analysis. Recall quality may be sharper for nullipara women (i.e., women who

have never carried a pregnancy beyond 20 weeks) undergoing fertility treatments to get pregnant than in women who already have a large family. Furthermore, all but two studies were conducted in high income countries. Maternal recall of birth events may present differently in different cultures, and birth outcome criteria based on Western norms may not be appropriate for non-Western countries.

General sources of error or bias in the research articles may be due to both incomplete hospital records data and recall errors. The absence of a record for a condition or procedure in the hospital birth records does not mean that the condition did not exist. In addition, a proportion of mothers, everywhere, may be unable or unwilling to divulge information about their past births or obstetric health. Therefore, it is impossible to know whether agreement discrepancies between maternal recall and hospital birth records arise from incorrect recording of birth information or due to some mothers' incorrect, or intentionally withheld, maternally recalled information.

The large dataset from the combined research articles provided information on the influence of ethnic, demographic and social factors on mothers' birth event recall. Some studies found significant associations between the recalled variables (mother-hospital records) and sociodemographic factors, others did not. Differences were, however, generally small.

Finally, the distribution of academic interest is inconsistent across the variables. Birth weight was by far the most investigated and reported variable, while stages in labour were the least investigated. Moreover, although diagnosis of labour onset is an important judgement in clinical care, no articles were found investigating maternal recall of when labour started with hospital records agreement. This is a gap in the literature which needs to be examined further.

This literature review provides an important insight into maternal recall agreement with hospital birth records of specific birth events. A summary of the reviewed articles shows that although agreement of maternal recall compared to hospital birth records may differ according to individual factors (such as maternal ethnicity, socioeconomic status and parity), the differences are small. Characteristics of the Western populations (27/29) of the reviewed articles were well represented. Participating mothers were of all ages, had various socioeconomic backgrounds and diverse maternity histories. Women who took part in long past research studies (Hewson & Bennett, 1987; Gayle *et al*., 1988) demonstrated similar levels of maternal recall agreement with hospital birth records as recent studies (Bat-Erdene *et al*., 2013; Liu *et al*., 2013). This may imply that women's memories of specific birth events remain reliable over time. The small magnitude of the differences between recalled and recorded birth event information suggests that maternal recall can provide accurate information and, in the absence of other data, may be relied upon.

3.10 Conclusions

This literature review compares, contrasts and synthesises 29 research studies on agreement between maternal recall and hospital birth records for a number of birth outcomes in a wide variety of settings and health systems. The results consistently show that agreement between maternal recall and hospital birth records for birth outcomes is high or moderate even 57 years after the birth (Catov *et al*., 2005). The lapse between birth and the recall date did not appear to influence agreement between the mothers' accounts and records of birth events. This literature review shows that there is evidence of good agreement between maternal recall and hospital birth records for a wide range of perinatal factors.

The following chapter is an empirical study on the maternal recall of distant first birth events. The study's aim was to explore agreement between maternal self-report of first labour and delivery events with data found in hospital birth records in Israel. The study will contribute to maternal recall literature by examining agreement of mothers' recalled birth events with hospital birth records for eight birth outcome variables, with particular focus on mothers' recalled length of labour.

Several recommendations for future maternal recall research can be made:

- Mothers should be asked to provide gestational age in weeks and days to determine whether the mother is using rounding in her responses.
- Studies in which reliability within sources and validity across sources are needed to identify a gold standard.
- As greater attention is paid to personalised maternity care, important information on obstetric data may be obtained from women for whom medical records are not available.
- Maternal recall of obstetric issues should be tested in large, representative samples in countries for which health records are easy to obtain.
- Further maternal recall research on what mothers remember about onset of labour would be useful.

Chapter Four: First Birth Events - Israeli Mothers' Recall Compared to Hospital Birth Records

4.1 Introduction

The literature review described in Chapter Three has indicated that accurate perinatal information can be provided by women from a range of cultural and demographic groups, with recall periods as long as 57 years, although differences between maternal retrospective report and medical birth records may vary across different types of perinatal events.

This chapter will present the methods and results of a comparative study of maternal recall of the events surrounding their first birth, with hospital records of the same birth, for women who gave birth in Israel. The rationale was to assess the degree to which maternal recall could be used in a subsequent study (the Similarities in Labour and Childbirth [SILC] study), which is reported in Chapter Five. These findings contribute to the achievement of the second objective of the thesis:

- To establish the accuracy of maternal recall for cardinal labour and birth events.

4.2 The Israeli Context and Public Health

The State of Israel is situated on the south eastern shore of the Mediterranean Sea and the northern shore of the Red Sea. It has land borders with Lebanon to the north, Syria to the northeast, Jordan to the east, the Palestinian territories of the West Bank and Gaza Strip to the east and west respectively, and Egypt to the southwest. The country contains geographically diverse features within its

relatively small area with desert conditions in the south and snow-capped mountains in the north. Israel's economy and technology centre is Tel Aviv, while its seat of government and proclaimed capital is Jerusalem.

The population of Israel, as of the first half of 2018 recorded by the Israel Central Bureau of Statistics (2018) was 8,855,000 people. The ethnic composition of the population consists of predominantly Jews (75%) and Arabs (21%), with significant minorities of Armenians, Assyrians, Black Hebrew Israelites, Circassians, Maronites and Samaritans. Israel also hosts a significant population of non-citizen foreign workers and asylum seekers from Africa and Asia, including illegal migrants from Sudan, Eritrea and other sub-Saharan African countries.

Israel is a developed country and has been an OECD (Organisation for Economic Co-operation and Development) member since 2010, having the 35th-largest economy in the world by nominal gross domestic product as of 2016. The country benefits from a highly skilled workforce and is among the most educated countries in the world with a high percentage of its citizens holding a tertiary education degree (OECD, 2017). The country has the highest standard of living in the Middle East and the third highest in Asia (Jahan, 2015).

Healthcare in Israel is universal. Israeli citizens are entitled to basic healthcare as a fundamental right and participation in a medical insurance plan is compulsory. The Israeli healthcare system is based on the National Health Insurance Law of 1995 which mandates that all citizens' resident in the country must join one of the four official health insurance services. These are run on a not-for-profit basis and are prohibited by law from denying any Israeli citizen membership. Israelis can increase their medical coverage and improve their options by purchasing private health insurance.

Among the OECD countries, Israel has the highest fertility rate (OECD, 2015a, 2015b). In a survey of 48 countries in 2013, the Israeli healthcare system was ranked fourth in the world in terms of efficiency, and in 2014 it ranked seventh out of 51 (Bloomberg, 2014). In 2015, Israel was ranked as being the sixth healthiest country in the world by Bloomberg rankings, and ranked eighth in terms of life expectancy (WHO, 2009).

4.2.1 Maternity Service Provision in Israel

In Israel, women usually give birth in hospital-based maternity units with midwives and obstetricians in attendance. According to the Israeli Association of Obstetrics and Gynaecology, more than 99% of all births occur in hospitals with no other legislatively approved options. The stated position of the Ministry of Health is that births in recognised and authorised delivery rooms are safer for both mother and child. It has been suggested that patriarchy has led to a particular social construction of women's reproductive health in Israel (Granek & Nakash, 2017), in parallel with excessive medicalisation which has become the norm (Benyamini *et al*., 2017). The Israeli Law of National Insurance, as amended 1995 (National Insurance Institute of Israel, 1995) entitles every birthing mother to a birth grant if she is hospitalised for the birth. By providing free maternity services, hospital care and maternity grants, the State of Israel compels and rewards women for giving birth in a hospital (Morgenstern-Leissner, 2006). With state ideologies favouring hospital births, there is broad acceptance of medical care and medicalisation in childbirth by the public at large (Benyamini *et al*., 2017).

Israeli maternity hospitals provide obstetric, anaesthetic and neonatal services, and are technologically supported. Women are hospitalised for an average of

2.5 days after a vaginal birth and 3.5 to 5 days after a caesarean section. Developments in Israeli maternity care have been heavily influenced by global trends in industrialised countries (principally the UK, USA, Australia and Canada) which endorse hospitalisation and the active management of labour (Hunt & Symonds, 1995; Gao *et al*., 2009). Although the childbirth rate of Israeli women is the highest among the 34 OECD countries (25% of Israeli women have six or more children), its rate of caesarean sections is the lowest. Nevertheless, Israel's caesarean section rate has been steadily increasing. In 1973 it averaged 5%, in 1994 it was 11%, 16% in 2000, rising to 18% in 2004 (Kupermintz, 2005). The current caesarean section rate in Israel is 19% (OECD, 2018), exceeding the 10-15% rate recommended by the World Health Organization (Gibbons *et al*., 2010).

4.2.2 The Research Sites

Data for this research study was collected over the two years of 2014 and 2015 from two Israeli public hospitals: the Lis Maternity Hospital at the Tel Aviv Sourasky Medical Center, and the Ma'aynei Hayeshua Hospital in Tel Aviv.

Both hospitals have a framework of obstetric clinical governance with high quality care standards. In January 2014, the Tel Aviv Sourasky Medical Center earned prestigious accreditation (Gold Seal of Approval) from the Joint Commission International (JCI), a global organisation that certifies hospitals for quality and safety. Both hospitals have a comparable number of annual births and similar health budgets, specialisations and use of technology.

The two research sites were chosen for pragmatic reasons; their geographical proximity and organisational similarities (i.e. both having antenatal clinics, obstetric triage systems and a similar number of births per annum, along with

the use of manual, archived and electronic birth records). In addition, the choice of research sites was influenced by the different caesarean section rates within the two settings.

The Lis Maternity Hospital has approximately 12,000 births a year (Lis Maternity Hospital, 2015, n = 11,862), which accounts for 7% of the total births in Israel. The current caesarean section rate at this hospital is 21.6% (2015) (of these, 47% were elective), which is slightly higher than the national statistic of 19% (OECD, 2018).

The Ma'aynei Hayeshua Maternity Hospital has approximately 12,000 births a year (Ma'aynei Hayeshua Maternity Hospital, 2015, n = 12,247) which accounts for 7% of the total births in Israel. The current caesarean section rate at this hospital is 9.5% (2015) (of these, 35% were elective), which is the lowest caesarean rate in the country.

The alarming increase in caesarean section rates worldwide (Betrán *et al*., 2016) has been recognised as a critical global problem by international organisations such as the WHO (2015) and FIGO (Visser *et al*., 2018). The WHO has stated that efforts should be made to provide caesarean sections to women in need due to the association with a range of short and longer term adverse clinical, emotional and psychological outcomes for both mother and baby when compared with the outcomes of spontaneous vaginal birth. At the same time, the WHO has shown that, at the population level, caesarean section rates of more than 10-15% are unlikely to improve maternal or perinatal outcomes (WHO, 2015) raising significant concern that caesarean delivery is overused. Furthermore, variation in the rates of nulliparous, term, singleton, vertex caesarean births also indicates that clinical practice patterns affect the number of caesarean births performed (ACOG, 2014). Specifically, for many

women in this study, guaranteed reproductive health following a vaginal delivery is a common belief. With the impact of religious restrictions on birth control, the ultra-orthodox community in the Ma'aynei Hayeshua Maternity Hospital have a high birth rate. For these mothers, avoidance of a caesarean section, especially for a first birth, is a priority.

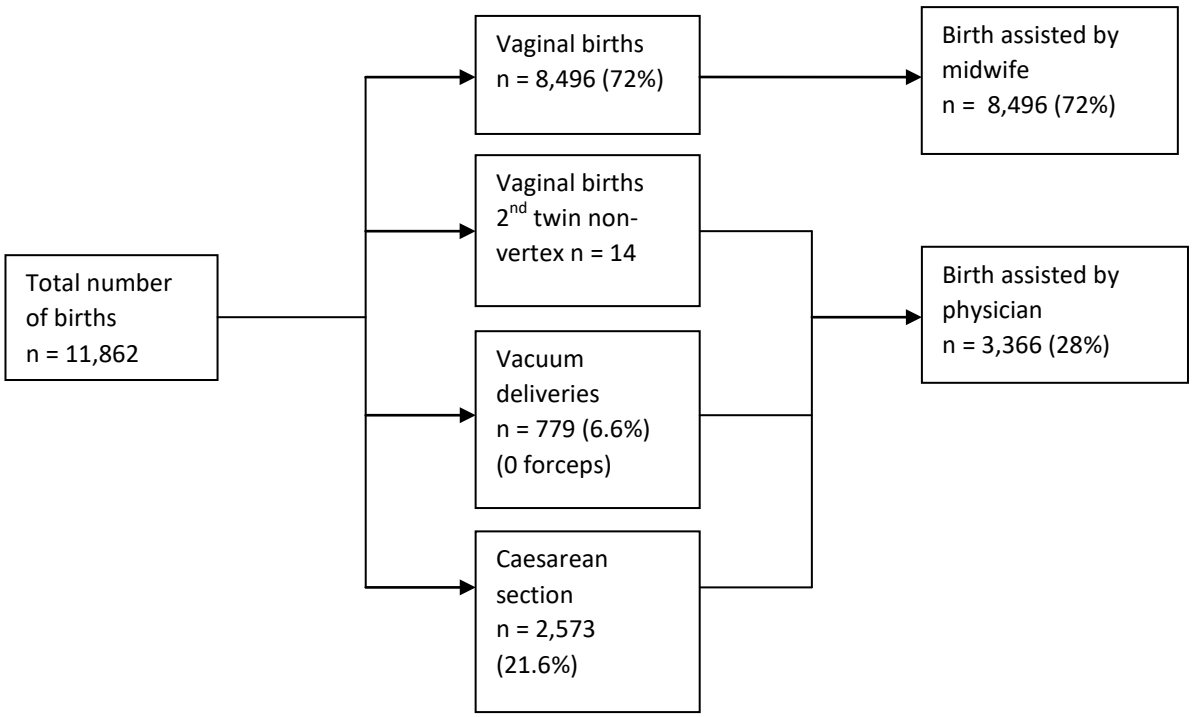
The two tertiary Tel Aviv hospitals selected have similar demographical and healthcare system characteristics. Caucasian residents are the majority ethnic group within the Tel Aviv area, with Hebrew-speaking Jews forming 93% of the population. Cultural and linguistic differences, as well as financial and personal time constraints, may have hindered minority participation, such as Muslims, Arab Christians and African/Asian foreign workers living outside the catchment area of the maternity facilities used by local people.

Both hospitals follow a shared-care model, with obstetricians overseeing clinical management through intrapartum care and qualified midwives attending uncomplicated vaginal births, participating in assisted births and caesarean sections, and providing immediate postpartum and neonatal care. Figure 4.1 shows the selection of vaginal, assisted and caesarean section births in the Lis Maternity Hospital according to the health professional (physician or midwife) in attendance. A summary of the number of annual births and attending physician/midwife for Ma'aynei Hayeshua Maternity Hospital was not available.

Active management of care in labour is common, with routine use of electronic foetal monitoring (EFM), and an epidural use rate of 73% (Lis Maternity Hospital, 2015) and 67% (Ma'aynei Hayeshua Hospital, 2015). Neonatologists work closely with the labour ward team and oversee the provision of care for the new-borns.

Although alternatives to the conventional hospital birth plan are being made increasingly available to Israeli women with some hospitals offering a 'natural birthing' room, most women comply with the expected care route within the medical establishment.

Figure 4.1: Annual Number of Births at the Lis Maternity Hospital (2015) and Number of Deliveries by Physicians and Midwives



Source: Lis Maternity Hospital (2015).

4.3 Aim

To measure agreement between hospital records and maternal historical reporting of mother's birth age, gravidity, onset of labour (including induction), use of pain relief, length of labour, birth outcome, birth weight and gestational age.

4.4 Research Methodology

4.4.1 Research Sample and Design

This was a cohort study of women who were accompanying parturients (daughters, granddaughters, daughters-in-law, other family members or friends) attending antenatal follow-up clinics at the Lis Maternity Hospital and Ma'aynei Hayeshua Maternity Hospital in Tel Aviv, Israel (2014-2015). Included women had given birth to their first born child in the hospital where they were accompanying the parturients. Of the women who were initially approached (n = 462), 67% of them gave birth to their first child at other hospitals, and so were excluded from the study as their records were not available for comparative analysis (see Figure 4.2).

The women's recalled first birth events were compared for agreement with data in their hospital records. They were asked to complete a questionnaire relating to their first birth history (see Appendix 3, Q1). The questionnaire was designed by my Director of Studies and myself, and approved by my on-site supervisor and university supervisor. Israeli identification numbers were used to trace archived birth records.

4.4.2 Research Ethics

Project approval was granted by the ethics committees for both the Lis Maternity Hospital and Ma'aynei Hayeshua Hospital, and also from the University of Central Lancashire (Helsinki Committees: Sourasky Medical Center, ref: 0039-14, 12.06.2014; Ma'aynei Hayeshua Hospital, ref: 72.14, 30.07.2014; and the University of Central Lancashire Research Ethics Committee, School of Health, UK, approval number ref: STEMH 255, 09.09.2014) (see Appendix 1).

4.4.3 The Pilot Study - Procedure and Data Collection Methodology

A pilot study was conducted to examine the feasibility of the methods and procedures. On two separate days in September 2014, I (as the research investigator) approached 12 women accompanying parturients attending the antenatal clinics of the two hospitals. Eligible women (those who had given birth to their first child in that hospital and were willing to take part in the study) received a copy of the questionnaire, participant information sheets and individual consent forms.

Ten women signed consent agreements and completed questionnaires. Some women returned their completed questionnaires immediately; other participant questionnaires were returned by the parturient at a subsequent visit to the antenatal clinic. A few participant questionnaires were returned by the 'Freepost' return envelope included in the participant pack.

The archived birth records for nine of these mothers were retrieved; but one set of birth records could not be found. Birth information from both the hospital archives and the maternal recall questionnaires were entered into a Microsoft Excel worksheet for analysis. Missing or ambiguous information from questionnaires/birth records was gathered through emails and telephone conversations. For mothers who had laboured for more than 10 hours, indications for labour onset were verified by telephone interviews and determined by the presence of strong, regular, painful contractions and/or hospital admission with ≥4 centimeters cervical dilatation.

The data collected from the pilot study confirmed achievability of recruitment procedures, questionnaire use and return of preliminary data. Methods were

thus not modified after the pilot. The data collection procedures for the pilot study were subsequently adopted for the actual study (see research methodology sections 4.4.4 [materials and methods], 4.4.5 [covariates], 4.4.6 [participants] and 4.4.7 [sample size calculation]). The pilot study participants with historical records (n = 9) are included in the main results.

4.4.4 Materials and Methods

On two separate days a week for a period of 24 weeks (September 2014 to March 2015) I approached 10-12 women accompanying parturients attending the antenatal clinics of the two hospitals. Eligible women were those who had given birth to their first child in that hospital and were willing to take part in the study.

Potential participants (60% were mothers whose pregnant daughters were participants of the SiLC study, presented in Chapter Five) were provided with a letter informing potential participants about the study, that their participation was voluntary and that their anonymity and confidentiality would be protected. A participant information sheet provided the contact details of the researchers (myself, my Director of Studies in the UK, my UK supervisor, and my on-site supervisor) should participants wish to seek further information. Participants were assured that they had the right to withdraw from the research at any time and contact details of mental health services were included for participants who might experience psychological distress or discomfort following memories of a difficult or traumatic birth. Participants were required to sign an informed consent agreement.

The 35 item questionnaire for this study (see Appendix 3, Q1) was developed by my Director of Studies and myself in collaboration with my two research

supervisors. The first 15 questions consisted of personal and demographic information, including mother's age, ethnicity, religious status, level of education and marital status. In addition, questions on health-related behaviours such as smoking and alcohol habits were included, because of their potential effects on the foetus.

These 15 questions were then followed by a logical sequence of 20 maternal history questions regarding the three main areas of birthing: (a) prenatal [during pregnancy], (b) perinatal [during birth] and (c) newborn outcomes. Maternal history items included: (a) the mother's age at first birth, delivery date, gravidity, weight gain during pregnancy, duration of pregnancy, (b) signs of labour, length of labour, use of pain relief medication, birth outcome (vaginal, assisted, or caesarean), and (c) gestational age at delivery, infant gender, birth weight, and Apgar of newborn.

Length of labour was measured on a categorical scale. The women were asked about the length of time they were in labour and responses were categorised as:

1) Less than 2 hours
2) 2 - 6 hours
3) 6 - 10 hours
4) More than 10 hours, please state the number of hours: _____

The four time intervals were based on the findings of a systematic review on active labour duration rates among 7,009 low-risk nulliparous women with spontaneous labour onset that reported a mean active labour duration of 6 hrs ± SD 3.5 hrs (Neal *et al*., 2010). We therefore created 4-hour end points (categories 2 and 3), as well as accounting for short (<2 hours) and long (>10 hours) labours.

Responses were either dichotomous or closed-ended questions with a limited set of responses. The final question was open-ended to allow participants to describe their first birth experience.

Data from the hospitals' birth records were extracted from microfiche. Hospital data records included age of parturient, gravidity, information on patient arrival at the labour ward (date and time), labour progress charts, physician and midwife progress notes and orders, mode of delivery (vaginal, assisted or caesarean), and infant outcome (gestational age at delivery, infant gender, infant birth weight and Apgar of the newborn).

4.4.5 Covariates

The following maternal covariates were collected: age at study entry, age at first delivery, ethnicity, family status, education, pregnancy history, onset of labour, use of pain relief medication, length of labour and birth outcome. Offspring covariates were gestational age, infant birth weight, gender and Apgar.

4.4.6 Participants

Eligibility criteria are presented in Table 4.1 below.

Table 4.1: Eligibility Criteria of Questionnaire Respondents

Inclusion criteria	Rationale
Participants must have given birth in the hospitals where the study is being conducted	Enabling access to birth records
Language competence (sufficient command of Hebrew reading and writing)	For self-report and questionnaire completion
Having had a first birth more than 17 years ago	To preclude very young womens pregnancies (pregnant women under 18 years of age are at higher risk of preterm birth and a low birth weight infant *)
Willingness to provide full name and national identity number	As a means of tracking hospital birth records
Willingness to sign informed consent	Ethical precaution and eligibility determination

* Khashan *et al.* (2010).

Exclusion criteria included unwillingness to provide informed consent and/or inability to complete the questionnaire because of language barriers or other response problems.

4.4.7 Sample Size Calculation

This is a retrospective cohort study using hospital birth records. The criteria that led to the use of convenience sampling were: 1) time considerations and 2) the existing available target population. A sample of 121 participants were recruited and the power of the study was calculated retrospectively. Known for its strong reported reliability, infant birth weight was selected as the primary outcome measure. Infant birth weight was the most researched birth outcome variable in the maternal recall of birth events literature review (Chapter Three). Moreover, birth weight, as a birth outcome measure, is the first outcome of interest to friends and family after birth (along with gender) and is often a self-reported outcome measure for women recalling their birth experiences.

In a similar population in Israel, Gofin *et al.* (2000) compared 259 maternally recalled infant birth weights with hospital records six years after delivery and found substantial kappa agreement for infant birth weight (k = 0.71) (for interpretation of kappa levels of agreement see description of measures after Table 3.1).

The power of this study was calculated based on the final number of women selected (101), at a significance level of 5% (α = 0.05), with an accuracy level of 78% and a kappa of 0.815. This provided a statistical power of 81.8%. The sample size was calculated using Winpepi software (Abramson, 2011).

4.4.8 Statistical Methods

All statistical analyses were performed using SPSS software SPSS 22.0.[1]

Descriptive statistics were reported for all variables. Continuous variables were reported in means and standard deviations (±*SD*), or medians and interquartile range (IQR) as appropriate. Categorical variables were reported in frequencies and percentages. Categorical birth weight and gestational age were compared with recorded infant birth weight and gestational age after categorising infant birth weight and gestational age into three groups consistent with cut-offs for clinical significance according to classifications defined by the US Centers for Disease Control (Martin *et al*., 2010). Infant birth weight groups consisted of low (≤2,499g), normal (2,500-3,999g) and high (≥4,000g). Gestational age groups consisted of preterm (≤36 weeks), term (37-40 weeks) and post-term (≥41 weeks). Multiple births were included in the analysis, with each child treated as a single unit.

[1] In the American Medical Association [AMA] citing style it is referred to as: IBM Corp. IBM SPSS Statistics for Windows, version 22.0. Armonk, NY; 2013.

Bland-Altman plots were used to determine agreement between questionnaires and medical records for infant birth weight and gestational age as continuous variables (Bland & Altman, 1986). Within Bland-Altman plots of the inter-source (maternal recall and hospital records) average (x-axis) versus inter-source differences for gestational age and infant birth weight (y-axis), 95% limits of agreement are denoted by two lines at +/- 1.96 x standard deviation (1.96 *SD*). Causes of discrepancies may be noted outside the limits of agreement.

To test the magnitude of agreement between questionnaires and medical records (adjusting for chance agreement of categorical variables) (Fleiss, 1981), categorised and dichotomised variables used kappa coefficients, confidence intervals of kappa and *p* values (the *p* value in kappa analysis shows whether the estimated kappa is not due to chance, not the strength of the agreement). Categorised infant birth weight and gestational age, onset of labour, pain relief, and mode of delivery (spontaneous vaginal delivery, use of forceps/ventouse, elective caesarean section, emergency caesarean section), and other dichotomised variables such as gravidity, epidural use and pethidine use and length of labour were evaluated. Kappa values of 0.81 to 1.0 represent almost perfect agreement, values of 0.61 to 0.8 represent substantial agreement, levels of 0.41 to 0.6 represent moderate agreement, levels of 0.21 to 0.4 represent fair agreement, levels of 0 to 0.2 represent slight agreement, and 0 represents poor agreement (Landis & Koch, 1977).

Logistic regression analysis was performed to assess the relationship between independent variables (such as immigrant status, maternal education, mother's age, and years elapsed since birth) with dependent variables (such as gravidity, onset of labour, any use of pain relief, epidural, pethidine, length of labour [≤10hrs or >10hrs], infant birth weight, gestational age and birth outcome). Dependent variables were converted into dichotomous variables to identify

inaccurate recall to questions about specific delivery events. The significance threshold was set at $p \leq 0.05$. Variables that had no effect were deleted from the regression analysis individually in a stepwise manner.

4.5 Results

4.5.1 Demographic Characteristics

A total of 150 questionnaires were distributed with an expected response rate of 70%. From the total of 150 questionnaires distributed (10 in pilot study, 140 in main study), 121 completed questionnaires were returned (81%), which attained a very high response rate (Groves [2006] construes a 'high' response rate as 70%). Fourteen out of the 121 had missing hospital birth records. Furthermore, six more women were excluded from the study since they had their first child less than 17 years prior to the study. Thus, 20 (n = 14+6) women were excluded from the sample, making a study sample size of 101. See Figure 4.2 for cohort profile.

Figure 4.2: Cohort Profile Maternal Recall Study

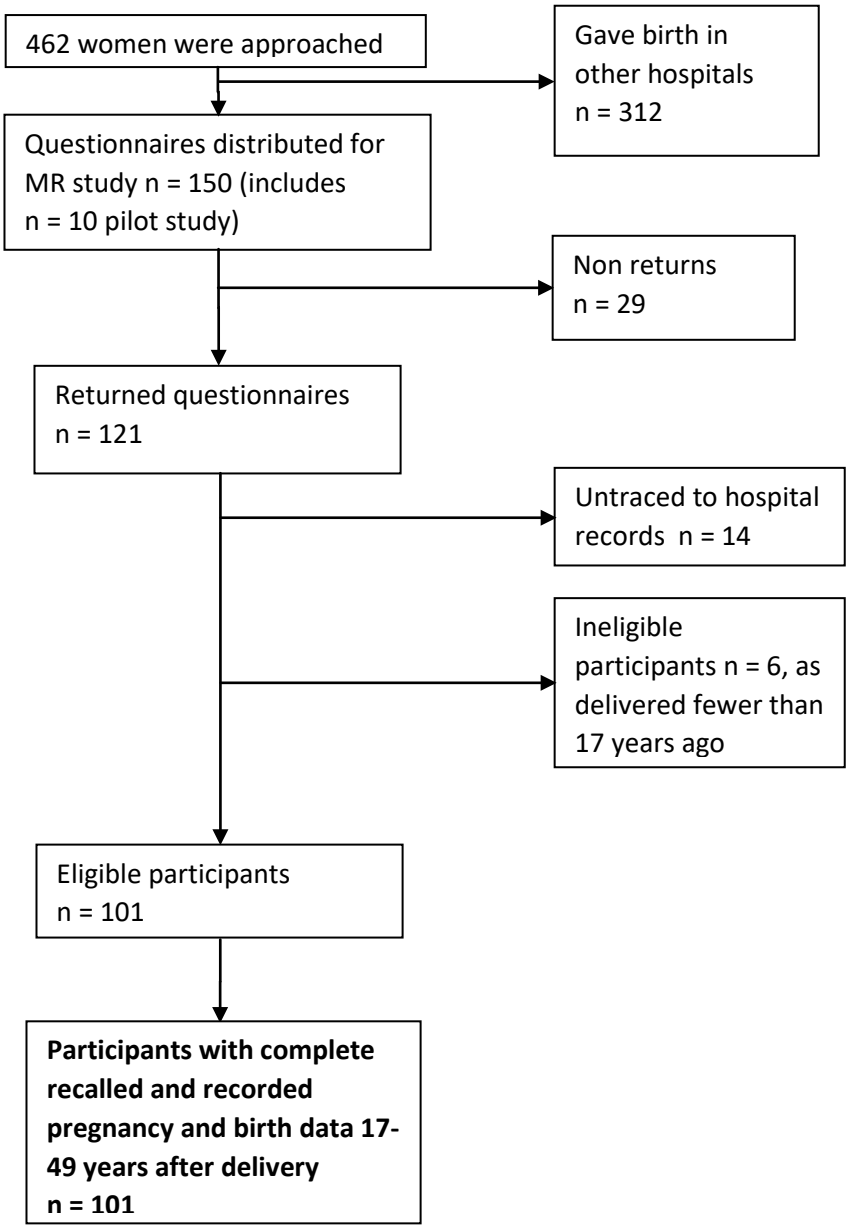


Table 4.2 presents those mothers (n = 101) who completed the maternal recall questionnaire and had retrievable and complete medical records of their first birth event.

The current study design recruited one third of all women who were eligible over the study period.

The mothers gave birth to their first child between 1967 and 1998. Participants were aged 37 - 70 years (*Mean* = 55.21, *SD* = 7.37), their age at first delivery was 18 - 41 years (*Mean* = 24.18, *SD* = 4.53), and the years elapsed since first birth was 17 - 49 years (*Mean* = 30.99, *SD* = 7.88). The mean age for women in Israel at first delivery in 1997 was 26.2 years (Israel Central Bureau of Statistics [ICBS], 2008).

The mean age of participants with missing birth records was 66 years (*SD* = 11.33), and the mean number of years elapsed since their first delivery was 42 years (*SD* = 7.77).

Of the 101 women in the study, 76 (75%) were Israeli. Other countries of origin included 5 (5%) from Africa and the Middle East, 15 (15%) from Europe, and 3 (3%) from the Americas. 2 (2%) were missing information (for parental origins of participating women, see Table 4.2). In a 1997 representative sample of Israelis, it was found that 61% of the Jewish population were born in Israel. The remaining population group were first-generation immigrants of African or Asian descent and European or American descent (ICBS, 2008) with their ethnic origins following that of their grandparents (35% African or Asian, 40% European or American, 25% mixed origin). Differences within the sample population of this study may be due to the multi-layered structure of ethnic identification within the Israeli immigrant society, ethnic identities' resistance to change, and ethnically mixed marriages eroding such ethnic identities and replacing them with national identities (Lewin-Epstein & Cohen, 2019).

Of the women who reported on educational status 10.9% (n = 11) had completed partial high school, 29.7% (n = 30) had completed high school, 27.7% (n = 28) had completed vocational school, and 27.7% (n = 28) had university degrees. Four women were missing information. Similar levels of

education of the general Israeli population in 1997 showed 33.6% of the population had completed high school and the proportion of women with vocational schooling was 30%. However, educational attainment for women with university degrees within Israel's populace was less than half (at 12.6%) compared with participants in the study (Israel Central Bureau of Statistics, 2008). This may be explained by the higher socioeconomic status within Tel Aviv society which provides higher standards of education than within the general Israeli population. The largest category of religious status was secular (n = 44/98, 43.6%) and most women were married (n = 84/101, 83.1%).

Fourteen participants smoked (13.8%), half of whom smoked 11-20 cigarettes per day. Five participants consumed alcohol, drinking 1-2 units per week. Although smoking and alcohol consumption during the prenatal period may be harmful and contributory factors to low infant birth weight (Oster *et al.*, 1988) and miscarriage (Thäle & Shlitt, 2011), these women were self-reporting on current use (≥ 17 years since birth). Former smoking and drinking habits during pregnancy were not questioned. In addition, Kreuter *et al*. (2009) found that respondents might underreport smoking and drinking habits by providing answers that comply with social norms, therefore these demographic data are not included in Table 4.2.

Table 4.2: Demographic Characteristics of Study Participants Based on Questionnaire Data (Maternal Recall)

		Participants	
Age	Total sample size (N)	101	
	Mean (*SD*)	55.17 (7.37)	
Age at first delivery	Number of usable replies (N) = 86	101	
	Mean (*SD*)	24.18 (4.53)	
	Median (IQR)	23.0 (5)	
Years elapsed since first birth	Number of usable replies (N)	101	
	Mean (*SD*)	30.99 (7.88)	
Country of origin	Number of usable replies (N)	99	%
	Israel	76	75.2
	Asia/Africa	5	5.0
	Europe	15	14.9
	Americas	3	3.0
	Missing	2	2.0
Mother's origin	Number of usable replies (N)	97	%
	Israel	24	23.8
	Asia/Africa	33	32.6
	Europe	35	34.6
	Americas	5	5.0
	Missing	4	4.0
Father's origin	Number of usable replies (N)	97	%
	Israel	21	20.8
	Asia/Africa	29	28.7
	Europe	43	32.6
	Americas	4	4.0
	Missing	4	4.0
Birth hospital	Number of usable replies (N)	101	%
	†Kiriya	90	89.1
	†Lis	4	4.0
	Ma'aynei	7	6.9
Education	Number of usable replies (N)	97	%
	Partial high school	11	10.9
	Full high school	30	29.7
	Vocational school	28	27.7
	University degree	28	27.7
	Missing	4	4.0
Family status	Number of usable replies (N)	101	%
	Married	84	83.1
	Divorced	10	9.9
	Widowed	5	5.0
	Other	2	2.0
Religious status	Number of usable replies (N))	98	%
	Secular	44	43.6
	Traditional	31	30.7
	Religious	7	6.9
	Ultra-orthodox	16	15.8
	Missing	3	3.0

† The Kirya Birthing Center closed when the new Lis Maternity Hospital opened in 1997. Archives and staff were relocated.

Recalled and recorded perinatal and newborn outcome information is presented in Table 4.3.

Table 4.3: Paired Data and Agreement Between Recalled and Recorded Intrapartum Data

		Mother's Recall N	% (out of the no. of valid responses)	Hospital Records N	% (out of the no. of valid responses)
IBW in grams (including multiple deliveries)	Low ≤ 2,499	16	15.2	12	11.9
	Normal 2,500-3,999	84	80.0	87	86.1
	High ≥ 4,000	5	4.8	2	2.0
	Missing	1 (0.9%)		5 (4.7%)	
GA in weeks (including multiple deliveries)	Pre- term ≤ 36w	11	10.7	7	9.5
	Term 37- 40w	75	72.8	56	75.7
	Postdate ≥ 41w	17	16.5	11	14.8
	Missing	3 (2.8%)		32 (30.2%)	
Gravidity	1	86	85.1	92	91.1
	2			6	5.9
	3			2	2.0
	4			1	1.0
	More than 1 (memory only)	15	14.9		
Onset of labour	Contractions	54	53.4	35	48.6
	Rupture of membranes	31	30.7	26	36.1
	Vaginal bleeding	2	2.0		
	Induction	11	10.9	8	11.1
	Elective CS	2	2.0	3	4.2
	Other	1	1.0		
	Missing	-		29 (28.7%)	
Reason for induction	Postdate	4	4.0	3	3.0
	PROM	2	2.0	5	5.0
	*Failure to progress-augmented	8	8.0	17	17.0
	Oligohydramnion	1	1.0	1	1.0
	Meconium			1	1.0
	PIH/Toxaemia	1	1.0	1	1.0
	No reason given	1	1.0		
	No induction	84	83.0	73	72.0
Rupture of membranes	Spontaneous	17	70.8	14	25.5
	AROM	-	-	22	40.0
	PROM	5	20.8	16	29.1
	OR	2	8.4	3	5.4
	Missing	77 (76.2%)		46 (45.5%)	

Anaesthesia	Epidural Pethidine Spinal No recall None General Missing data	46 12 2 3 33 2 3 (3%)	45.9 12.2 2.0 3.1 33.8 2.0	42 13 1 17 3 25 (24.8%)	55.3 17.1 1.3 22.4 3.9
Length of labour in hours	< 2 2 – 6 6- 10 > 10 Missing data	6 34 16 39 6 (5.9%)	6.3 35.8 16.8 41.1	1 15 29 13 43 (42.6%)	1.7 25.9 50.0 22.4
Birth outcome	Spontaneous vaginal Vacuum/Forceps Elective CS Emergency CS Missing data	69 18 2 12	68.3 17.8 2.0 11.9	67 19 4 10 1 (1.0%)	67.0 19.0 4.0 10.0
Presentation (including multiple deliveries)	Cephalic Breech Footling Missing data	97 3 1 5 (4.7%)	96.0 3.0 1.0	88 3 15 (14.2%)	96.7 3.3
Gender (including multiple deliveries)	Male Female Missing data	43 61 2 (1.9%)	41.3 58.7	44 62	41.6 58.4
APGAR (including multiple deliveries)	Normal Abnormal Don't know Missing data	92 1 2 11 (10.4%)	96.8 1.1 2.1	80 26 (24.5%)	100.0
Placental expulsion	Spontaneous Manual removal in L&D (revision/lysis) Surgically removed (CS) Missing data	84 3 13 1 (1.0%)	84.0 3.0 13.0	66 14 21 (20.8%)	82.5 17.5

Legend: L&D: labour and delivery rooms.

*Cases of augmented labour with Pitocin (oxytocin) were excluded from the induction analysis (kappa).

Singletons and multiples were included in infant birth weight and gestational age analysis (multiple births included one set of triplets and three sets of twins, total n = 106 infants).

Table 4.3 compares intrapartum variables by maternal report and hospital birth records. Women's reported data showed higher prevalence rates for all outcomes, by 1% for reason for induction/post-date to 25.7% for length of

labour >10 hours, except infant birth weight, gravidity, elective caesarean section, reasons for induction/premature rupture of membranes, pethidine and length of labour 6-10 hours.

4.6 Level of Agreement Between Maternally Recalled Events and Hospital Birth Records

4.6.1 Assessing Agreement for Continuous Variables

The agreement between maternally recalled gestational age and infant birth weight with hospital records was assessed using Bland-Altman plots (Bland & Altman, 1986); these are shown in Figures 4.3 and 4.4 respectively.

Figure 4.3 shows the differences between maternally recalled and recorded gestational age plotted against the mean of the two values together, with 95% limits of agreement. The bias (mean difference) is equal to zero and an agreement interval (±1.766 weeks) shows a very strong agreement between maternally recalled and recorded gestational age (as concentration points above and below 0, which is perfect agreement, depict tendencies). The graph looks bare since many of the points fall on identical locations. However, a distinct pattern of agreement according to gestational age at birth shows a trend towards underestimation between 39 and 41 weeks of gestation, and a slight trend towards overestimation for infants who have extended their expected date of delivery.

Figure 4.3: Agreement Between Maternally Recalled and Recorded Gestational Age with 95% Limits of Agreement

Mean difference = 0, SD = 0.90, 95% limits of agreement (-1.766, 1.766).

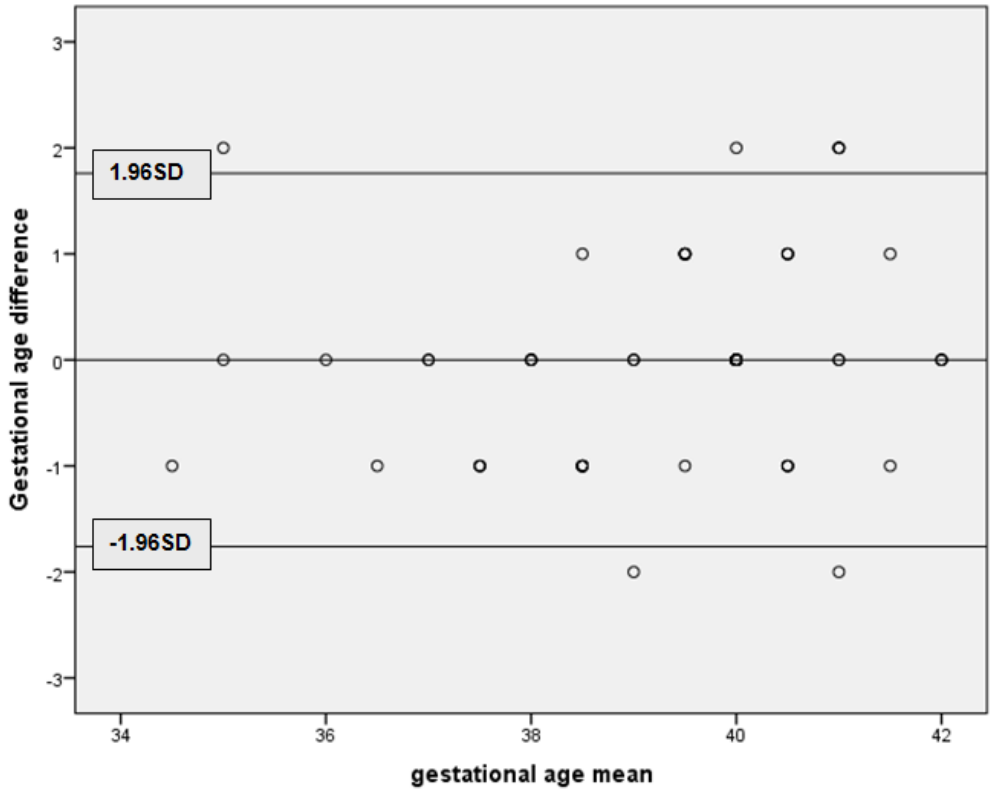
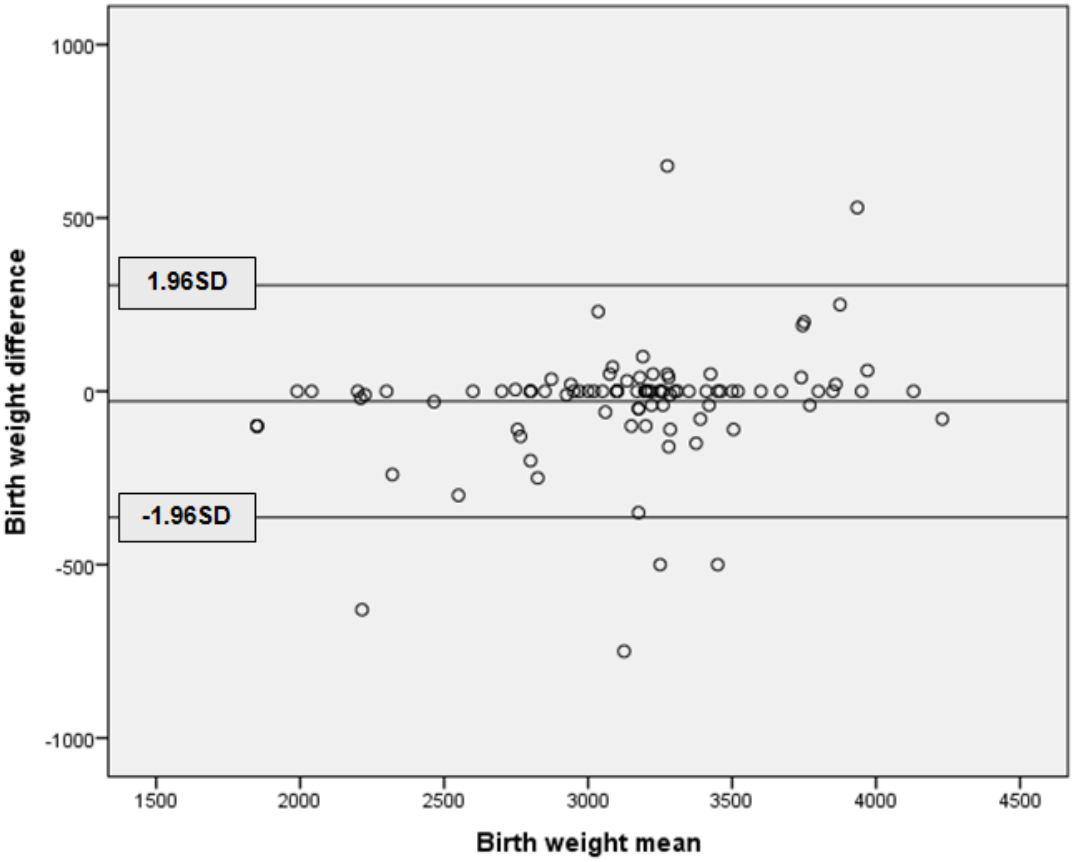


Figure 4.4 shows the evaluation of the agreement between maternally recalled and recorded infant birth weight plotted together with 95% limits of agreement. Most of the points are concentrated around the line of mean difference close to zero. The bias, estimated as the mean discrepancy between the two methods, is -28.69g and can be considered as a negligible difference between recalled and recorded infant birth weight. The limits of agreement show that most of the differences would be expected to lie between -363.7g and 306.3g. A study by Wilcox *et al.* (1993) of 41,718 newborns within a multicultural British population showed that the average term birth weight for babies in the normal range was 3201-3753g (range, 552g). Based on this study, differences within the 500g mark may be regarded as of no clinical significance. In our study, infant birth weight recalled by mothers may be 363.7g below hospital records or 306.3g

above hospital records, which is within the range of no clinical significance. This estimated agreement interval, together with a small bias between the mean differences, demonstrates a strong agreement between maternal recall and hospital records. In comparing the concentration points above and below 0 (perfect agreement), a slight tendency towards underestimation among normal birth weight infants, especially from 2,700 - 3,500g (around the value 3,300g), was observed.

Figure 4.4: Agreement Between Maternally Recalled and Recorded Infant Birth Weight with 95% Limits of Agreement

Mean difference = -28.69g, and SD = 170.91, 95% limits of agreement (-363.66, 306.28).



4.6.2 Assessing Agreement for Categorical Variables

For the categorical variables, gestational age, infant birth weight, onset of labour, pain relief and mode of delivery, kappa coefficients were calculated to evaluate the level of agreement between maternally recalled and recorded events (see Table 4.4). Strength of agreement was evaluated according to Landis and Koch (1977).

Table 4.4: Agreement Between Maternal Recall and Hospital Birth Records

Variable	Kappa	Strength of agreement*	*p*	95% CI
Gestational age	0.563	Moderate	0.001	0.342, 0.784
Infant birth weight	0.830	Almost perfect	0.001	0.641, 0.989
Onset of labour	0.790	Substantial	0.001	0.601, 0.979
**** Any pain relief**	0.618	Substantial	0.001	0.477, 0.759
Mode of delivery	0.919	Almost perfect	0.001	0.842, 0.995

* Landis & Koch (1977).
** The 'any pain relief' variable includes any combination of pain relief (yes/no)

Among the five categorical variables that were analysed for agreement between maternal recall and hospital birth records using kappa coefficient for strength agreement analysis, infant birth weight and mode of delivery had the highest level of agreement between recall and hospital records. Infant birth weight, including multiples, showed an exact match in 42% of women. In 30%, 15% and 7% of the women there was up to 100g difference, between 101 to 300g difference and >300g difference respectively. Missing data accounted for 6%.

Table 4.5 shows the margin of error (with *SD*s) within the different infant birth weight categories. Mothers of low (≤2,499g) and high (≥4,000g) birth weight babies tended to recall them as being smaller or larger respectively than recorded in the hospital records. Mothers of average birth weight babies (the

largest group) tended to have good agreement with birth weight as recorded in hospital records.

Table 4.5: Agreement of Maternal Recall and Hospital Birth Records of Infant Birth Weight

Infant Birth Weight (g)	IBW error (g) mean (SD)		n
≤2,499	136.15	(186.84)	13
2,500-3,999	71.73	(141.32)	81
≥4,000	184.00	(214.55)	5
Total	85.86	(153.13)	99

An exact match was found for mode of delivery in 95% of women (k = 0.919).

For onset of labour and pain relief, an exact match was found in 61% and 57% of women respectively. Categories were mismatched in 10% of women for onset of labour and 17% of women for pain relief.

Of the five variables, gestational age had the lowest level of agreement (k = 0.563). An exact match was found for gestational age in 35% of women, with 29% and 6% of women reporting a one-week difference and two-week difference respectively. Some 30% had missing data, the majority of which were in records.

4.6.3 Assessing Agreement for Dichotomous Variables

Agreement between maternally recalled length of labour, gravidity, induction, epidural use and pethidine with hospital records was explored. Table 4.6 presents results of all the dichotomous variables.

Table 4.6: Agreement Between Maternal Recall and Hospital Birth Records for Dichotomous Variables

Variable	Kappa	Strength of Agreement*	*p*	95% CI
Length of labour ≤10hrs/ >10 hrs	0.536	Moderate	0.001	0.305, 0.767
Gravidity	0.437	Moderate	0.001	0.176, 0.698
Induction	0.758	Substantial	0.001	0.556 - 0.960
Epidural	0.759	Substantial	0.001	0.632, 0.886
Pethidine	0.224	Fair	0.024	-0.035, 0.448

* Landis & Koch (1977).

Two variables were found to have substantial agreement, notably induction (k = 0.758) and epidural (k = 0.759). Although 17 women recalled receiving induction, only ten concur with hospital records. Of the 46 women who recalled receiving an epidural, 38 concurred with hospital records.

Although there was moderate agreement for gravidity (k = 0.437), 85% of women had an exact match between recall and records. Three women claimed to have had no previous pregnancy, but records showed a second pregnancy in all three cases.

There was moderate agreement for length of labour (≤10hrs / >10 hrs). It is not surprising that length of labour had the largest proportion of recorded missing data among the variables (43%). Medical record documentation was typically poor for labour progress in the days before electronic records. The time intervals used for dichotomising the length of labour variable into short and long labour for agreement between recalled and recorded length of labour were chosen for assessing labours of ≤10 hours and >10 hours. Calculating labour progress in the already compromised recorded dataset using smaller categories

would have further reduced the sample size in each category and introduced potential errors in calculation. In addition, understanding what constitutes normal labour progress and providing the appropriate care requires reducing unnecessary interventions prevalent in high-level facilities for longer than normal labour progress.

Only fair agreement was found for pethidine (k = 0.224), yet results from a study by Hewson and Bennett (1987) for women up to one year after birth show near perfect agreement (k = 0.85). Pethidine users in this study may have less accurate recall of labour events in the long term (>17 years). Moreover, the low kappa value may reflect low prevalence of its use (n = 12) as well as under-reporting. Under-reporting may be partly explained by known side effects to pethidine, which can include drowsiness, confusion and blurring of memory (British National Formulary, 2016).

4.7 Analysis with Logistic Regression

Logistic regression analysis was used to investigate whether independent variables were associated with discrepant recall of dependent variables. The test was carried out on all potential independent variables and outcomes (maternal recall of dependent variables). Continuous and categorical variables were converted to binary variables (i.e., inaccurate or accurate, coded as 0 and 1 respectively). Adjustment for the independent variables of maternal education, age of mother and years elapsed since delivery showed significant variable effects on the following dependent variables: gestational age, birth weight, gravidity, onset of labour, any pain relief, epidural, pethidine, and mode of delivery (see Table 4.7). There was no significant adjustment by immigrant status. The impact of the independent variables is explained in odds ratios (OR) and *p* values.

Table 4.7: Univariate Logistic Regression Between Maternal Recall and Hospital Records for Different Factors Relating to Each Other

*Dependant variable	Independent variable	*B*	OR Exp(*B*)	95% CI	*p*
Infant birth weight (± 100g)	Education	-1.090	0.336	0.114-0.987	0.047
Onset of labour	Age of mother	0.175	1.191	1.021-1.389	0.026
**** Any pain relief**	Years since delivery	0.082	1.086	1.0003-1.175	0.041
Epidural	Years since delivery	-0.156	0.856	0.758-0.966	0.012
Pethidine	Years since delivery	0.101	1.106	1.018-1.201	0.017
Mode of delivery	Age of mother	0.226	1.253	1.006-1.561	0.044

*ref. category DV = 0 (recalled incorrectly)
** The 'any pain relief' variable includes any combination of pain relief (yes/no)
$p \leq 0.05$ is a significant finding.

Among the six variables analysed in the univariate logistic regression, three pain relief variables (any pain relief, epidural, and pethidine) were influenced by time elapsed since delivery. Women who had more years elapsed since birth (*Mean* = 33.1, *SD* = 7.68 and *Mean* = 36.65, *SD* = 7.11 respectively) showed less agreement between recalled and recorded 'any pain relief' and use of 'pethidine' than women who had less years elapsed since birth (*Mean* = 28.1, *SD* = 5.88 and *Mean* = 29.85, *SD* = 6.06 respectively). However, in the case of epidural analgesia, women who had *less* years elapsed since birth (*Mean* = 25.33, *SD* = 5.76) showed *less* agreement between recalled and recorded epidural use than women who had more years elapsed since birth (*Mean* = 31.75, *SD* = 5.16). This unexpected finding may be explained by the fact that Israeli women are likely to receive an epidural (use in both the Lis Maternity Hospital and Ma'aynei Hayeshua Maternity Hospital exceeds 75% among first

time mothers) (Lis Maternity Hospital, 2015; Ma'aynei Hayeshua Maternity Hospital, 2015). Routine administration of a high number of epidurals may imply that epidurals are taken for granted and therefore perhaps not maternally recalled or are routinely recorded in the notes, even if they are not administered.

Two variables were influenced by age of mother at first birth. Women who were older at delivery (*Mean* = 27.9, *SD* = 6.08) showed less agreement between recalled and recorded onset of labour than younger women (*Mean* = 23.95, *SD* = 4.02). Likewise, older women at time of delivery (*Mean* = 25.8, *SD* = 5.36) showed less agreement between recalled and recorded mode of delivery than younger women at time of delivery (*Mean* = 24.1, *SD* = 4.49).

Finally, better agreement between recalled and recorded infant birth weight was associated with higher education. Women who had only partial or incomplete high school education showed less agreement between recalled and recorded infant birth weight by more than 100g than their better educated counterparts.

4.8 Discussion

In this study, agreement of maternal recall with hospital birth records for mode of delivery and infant birth weight of first births, over 40 years later, was remarkably accurate (k 0.92, agreement 96%; and k 0.83, 42% exact match, 30% <100g difference, 21% >300g difference, 6% missing respectively). Furthermore, maternal recall of these two variables was stable even when adjusted for time elapsed since birth (17- 49 years). This finding adds to existing evidence that infant birth weight and mode of delivery are among the most accurately recalled perinatal variables (Olson *et al*., 1997; Yawn *et al*., 1998; Tomeo *et al*., 1999; Sou *et al*., 2006).

Consistent with findings from five other studies (Gayle *et al*., 1988; Githens *et al*., 1993; Buka *et al*., 2004; Catov *et al*., 2005; Rice *et al*., 2006), discrepancies between questionnaire responses and birth record documentation of infant birth weight were found in less educated mothers ($p = 0.047$).

Maternally recalled and hospital records of infant birth weight and gestational age were in almost perfect and moderate agreement ($k = 0.83$ and $k = 0.563$ respectively) a finding consistent with nine studies that investigated maternal recall of ≥10 years from delivery. Agreement was reported to be higher for infant birth weight than for gestational age (Oates & Forrest, 1984; Gayle *et al*., 1988; Casey *et al*., 1992; Olson *et al*., 1997; Yawn *et al*., 1998; Buka *et al*., 2004; Adegboye & Heitmann, 2008; Troude *et al*., 2008; Liu *et al*., 2013). A high level of maternal recall of infant birth weight may not be surprising since birth weight information (and the infant's gender) is always eagerly awaited by parents and family members after delivery and is therefore more likely to be remembered (Yawn *et al*., 1998). The lack of social value for gestational age, together with the mother's possible lack of information on definitions of preterm and post-term delivery, could explain why some mothers in this study were unable to give an exact estimate of gestational age. In addition, some imprecision may have been introduced in this study due to the rounding off of gestational age to whole weeks in hospital records to correspond with maternally recalled gestational age. Moreover, maternal report of gestation was often in months, with descriptions of the child being born "on time" (which was taken to be 40 weeks), or born "late" or "early" (by a number of days or weeks). Thus, the effect of differential maternal recall (however small) may have been compounded by margins of error on both sides of the specific gestational age at birth.

Poor agreement between hospital records and maternal recall for pethidine was observed (k 0.224; *p* = 0.024). Due to the small number of women in the dataset (n = 12), conclusions could not be drawn as to the possible reasons for this (discussed in section 4.6.3).

There was substantial agreement between the two sources of information for induction (k 0.758) and onset of labour (k 0.790). To the best of my knowledge, this is the first study that has investigated these two variables for distant birth events and further/repeat studies are needed to confirm these findings. One other study (Elkadry *et al*., 2003) investigated induction in mothers only ten weeks after delivery; however, frequencies were small and findings were imprecise.

Labour onset may not have been previously investigated because important data may be missing from hospital birth records. In the present study, maternally recalled rupture of membranes (as a sign of pre-labour or early labour onset) was the most commonly missing data item (74.2% missing). Missing reports on induction and labour onset may preclude any reasonable conclusions.

By convention, hospital births are ‘managed’. Disparities and inequities within recalled and reported birth events may indicate a breakdown of communication between birthing mothers and care providers. For cases where recalled birth information is missing but clinical treatments are reported in hospital birth records, practitioners may have underestimated women’s preferences to participate in maternity-care decisions, or may have simply administered treatment without informed consent. Most of the women in the study sample (75%) gave birth between 1970 and 1990. Paternalistic attitudes in 20th century state-sponsored hospitals maintained levels of control on birthing women.

Studies by Joffe and Grisso (1985) in the UK, and Tomeo *et al*. (1999) and Buka *et al*. (2004) in the US found that mothers' disagreement with hospital records was greatest for events involving technical knowledge or medical intervention. In the present study, only eight women claimed to have received Pitocin to augment labour, but records show augmented labour administration for 17 women. This study is unable to elucidate the reasons for the discrepancy. There is a possibility that the nine women with no recall of the event were never informed that they had been induced so information in the hospital birth records may never have been disclosed to these mothers.

Statistical differences between the dependent variables (infant birth weight, onset of labour, any use of pain relief/epidural/pethidine and mode of delivery) related to education, age of mother, years since delivery, and age of mother respectively suggest that maternal factors may contribute to the discordance between recalled and recorded information.

Maternally recalled and hospital records of length of labour showed moderate agreement (k = 0.536). There is no preferred source for collecting intrapartum information. Deciding which data source to use for length of labour depends solely on the maternity carer. For acquiring a birth history, a woman's self-report is the more frequently used method. Implications for choosing self-report versus medical records for length of labour should be carefully considered when assessing maternity services for clinical practice. Judgements on the validity of either source have not been made, it has only been reported how they compare with each other. However, hospital record documentation was typically poor for labour progress, as observed by the large amount of missing data. Moreover, labour onset is most commonly defined through a woman's report of regular painful contractions. Even so, there is considerable discrepancy about what constitutes onset of labour, how to measure length of labour (normal or

prolonged) and whether vaginal examinations are a precise method to chart labour progress. This study's findings suggest that either method, recalled or recorded data, is useful for assessing women in the intrapartum period. Paradoxically, in many cases birth history documentation relies on the woman to give birth history information.

Childbirth is a highly memorable experience. It is perhaps not surprising that, in maternally recalled birth events, mothers are accurate in their descriptions for pregnancy outcomes. Furthermore, some discrepancies may be due to medical record omissions rather than to over-reporting by women. The best approach to obtaining accurate birth data is probably through the use of more than one source of information (Lydon-Rochelle *et al*., 2005). As this is not always possible, the limitations of each single data source should be recognised and taken into account. For data collection of specific birth events, women's recalled information offers a simple and reliable method. Women's recall is a useful first line of enquiry; after which it may be complemented by medical records data (when available) to rectify omissions occurring in the reporting system. In light of these findings, mothers' maternal recall data will be used to examine similarities in mother-daughter birth characteristics in the main study of this thesis (see Chapter Five).

Finally, agreement between mothers' self-reports and birth records may be lowest for normal births. Many of the options for women having a normal birth have not been studied in clinical trials. Most midwives base their treatment decisions for normal births on their clinical experience and subjective judgement. Recorded information for women having normal births may be minimal or missing. Deciding upon which information to record will often depend on the midwife, type of birth and birth outcome. Surveillance, patience and a 'hands off' policy is often not recorded.

4.8.1 Strengths and Limitations

The study depended upon recalled and recorded data collection. A strength in this study was the research investigator's (my own) personal role in searching through archived files. Particular care was taken to verify hospital birth records against self-reported questionnaires. By this method, errors in chart abstraction were minimal. In addition, while both maternal recall and hospital birth records were used as sources of information for agreement analysis, neither was considered a perfect 'gold standard'.

In this study, agreement between maternal recall and hospital birth records of distant birth events used several statistical methods for agreement analysis. The combined use of Bland-Altman plots and kappa coefficients provided a thorough analysis. The Bland-Altman graphs identified patterns of agreement for continuous variables and their characteristics. The kappa statistic for categorical variables considered agreement by chance. Logistic regression allowed inferences to be drawn about associations.

Prior to this study, the most comparably comprehensive study (Buka *et al*., 2004) examined six postpartum birth outcomes 20 years later. This study has extended that scope by examining eight variables on average 33 years after delivery. It sets the stage for investigating a larger number of variables over a longer post-birth period using birth data from recalled and recorded sources.

The data presented are based on convenience samples from antenatal clinics within the two hospitals. Despite the obvious advantages of selecting study participants who were accompanying pregnant women to antenatal clinics (they may have been more likely to be eager, or motivated to consent to participate in

birth-related research), these women may not have been typical, nor a probability sample of all potentially suitable cases within the local population base. For this reason, findings may not be generalisable to all women across Israel or other countries. Comparing maternally recalled factors between women who did and did not enrol in the study may have potentially given an indication of whether selection bias affected the representativeness or generalisability of the results.

Limitations of using data obtained from birth records include incomplete or missing personal and demographic data within the records, hospital record omissions or errors, and variability in the quality of documentation. Conversely, discrepancies between the two sources of information may have been equally due to over/under-reporting by mothers.

Other limitations of the present study may be participants' limited understanding of clinical diagnoses (Sou *et al*., 2006). The study design elicited maternal report by questionnaire of diagnostic criteria of perinatal events or interventions which may have affected the levels of agreement obtained. Similarly, women who suffer emotional distress may be more or less likely to recall specific perinatal details (Buka *et al*., 2004), further influencing maternal questionnaire responses. Furthermore, despite assurances of confidentiality, respondents may have decided not to share all the information requested in the questionnaire. Women who had had abortions or a termination of pregnancy may have declined to disclose their own maternity histories in the questionnaire (and, more likely, in hospital records). In addition, the relatively small sample size and homogenous population may not have allowed for detection of differences in agreement by women's or practice characteristics.

Finally, the highest proportion of discrepancy was found for length of labour (see Table 4.3). As section 4.8 illustrates, there is no standard way of measuring labour duration. Women who began latent phase labour at home may have counted this period of time within their overall assessment of the length of their labour, but this may not have been included in hospital records, as they may have only included the time from when the woman arrived in hospital in more advanced labour. Conversely, women who arrived at the labour ward in the final stages of labour may have seen their time in hospital as the 'official' length of labour, and so reported this, while the hospital staff may have made a judgement about when active labour started (prior to hospital admission) and recorded this as the length of labour. In a recent systematic review of the research literature on diagnosing labour onset, Hanley *et al.* (2016) report that there is considerable discrepancy among studies. Although four types of labour onset were identified in 62 studies in a population of healthy women with term births, labour onset was not generally evidence-informed, as there is no agreed evidence base in this area, and consensus concerning definitions of labour onset was universally lacking. Lack of diagnostic criteria and inconsistency of interpretation may be the reason for poor documentation of labour onset in birth records.

Despite these limitations, this study makes an important contribution to the expanding research and literature on maternal recall agreement with hospital birth records for a number of perinatal factors.

4.8.2 Implications for Practice and Research

This study investigated maternal recall of first delivery perinatal outcomes over a period of 17-49 years. Past studies have found increased agreement in a mother's recall of her first delivery compared with subsequent deliveries

(Seidman *et al*., 1987; Casey *et al*., 1992; Catov *et al*., 2005), further supporting the use of maternal recall for first birth events. In addition, a first birth is by definition a new experience which is not the case with a second or subsequent birth. Seidman *et al*. (1987) suggest maternal recall of first births may be interlaced with recollections of this uniqueness leaving a 'special mark' in maternal memory. Researchers requesting maternally recalled information per child for larger families should consider that maternal recalls may be slightly less reliable. Furthermore, when requesting information on length of labour, women should be encouraged to report on distinct signs of labour onset and timing. In addition, when requesting information on gestational age, researchers should consider defining and specifying length of gestation in weeks and days in the questionnaire for greater reliability.

Finally, although the multiple births in this study (one set of triplets and three sets of twins) may have been representative of the prevalence of triplets and twins in the sample, frequencies were too low for agreement analysis. Although current maternal recall literature has varied sample populations and broad measures of interest, only one study (Liu *et al*., 2013) examined maternal recall with a focus on mothers with twins. Future studies may wish to research maternal recall of twin and triplet birth outcomes more thoroughly and independently of single birth outcomes.

Although this study is based on specific perinatal outcomes, the findings are likely to be applicable to the use of maternally recalled data that includes other reproductive outcomes, such as weight gain in pregnancy.

4.9 Conclusions

Consistent with previous studies, the findings in this study suggest that maternal recall is remarkably in agreement with hospital birth records for most perinatal factors. Mothers are willing to provide perinatal information about their first births. This information may be used as a supplement to, or in replacement of, hospital birth records.

A recall period of 17-49 years does not appear to be a disadvantage in an event as salient as the birth of a first child. However, for certain outcomes such as birth weight, onset of labour, any use of pain relief/epidural/pethidine and mode of delivery, maternal recall may be influenced by education, age of mother and years since delivery. To improve the reliability of the results on length of labour and gestational age, modifications to the response options in the questionnaire may be necessary.

Chapter Five: Mother-Daughter Similarities in Labour and Birth Characteristics (SiLC): a Linked Comparative Cohort Study

5.1 Introduction

This chapter presents the primary data for this thesis. It describes the methods and results of a comparative linked cohort study that was designed to explore similarities in labour and childbirth characteristics between nulliparous women and the first birth of their mothers. Other factors influencing daughters' first labour and birth were also investigated.

5.2 Background

As suggested in previous chapters, an alternative to individual labour history for nulliparous women could be family history. Examples of documented mother-daughter similarities in pregnancy and birth outcomes include gestational age, birth weight, prolonged pregnancy, labour dystocia, assisted vaginal birth and caesarean section (see Chapter Two).

These studies show that there are familial factors related to recurrence of pregnancy and birth outcomes across generations, with a strong maternal component. However, to the best of my knowledge, there are no matched cohort studies on length of labour of nulliparous women taking account of their mothers' first births. Whilst previous labour length can be a useful guide to subsequent labours, nulliparous women have no birth history and are more likely to be diagnosed as having atypically slow labour progress (Neal *et al*., 2010; Souza *et al*., 2015).

In 2018, Oladapo *et al*. reported prospectively plotted labour curves for 5,606 Nigerian women, along with outcomes data, and concluded that average population labour curves do not reflect the variability associated with labour progress and outcomes for individuals. It appears that physiological length of labour is highly variable (WHO, 2018) and that population norms may not be relevant for clinical decision-making related to particular women in labour (Abalos *et al*., 2018). There is also concern that overly conservative definitions of labour dystocia are associated with rising caesarean section rates (Visser *et al*., 2018), despite new evidence showing that cervical dilation over time serves as a poor predictor of adverse birth outcomes (Souza *et al*., 2018). Differences in risk thresholds for intervention may be as much responsible for these variations as actual underlying pathology.

At present, assessment of progress in labour is based on health provider expertise, knowledge and population norms. Since evaluation for labour progress by population norms has low sensitivity and specificity for individuals, a mother's birth history might provide a basis for individualised assessment of labour progress in her nulliparous daughter.

The aim of this study was to investigate the relationship between length of labour in nulliparous daughters and in their mothers' first birth, as a basis for constructing individualised labour prediction models in the future. A new standard for measuring physiological progression of labour in nulliparous women may enhance clinical practices and inform strategies to avoid unnecessary interventions and caesarean sections. As suggested in Chapter One, a mother's familial history may be relevant to guide decisions made for a nullipara in labour. Maternity carers face complex obstetric decisions in everyday practice. Multiple inter-related factors may influence a nullipara's labour progression.

5.3 Objectives for the Linked Comparative Cohort Study

The objectives for this linked comparative cohort study (as noted in section 1.6.1) include:

- to analyse associations between the labour and birth characteristics and outcomes of nulliparous women and the first birth of their mothers;
- to examine variables associated with length of labour of nulliparous women, taking account of the length of labour of their mothers' first birth.

5.4 Study Population

Index women (daughters) were a cross-sectional cohort of women resident in the Tel Aviv conurbation area. Mothers of these index women were found to be resident in many different areas of Israel (see Table 5.1 for participant inclusion criteria).

Index women were excluded if they were under 18 years old, below 32 weeks' gestation or unwilling to include their mother. Mothers were excluded if they had a first birth less than 17 years ago or were not the biological mother of the index woman.

Table 5.1: Inclusion Criteria for Participants

Inclusion criteria, index women (daughters)	Rationale	Inclusion criteria, mothers	Rationale
Participants must have given birth in one of the hospitals where the study is being conducted	Enabling access to birth records	Participants must be the biological mother of the index woman	Confirmation of biological family structure for expected familial effect
Language competence (sufficient command of Hebrew reading and writing)	For self-report and questionnaire completion	Language competence (sufficient command of Hebrew reading and writing)	For self-report and questionnaire completion
Nulliparous women of at least 18 years old and >32 weeks gestation	To preclude pregnancies in very young women (below 18 years old), and cases above 32 weeks gestation at time of study recruitment to preclude prematurity and neonatal complications	Having had a first birth more than 17 years ago	To preclude pregnancies in very young women (pregnant women under 18 years of age are at higher risk of preterm birth and a low birth weight infant) *
Willingness to provide full name and national identity number	As a means of tracking hospital birth records	Willingness to complete the questionnaire	For birth history information
Willingness to sign informed consent	Ethical precaution/eligibility determination	Willingness to sign informed consent	Ethical precaution/eligibility determination
Willingness to contact their mothers	For paired mother-daughter data		

* Khashan *et al*. (2010).

This study aimed to collect empirical data on women who lived in the Tel Aviv area, and their mothers. Women who did not patronise the study hospitals were not offered study participation. Feasibility, in terms of time and resources, dictated the choice of sampling methods. The data presented are based on convenience samples from antenatal clinics within the two hospitals. Despite the obvious advantages of selecting study participants who were attending, and in some cases accompanying, pregnant women to antenatal clinics (they may

have been more likely to be eager or motivated to consent to participate in birth-related research), these women may not have been typical, nor a probability sample of all potentially suitable cases within the local population base. Restriction to Hebrew language speakers was pragmatic, as there were insufficient resources for translation. As the majority (96%) of all women frequenting the study hospitals were Hebrew speakers at the time of data collection (taken from the 2016 hospital census), the language restriction was unlikely to have had a detrimental effect on recruitment and participation to the study, but may limit generalisability to the wider Israeli population.

5.5 Research Design

A cross-sectional cohort design was used. Cohort study designs are recommended for specific groups of people selected according to some defining characteristics and/or health outcomes (Altman, 2014). Cross-sectional study designs have been used to investigate risk factors for disease (Glasziou *et al*., 2001). A cohort study is still susceptible to bias because of losses due to follow-up and confounders (Carr *et al*., 2007). In this study, both mothers' and daughters' labour and birth variables were evaluated simultaneously. Data were collected consecutively - retrospectively with regard to the mothers, and prospectively with regard to the index women (daughters).

5.6 Methods

5.6.1 Recruitment

The hospital sites for participation recruitment were located in the central area of Israel and each averaged around 1,000 births a month (see section 4.2.2 for context). In terms of intrapartum care, they provide maternity triage, midwife

and/or doctor-led delivery rooms, obstetric operating rooms, and maternity/newborn wards.

Recruitment took place in two Israeli hospitals between September 2014 and June 2015 on one day a week at each hospital, alternating weekly between the two hospitals over a period of 42 weeks. All eligible women were approached on these recruitment days. Ten to twelve questionnaires (in Hebrew) were distributed by myself (as the research investigator) to 10-12 nulliparous (index) women, each at least 18 years old, at >32 weeks' gestation, attending antenatal clinics (Sunday through Thursday during antenatal clinic hours, 07:30-14:00). Eligible women received questionnaires, participant information sheets for themselves and their mothers, and individual consent forms.

5.6.2 Instrumentation, Procedures and Birth Data Collection

The self-completion questionnaire is a widely used research tool that has a number of advantages: it reduces interviewer bias, collects large amounts of data relatively quickly and is fairly straightforward to analyse (Oppenheim, 1992; Robson, 1993).

The Similarities in Labour and Childbirth (SiLC) research questionnaire for mothers was identical to the maternal recall questionnaire described in Chapter Four (a copy of the mothers' questionnaire can be found in Appendix 3). The index women's 23 item questionnaire included personal information (full name and national identity number as a means of tracking medical records), expected date of delivery and sociodemographic information (a copy of the daughters' questionnaire can also be found in Appendix 3).

Potential participants selected from nulliparous women who were at least 18 years old, of more than 32 weeks' gestation attending antenatal follow-up at the Lis Maternity and Ma'aynei Hayeshua hospitals were approached by the research investigator (myself) and provided with a participant information sheet for themselves and their mothers. Mothers were either accompanying the index woman at the antenatal clinic or were recruited via the index woman. A covering letter explained the research aims, assured that involvement in the study was voluntary and guaranteed confidentiality of responses. Participants were made aware that they were free to withdraw from the study at any time and were asked to sign a consent form. Completed questionnaires were returned by the index women at subsequent follow-up visits to the hospital or via a 'Freepost' envelope provided. Prenatal, perinatal and newborn outcome information for the index women was collected from electronic hospital records after the birth of their babies.

Birth information collected from both mothers and daughters included age at first period, height, education, marital status, weight gain in pregnancy, signs of beginning labour, analgesia in labour, augmentation in labour, length of labour, age at first birth, delivery outcome, foetal birth weight, gestational age, Apgar and gender. The length of labour variable was measured on a self-reported categorical scale in mothers (from questionnaires), and on a continuous scale for the index women (from birth records).

Mothers were asked about the length of time they were in labour and responses were categorised as:

1) Less than 2 hours
2) 2-6 hours
3) 6-10 hours
4) More than 10 hours, please give the number of hours: _____

The four time intervals were based on findings from a systematic review of active labour duration rates among low-risk nulliparous women with spontaneous labour onset (Neal *et al*., 2010) and are described in section 4.4.4.

The mothers were not asked to record the length of their births in hours and minutes because some women include the latent phase in this assessment, which can last many days. For this study, the particular interest was in longer labours as a category, rather than the precise hours and minutes a labour may continue for. Mothers' length of labour was determined by self-report. For mothers who had laboured for more than 10 hours, indications for labour onset were verified by telephone conversations and determined by the presence of strong, regular, painful contractions and/or hospital admission with ≥4 centimetres cervical dilatation.

Daughters' onset of labour was determined from a starting point of 4 centimetres cervical dilation following hospital admission, and whether they were also experiencing regular uterine activity and intense, painful contractions (taken from birth records). Daughters who were admitted to hospital with a cervical dilatation >4 centimetres were questioned as to what time they started feeling strong, regular, painful contractions to determine onset of labour. Mothers' and daughters' length of labour was measured from onset of labour to childbirth.

Once linkage between mothers and daughters had taken place, the questionnaire and birth record data were anonymised, numbered, assessed manually for errors and entered into Excel spreadsheets. Mothers' and daughters' missing data were queried by telephone interviews and the data obtained and entered.

5.7 Sample Size Calculation

A sample of 360 mother-daughter dyads were recruited; 323 dyads were retained through all stages of the study. The power of this sample size to answer the primary study question (risk of long labour in daughters) was calculated retrospectively and it provided a guidance to the number of variables to be included in the model. Calculating sample size for logistic regression is a complex problem and was not feasible in this study, as the information required for it was not available. However, Peduzzi *et al.* (1996) suggest the following formula for estimating the minimum number of cases to include within a study:

n = 10* (k/p),

where k is the number of covariates and p is the smallest proportion of negative or positive cases within the population (short or long labour cases). Based on the planned regression with 14 variables, the number of daughters required for the study would be n = 311, with 14 factors and p taken as 0.45 (proportion of short labour cases in daughters). Estimated relative to the number of variables in the study, the amount of data collected for this study is satisfactory for conducting logistic regression analysis and building the model with a reasonably large number of factors.

The original calculation of the sample size for this study used NQuery Advisor and reached a sample size of 500. The calculation was granted ethics approval and is presented within the thesis proposal (see Appendix 1). However, the sample size protocol was subsequently not followed for logistical reasons. It was updated to adjust for the variables and data collected during the conduct of the research with no difference to the study design.

5.8 Research Ethics

Project approval was granted by the Ethics Committees of the Lis Maternity Hospital, the Ma'aynei Hayeshua Hospital and the University of Central Lancashire (see section 4.4.2 and Appendix 1).

The main ethical concerns for this part of the study were ensuring the participants' confidentiality, attaining security of information storage, and the possibility that participants may suffer from negative or painful memories. The following steps were therefore taken to mitigate these concerns:

Disclosure: for participants' protection, confidentiality was strictly maintained by using name codes. Assurance was given that names would not be used in any published reports of the study.

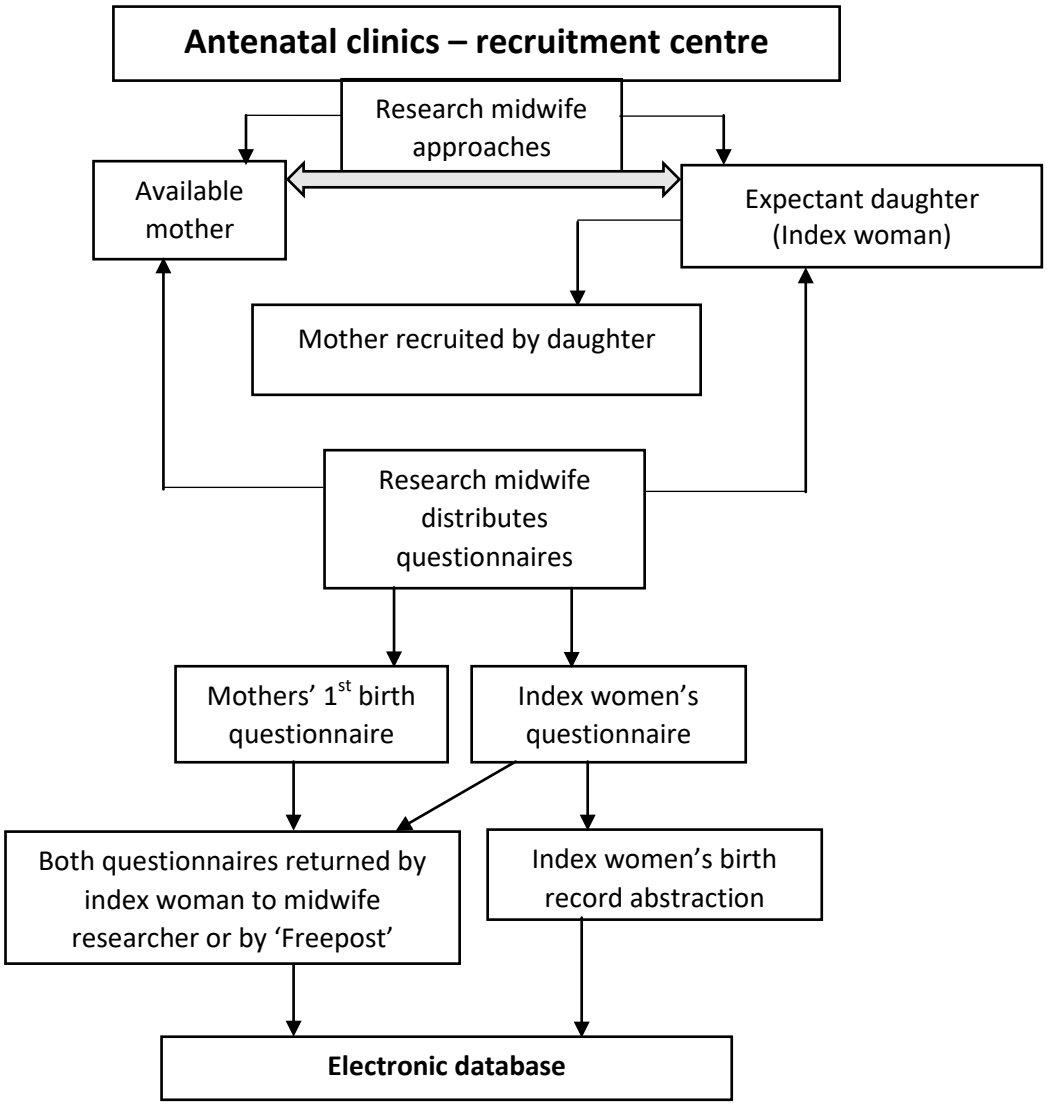
Data management: all identifiable data were kept in a locked cabinet in a locked office and the database was protected using a secured password accessible only to myself.

Reawakening of painful memories/experiences: emotional support for participants was made available. The questionnaire front cover (see Appendix 3) states: *"Should you experience anxiety or distress following memories of a difficult or traumatic childbirth and wish to discuss your feelings or seek emotional support, please contact the Women's Mental Health Services, Sourasky Medical Center TA, located in the rehab building on the ground floor. Consultations are free of charge. For appointments call: 03-6974707)."*

5.9 Pilot Study

A pilot study was conducted prior to initiating the main study to test the feasibility and logistics of the study design, recruitment of subjects, inclusion and exclusion criteria, questionnaire design and the availability of information from birth questionnaires and data abstraction postnatally. The data collection process is presented in Figure 5.1. In September 2014, 20 nulliparous index women in their third trimester of pregnancy were recruited while attending maternity triage at either of the two hospitals where the research was being conducted. After consenting to participate, ante-natal questionnaires were distributed to these index women, and birth information questionnaires were included for their mothers. Completed questionnaires were returned by the index women at a subsequent follow-up visit to the hospital or via the 'Freepost' service offered in the research package. The pilot study provided the groundwork to test the project design (questionnaire distribution and return) and demonstrated that the study protocol was feasible.

Figure 5.1: Flow Chart of the Data Collection Process and Information Flow



5.9.1 Findings

Most daughters (99%) who were asked, and mothers when present, readily volunteered to join the study. The project did not appear to be disruptive to either of the antenatal clinics. No changes were deemed necessary to the questionnaire and no logistical issues were raised. After the births of the 20 index women's babies, electronic hospital birth data were collected. All data were coded into mother-daughter pairs and entered into Excel for primary analysis. The data content of this pilot was included in the main study findings.

5.10 Data Management

Data from questionnaires and birth records were entered into Excel spreadsheets. The birth outcome data from Excel were cleaned, divided into mother-daughter datasets, then transferred to the statistical software package 'SPSS' (version 24.0, Armonk, NY, IBM Corp.) using the 'copy and paste' method, with a subsequent check of copied data for consistency with the original Excel file. Raw data were entered solely by myself, the research investigator. Double data entry by another researcher was not performed due to a lack of resources. However, to reduce input errors, all data from questionnaires and birth records were checked for validity of entry by double checking against the source document. Where conflict existed in any of the data fields, validation was carried out by referencing the questionnaire/birth records. Missing or ambiguous information from questionnaire/birth records was gathered through emails and telephone conversations. Prior to data analysis, data were cleaned and corrected in order to address errors that might have occurred.

5.10.1 Data Cleaning

Decisions were made prior to data screening on how to handle problematic observations (such as missing data or outlier data-points). For missing data in this study, the available case analysis method was used (i.e., use of the data available for each analysis) because it may be applied if less than 5-10% of the data is missing (Bennet, 2001), in which case it does not pose a major threat to statistical power. In this study, the proportion of missing data was less than 10%, therefore, excluding observations that have missing information should not have led to a substantial loss of statistical power. In addition, there are circumstances in which the available case analysis method is advocated as an improvement over imputation of data. For instance, when the available data

matches the out-of-sample missing data, no imputation is needed (White & Carlin, 2010). In this case, there is no direct indication of bias due to systematic differences among the respondents and non respondents. Moreover, Hughes *et al*. (2019) suggest that the available case analysis method is an appropriate choice for epidemiological style studies and often the preferred choice over imputation of data.

The case analysis method is a commonly used method in statistical analysis using SPSS (Kwak & Kim, 2017) and was employed for the treatment of missing values within this study. Outliers that were identified were checked for human error and corrected if appropriate.

The data were screened to ensure that the total number of participants in each dataset (mother-daughter) corresponded to each other and to the number on the database. Code numbers (ID) and initials on each completed questionnaire were cross-checked with those on the database. In addition, unexpected patterns in data distributions were identified.

By arranging data in both ascending and descending order, erroneous or impossible values (such as ‘age 106’) were checked against the source document and replaced with the actual value from the questionnaire/birth records or after verification with the mother-daughter by telephone or email.

5.11 Exploratory Data Analysis

An exploratory data analysis approach was adopted. This approach allowed for a step-wise analysis towards model selection at a later stage. The methods used are summarised in Table 5.2. The exploratory steps taken for statistical analysis are described. Information in this section is divided into three main

sections: logistic regression analysis, linear regression analysis and common methods used to check assumptions. Other relevant statistical tests and findings are also presented. Finally, section 5.17 discusses statistical analyses in the light of these explorations, adding more breadth and depth to the findings.

A summary table of key steps in the exploratory data analysis is presented at the end of the methods section (see Table 5.2).

5.12 Statistical Analysis

This section presents the chosen methods and outcome models that are used to answer the research objectives. Both logistic and linear models are used.

5.12.1 Description of Statistical Methods for Preliminary Analysis

To address research objective 3 (mother-daughter birth characteristic associations), descriptive statistics were used to describe the personal and demographic characteristics and birth history information of the respondents using a central tendency measure (mean) and measure of dispersion (standard deviation [*SD*]) for continuous variables. Continuous variables were also checked for normality of distribution. These included age at first period, height, weight gain in pregnancy, age at first delivery, foetal birth weight and gestational age. The percentage and frequency were calculated for categorical variables (for example, education and length of labour categories).

5.12.2 Statistical Analysis for Mother-Daughter Health and Maternity Associations

Tests for associations between mother's and daughter's health and maternity variables were conducted. Appropriate statistical tests were chosen according

to the type of variable. Paired *t*-test and Wilcoxon tests were used to compare continuous variables. McNemar's test was used for binary variables. For categorical variables with more than two responses, the marginal homogeneity test was applied, which is a generalisation of McNemar's test. Significance was defined as $p<0.05$.

5.12.3 Statistical Analysis with Logistic and Linear Regressions

To address research objectives 3 and 4 relating to similarities and differences in characteristics, outcomes, and length of labour between mothers and daughters, logistic and linear regression analyses were conducted.

5.12.3.1 Methods for Logistic Regression Model

Logistic regression analysis was used to predict the probability of daughters' long length of labour. To interpret the results of the prediction of daughters' long length of labour, a preliminary analysis of the cleaned dataset was conducted to observe if the assumptions of logistic regression were met. The assumptions are satisfied and are presented in the results section (section 5.17) after regression modelling.

Logistic regression analysis can be used to determine the probability of an event occurring given a select number of explanatory continuous and categorical variables. It can handle data where the multivariate normality assumption does not hold (Sharma, 1997). However, logistic regression can only be used when the predictor variables are independent of each other. In addition, the Hosmer-Lemeshow goodness-of-fit test (Hosmer *et al*., 2013) was used with the logistic regression analysis.

As a result, logistic regression for the binary dependent variable ‘daughters’ length of labour’ was the first line of enquiry used to explain the relationship between ‘mothers’ length of labour’ (and other independent variables) and ‘daughters’ length of labour’.

Daughters’ length of labour was dichotomised (≤10hours / >10hours) and analysed with logistic regression. Clinically, dichotomisation of length of labour offers a risk classification into high versus low, which may assist in making treatment recommendations and in setting diagnostic criteria for women whose labour patterns are prolonged (i.e. slower from that observed in the majority of women). A cut-off point of >10 hours was chosen to define longer labour taken from the end point in category ‘3’ of the mothers’ questionnaire question on length of labour.

To examine length of labour in daughters, multivariable logistic regression was used to determine the predictability of ‘daughters’ length of labour’ by ‘mothers’ length of labour’ and other independent variables. The following model was used to calculate the odds ratio:

$$\text{Logit}(p) = \ln(\text{Odds}) = \ln\left[\left[\frac{p}{1-p}\right]\right] = \beta_0 + \beta_1 x_1 + \beta_2 x_2 + \ldots + \beta_k x_k$$

where “*p*” is the predicted probability of long length of labour in a daughter influenced by her mother’s length of labour and other independent variables (denoted by the vector x’ = (x_1, $x_{2...}$, x_k)).

In order to categorise length of labour, the dependent variable (daughters’ length of labour) was coded dichotomously (≤10hrs/>10hrs). This created two defined groups: women who had a ‘shorter labour’ and gave birth in under 10 hours, and women with a ‘longer labour’ (in this study defined as a labour

lasting more than 10 hours). Either group may or may not have received oxytocin augmentation to speed up labour. In the dataset, all daughters' length of labour ≤10 hours were coded "0" (shorter labour) and >10 hours coded "1" (longer labour).

To answer the research objectives, a logistic regression model was created using the forward selection procedure to ascertain what variables are most related to daughters' length of labour. First, for comparison of mother-daughter length of labour, mothers' four-category self-reported data (taken from questionnaires) were converted into two and three categories, and daughters' continuous length of labour data (taken from electronic hospital records) were categorised into two, three and four categories. Second, the dichotomised (≤10hrs/>10hrs) independent variable (daughters' length of labour) was explored using univariate logistic regression with all the independent variables. Utilising significant results (p ≤0.05) from univariate logistic regression analysis, the regression was re-run controlling for the gender of the baby in the case of both mother and daughter. The statistically significant variables were: mothers' length of labour (binary), foetal birth weight and gestational age, and daughters' height, education, age, weight gain, induction, augmentation, use of anaesthesia, foetal birth weight, gestational age (rounded off to the nearest week), and type of birth. These variables were used in a multivariable logistic regression model with standard method of variables entry in SPSS.

Using a manual stepwise regression method, candidate variables were systematically entered and removed to find the best model fit based on the predetermined p-value. This method was chosen for its convenience for data collected within different settings (mother/daughter data), for its ability to manage large amounts of potential predictor variables, for fine-tuning the model to choose the best predictor variables from the available options, and because it

is more controlled than automatic model-selection methods. The performance of the model was investigated using 'percentage correct predictions' (Hosmer *et al*., 2013).

There are different recommendations in the literature regarding *p*-value for including predictor variables into the model, in a range between 0.1 to 0.2. Hosmer and Lemeshow (2000) recommend that independent variables should have a significance level of $p < 0.15$ to enter the model. A 0.1 significance level was used when assessing predictor variables for model inclusion. Once variables entered the model, the Hosmer-Lemeshow goodness-of-fit test showed best goodness-of-fit. The process was repeated by manually fitting selected predictors into the model until all predictors that contributed to the improvement of the model were included. Once the Hosmer-Lemeshow goodness-of-fit test showed that the final model was correctly specified, the Area Under the Curve (AUC) (Hosmer *et al*., 2013) was applied. AUC = 0.5 – 0.6 means discrimination was poor and no better than chance, $0.7 \leq AUC < 0.8$ means acceptable discrimination, and $0.8 \leq AUC < 0.9$ means excellent discrimination (Hosmer *et al*., 2013). The Receiver Operating Characteristic (ROC) curve was plotted to identify daughters' long length of labour, given by the reported presence of the mothers' length of labour variable.

In addition, several manipulations were applied to the model using variables that may be expected to have direct effects on the outcome variable. The following quadratic regression terms were introduced to the model: daughters' age and daughters' height; and the following potential interactions were tested for in the model in the following combinations: foetal birth weight/induction, foetal birth weight/gestational age, gestational age/augmentation and signs of labour/mode of delivery. These predictors were not significant, did not improve the goodness-of-fit and were not included in the final model.

The final predictive model for daughters' length of labour (binary) included mothers' length of labour binary, daughters' age, daughters' weight gain in pregnancy, and daughters' use of anaesthesia (categorical). No imputation was performed for missing data.

5.12.3.2 Methods for Linear Regression Model

Linear regression modelling is a good method for numeric prediction. Linear regression analysis was applied to test the relationship between daughters' length of labour (continuous) with other variables (continuous or binary), and for individual predictive value for daughters' length of labour. The initial judgement of a linear relationship between daughters' length of labour and daughters' age at delivery (continuous dependent variable and continuous independent variable respectively), and daughters' length of labour and weight gain in pregnancy (continuous dependent variable and continuous independent variable respectively) was made on the basis of two scatterplots (see Figures 5.9 and 5.10).

In the multivariable regression model, the dependent variable (daughters' continuous length of labour) is described as a linear function of the independent variables X_i, as follows: $Y = a + b_1 \times X_1 + b_2 \times X_2 + \ldots + b_n \times X_n$. The model permits the computation of a regression coefficient b_i for each independent variable X_i (Y = dependent variable, Xi = independent variables, a = constant intersect, and b_i = regression coefficient of the variable X_i).

To interpret the results of the prediction of daughters' length of labour, a preliminary analysis of the cleaned dataset was conducted to observe whether the assumptions of linear regression were met. The assumptions are satisfied

and presented in section 5.18.1, after linear regression modelling. Variables that were found to be statistically significant in the univariate analysis (p <0.1) were explored in a multivariable linear regression model. A predictive model for daughters' length of labour included mothers' length of labour in three 'long' labour time intervals (0-12 hrs, 12-18 hrs, 18+ hrs) (as dummy binary variables), daughters' age (continuous variable), daughters' weight gain in pregnancy (continuous variable) and daughters' use of anaesthesia (binary). Using alternative categorisation of mothers' length of labour, a predictive model using three 'short' labour time intervals (0-6 hrs, 6-10 hrs and 10+ hrs) with the same variables was also explored.

The three 'long' time interval categories were chosen because longer labours (as seen in the latter two categories; 12-18 hours and above 18 hours) are those which are likely to trigger interventions, even if there is no actual pathology present. This may be because the attending physician believes that, in this particular case, there is a real threat to either the mother or baby. However, interventions for longer labours also occur regularly just because a guideline or protocol indicates a course of action is necessary based on time elapsed, and not because the particular mother or baby are at any additional risk. Although prolonged labour (above 12 hours), especially among primiparae may be common, it constitutes the major indication for instrumental deliveries and delivery by caesarean section (Lowe, 2007; Shields *et al*., 2007).

The three 'short' time interval categories were chosen for linear regression analysis to compare results of the 'long' and 'short' time interval categories at different points in time using the same parameters.

A summary table of key steps in the exploratory data analysis is presented below (Table 5.2).

Table 5.2: Key Steps in Exploratory and Inferential Data Analysis and Typologies of the Study Design

Step	Action/Findings
1 Data preparation and transfer	Birth outcome data from questionnaires and birth records were entered into Excel spreadsheets
2 Data transport	Birth outcome data from Excel were cleaned and transported to Data Statistical Package for the Social Sciences (SPSS) version 24.0.
3 One full mother-daughter dataset was constructed. One physiological m-d dataset was constructed. Variables were defined for SPSS into nominal, ordinal and scale fields.	1) Index/mother full dataset (n = 337) (excluding multiple births in either mothers or daughters). This was subsequently filtered to exclude elective caesarean sections (n = 14) in either mothers or daughters (n = 323) and will be referred to as the full dataset. 2) A physiological dataset (n = 21) consisting of mothers and daughters who took no analgesia, had no interventions throughout labour and had normal labours and deliveries, and will be referred to as the physiological dataset.
4 Frequency analysis	Used for personal and demographic characteristics and birth history information of the respondents. Table 5.3 presents the frequencies and differing percentages of the interesting categorical and continuous variables. Table 5.6 shows the same for physiological births. Table 5.7 shows length of labour of index women dichotomised and categorised to yield the appropriate number of categorical observations for comparison with mothers' length of labour data. Table 5.8 shows the same for the physiological births.
5 SPSS output process includes graphic figures for each category	Pie charts for nominal variables, bar charts for ordinal variables and histograms with a parametric curve for scale variables. Pre-screening analysis examined normality, homoscedascity, skewness and kurtosis in the data.
6 Application of statistical tests to analyse index woman and mother associations	Tests were chosen according to the characteristic of the variable, namely, for scale normally distributed variables - paired t-tests; for scale not normally distributed variables - Wilcoxon signed-rank test; for binary variables - McNemar's test and, for categorical variables with more than two responses, the marginal homogeneity test was applied. For continuous statistically significant results effect sizes were calculated. Statistical significance was assessed using $p < 0.05$. Table 5.4 presents a comparative analysis of mother-daughter reproductive outcomes (excluding caesarean sections).
7 Re-categorisation for length of labour	For comparison of mother-daughter length of labour, mothers' four-category self-reported data (taken from questionnaires) were converted into two and three categories, and daughters' continuous length of labour data (taken from electronic hospital records) were categorised into two, three and four categories. Analysis of variance (ANOVA) was used to show differences in the distributions of daughters' length of labour between groups defined by mother's length of labour.

8 Univariate logistic regression using dependent variable length of labour index woman binary (outcome variable) and independent variables from both index and mother (predictor variables) Multivariable model	Logistic regressions (for binary variables) with calculated odds ratio (OR), *p* value and 95% confidence interval (CI). 1) Univariate logistic regressions 2) Multivariate logistic regression 3) Model including quadratic variables 4) Model including interactions 5) Test for sensitivity and specificity Univariate logistic regression: the following variables were assessed: age at first period, height, education, marital status, weight gain in first pregnancy, age at first birth, labour onset, use of analgesia in labour, augmentation in labour, gestational age, foetal birth weight, type of delivery, gender. Table 5.5 shows univariate logistic regression with daughters' binary length of labour variable and independent predictor variables. Findings ($p \leq 0.1$): length of labour binary mothers ($p = .011$), and weight gain index woman, age at first birth index woman, analgesia index woman, augmentation of index woman, type of delivery index woman. When logistic regression is filtered for gender analysis (gender index = gender mother), $p = 0.002$. Significant results from univariate analysis were selected and used in the multivariable logistic regression model (length of labour mother binary and daughters' age, weight gain in pregnancy, anaesthesia [binary], and augmentation). Hosmer-Lemeshow goodness-of-fit test showed $p = 0.810$. When augmentation daughter was removed, Hosmer-Lemeshow goodness-of-fit test showed best goodness-of-fit $p = 0.943$. Quadratic variables: age index woman, Hosmer-Lemeshow $p = 0.455$, & height index woman Hosmer-Lemeshow $p = 0.708$ did not improve the goodness-of-fit. Interaction variables: foetal weight/induction Hosmer-Lemeshow $p = 0.796$; gestational age/augmentation Hosmer-Lemeshow $p = 0.832$; foetal weight/gestational age Hosmer-Lemeshow $p = 0.281$; and signs of labour/mode of delivery Hosmer-Lemeshow $p = 0.541$ did not improve the goodness-of-fit.
9 Checking assumptions for logistic regression	Assumptions for logistic regression analysis: 1) No multicollinearity correlations 2) The continuous independent variables are linearly related to the log odds 3) Residuals are approximately normally distributed and include independence of errors 4) No influential observations
10 Linear regression model	Linear regression (for continuous dependent variable) *Conversion of four categories mother's length of labour from the questionnaire into three dichotomous dummy variables, of 0-12 hours, 12-18 hours and 18+ hours (long labour categories); and 0-6 hours, 6-10 hours and 10+ hours ('short' labour categories) respectively. Each categorical group ('long' and 'short' labour categories) was used as a variable in independent linear regressions. Significant results were found in both regression models.

11 Checking assumptions for linear regression	Assumptions for linear regression: 1) Linear relationships between outcome and continuous independent variables. 2) Homoscedasticity/residuals are approximately normally distributed. 3) No multicollinearity 4) No significant outliers 5) Normally distributed residuals
12 Physiological M-D datasets (attempted identical statistical analysis as mother-daughter dataset)	Physiological M-D datasets proved too small for significance testing. Difference in mother-daughter age was identical in both physiological and full datasets (i.e., daughters were on average six years older than mothers had been). Almost identical in the physiological dataset were m-d weight gain, gestational age, foetal birth weight and gender distribution of offspring.

5.13 Description of the Population, and Results of Exploratory and Preliminary Data Analysis

This section presents the findings of the descriptive statistics, along with some commentary. Preliminary analysis included univariate statistics and univariate modelling as a preparation for multivariable logistic and linear regression modelling. The focus of the analysis in the logistic and linear regressions was the relationship between daughters' length of labour (dependent variable) and mother-daughter birth characteristics (independent variables). The models included significant independent variables to give best predictive power in the analyses. In the discussion section, the findings were discussed by variable across the models, highlighting expected, unexpected and consistent effects, and attempting to reconcile or explain divergent or unexpected findings.

Of the 452 parturients approached, two daughters declined to take part due to the fact that their mothers were no longer alive. No mothers of consenting daughters refused to take part in the research study. Of the 450 paired questionnaires distributed, 360 paired completed questionnaires were returned (a response rate of 80%). Twenty-three (6%) of paired participants were excluded; 15 had incomplete questionnaires (unclear or indecipherable data, or missing information), and eight were women with multiple gestations. Excluded

from the statistical modelling dataset (but retained for the frequencies dataset in order to describe the sample) were mother-daughter pairs of which either participant had had an elective caesarean section (4%, n = 14) (see Figure 5.2), since the question of interest related to the characteristics of labour as well as the birth itself. Women who had an elective caesarean section had no labour process and the births had no relevance with regard to perinatal characteristics, labour duration and timing. The final analysis for statistical modelling thus included 323 paired mother-daughter women who gave birth to first birth singleton live infants.

Figure 5.2: Flow Chart of Inclusion in the Analysis

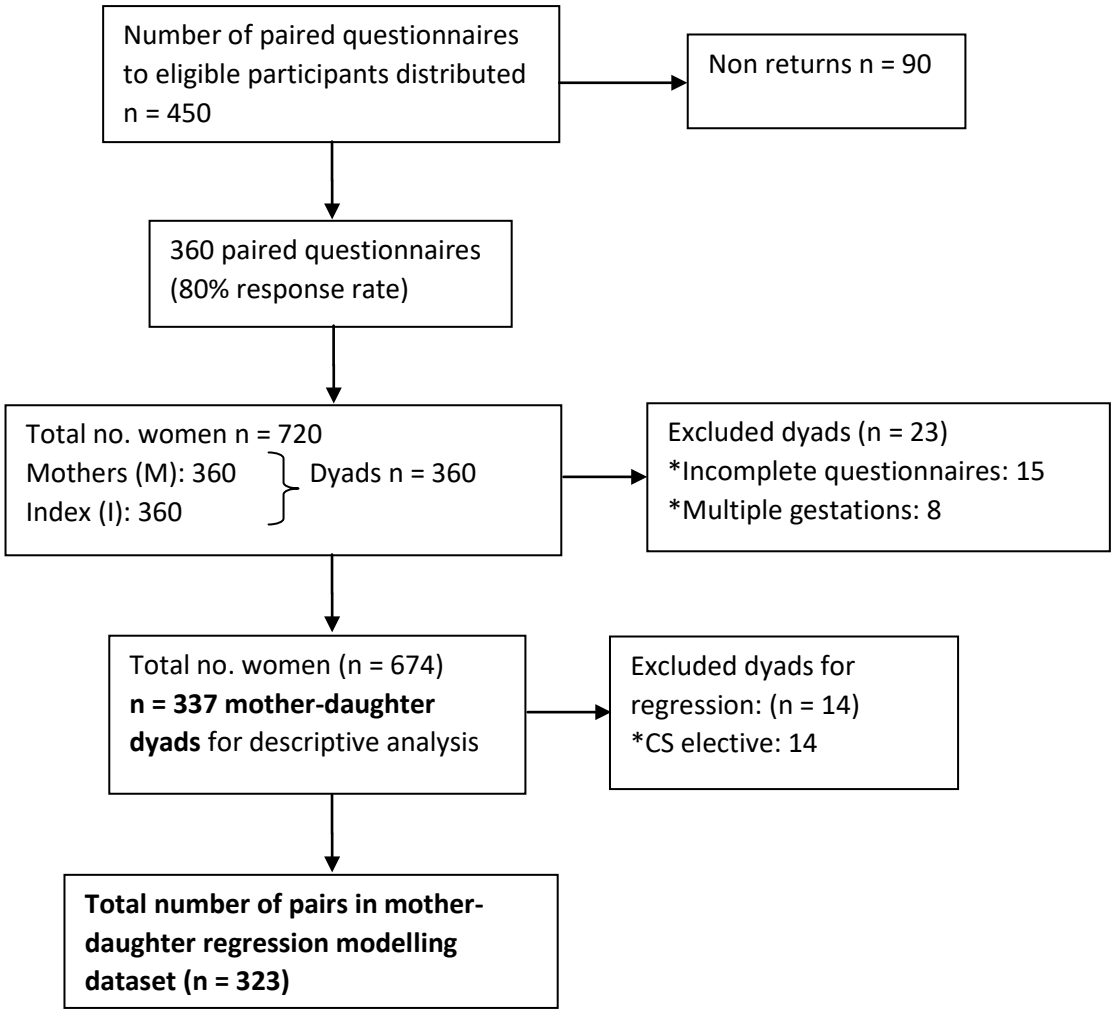


Table 5.3 provides the demographic characteristics and clinical outcomes of the 337 paired respondents.

Table 5.3: Characteristics of the Population and Clinical Outcomes

(Daughters in 2015; Mothers in 1967-1998)

Variable		**Daughters n**	***% out of valid responses***	**Mothers *n***	***% out of valid responses***
Country of birth	Israel	308	*91.4*	220	*67.9*
	Other	29	*8.6*	104	*32.1*
	Missing			13	
				(3.9%)	
Education	≤ Trade/tech school	118	*35.3*	193	*60.5*
	Academic	216	*64.7*	126	*39.5*
	Missing	3		18	
		(0.9%)		(5.3%)	
Marital status	Married	294	*87.2*	255	*82.8*
	Other	43	*12.8*	53	*17.2*
	Missing			29	
				(8.6%)	
Signs of labour	Contractions	164	*48.7*	190	*56.6*
	Amnion rupture	78	*23.1*	81	*24.1*
	Bleeding	10	*3.0*	30	*8.9*
	Induction	69	*20.5*	26	*7.7*
	CS (emergency/elecive)	16	*4.8*	9	*2.7*
	Missing			1	
				(0.3%)	
Induction	None	266	*78.9*	311	*92.3*
	Induced	71	*21.1*	26	*7.7*
Augmentation	None	297	*88.1*	313	*92.9*
	Augmented	40	*11.9*	24	*7.1*
Analgesia	Epidural	274	*81.5*	50	*16.0*
	Pethidine	0	*0*	70	*22.4*
	None	39	*11.6*	180	*57.5*
	Spinal	23	*6.9*	13	*4.1*
	Missing	1		23	
		(0.3%)		(6.8%)	
Mode of delivery	Normal	232	*68.8*	266	*79.2*
	Vacuum/forceps	57	*16.9*	43	*12.8*
	CS elective	10	*3.0*	4	*1.2*
	CS emergency	38	*11.3*	23	*6.8*
	Missing			1	
				(0.3%)	
Gender	Male	184	*54.6*	107	*31.8*
	Female	153	*45.4*	229	*68.2*
	Missing			1	
				(0.3%)	

Q = questionnaire

	Daughters				Mothers			
Variable	Mean (SD)	Median (IQR)	Min	Max	Mean (SD)	Median (IQR)	Min	Max
Age at Q (Missing 4)	29.54 (5.46)	30 (7)	18	46	57.81 (7.65) (Missing 3)	59 (10)	40	87
Age at 1st birth (Missing 4)	29.54 (5.46)	30 (7)	18	46	23.9 (3.70) (Missing 1)	24 (5)	18	41
Weight gain kg (Missing 12)	12.99 (5.17)	13 (6)	0	31	13.47 (6.11) (Missing 40)	12 (6.25)	2	45
Gestational Age (Missing 1)	40.08 (1.40)	40.08 (2)	34	42	39.76 (1.94) (Missing 9)	39.76 (2)	26	43
Foetal body weight g (Missing 1)	3273 (443.9)	3273 (557.5)	1872	4665	3176 (523.7) (Missing 6)	3176 (625)	920	4700

Missing data are presented as numbers together with percentages in brackets.

Daughters were older than their mothers had been at time of first birth (daughters' mean age = 29.5 yrs, SD 5.5; mothers' mean age = 23.0 yrs, SD 3.7). Daughters were also slightly older than the average age for an Israeli woman having her first child in 2016 (27.6 yrs). The majority (87%) of the sample self-classified as married which is higher than the nationwide average of 63% among the Hebrew speaking Israeli population (Israeli marital history data, 2016). This may be explained by the fact that the marriage rate in the ultra-orthodox population (aged 20 and above) stands at 82%.

Two thirds of the daughters had a university education compared with just one third of the mothers, and this compares to 50% for the Hebrew speaking Israeli population in 2016. One explanation for this difference may be because Tel Aviv is the economic and technological centre of Israel, has the largest university in the country and is home to younger, more educated residents than other cities in the country.

The most common sign of labour onset overall was contractions (daughters 48.7%; mothers 56.4%) followed by a similar number of spontaneous rupture of membranes or premature rupture of membranes (PROM) (daughters 23%; mothers 24%).

Compared to their mothers, the daughters had almost three times the rate of inductions (daughters' n = 21.1%; mothers 7.7%), more than one and a half times the rate of augmentations (daughters 11.9%; mothers 7.1%), five and a half times the rate of epidural analgesia use (daughters 81.3%; mothers 14.8%), and over one and a half times the rate of emergency caesarean (daughters 11.3%; mothers 6.8%). The average rate of all first caesarean sections in Israeli women in 2016 was 9.8% (range by hospital 3.1% - 14.6%). The upper end of this range equates to the 14% figure for the combination of elective and emergency caesarean sections for daughters in this study (see Table 5.3).

Daughters gained less weight overall than their mothers (mean weight gain daughters = 12.9 kg; mothers = 13.5 kg), and their babies were born on average one day earlier than their mothers. Daughters and mothers had ±100 g difference between mean and maximum foetal birth weights (daughters' mean foetal birth weight = 3,273 g, mothers' = 3,176 g). Mothers gave birth to over double the number of females than males (females n = 229, 68% and males n = 107, 32%) whereas daughters had a more similar gender distribution among their firstborn offspring (females n = 153, 45% and males n = 184, 55%). This approximately equates to the national statistic of 51.5% of male babies born to Jewish women in 2016. The apparent skew in the data on gender of the baby for the mothers' cohort may be at least partly explained by the fact that only women who had at least one daughter were recruited to the study (since their recruitment was dependent on that of their parous daughter).

Overall, more daughters (n = 171, 51%) laboured for over 10 hours than mothers (n = 123, 36%). Of the total dataset, 21 mother-daughter pairs had vaginal deliveries with spontaneous labour onset and no augmentation or pharmacological pain relief. For this subgroup, there was an almost equal percentage of mothers and daughters who laboured for less than 10 hours. This may be at least partly explained by the fact that, at both time points, labours of less than 10 hours were deemed 'normal', so there was less clinical pressure to intervene.

Daughters' length of labour was calculated for babies born at ≤38 weeks and >38 weeks, and for babies born ≤3,500g and >3,500g by taking a mean length of labour of each of the categories. Daughters' length of labour did not differ for babies born ≤38 weeks and ≥38 weeks. However, daughters' length of labour was shorter for babies born ≤3,500g compared to babies born ≥3,500g, (mean 11.15 hrs, SD 5.32; and mean 12.16 hrs, SD 5.58 respectively).

Table 5.4 presents the levels of association between mothers' and daughters' health and maternity variables analysed using parametric and non-parametric tests.

Table 5.4: Comparative Analysis of Mother-Daughter Reproductive Outcomes (Excluding Elective Caesarean Section)

Total mother-daughter pairs n = 323.

Variable	Mother-daughter pairs (n)	Mother	Daughter	Statistical test	Test statistic	*p*-value
Age at 1st period, median (IQR)	295	13 (2)	13 (2)	Wilcoxon	-0.761	0.447
Natural conception (Y), n(%)	323	314 (97.2)	278 (86.1)	McNemar's	24.5	**<0.001**
Abortions/missed (Y), n(%)	321	33(10.3)	51(15.9)	McNemar's	4.516	**0.033**
Induction (Y), n(%)	319	26(8.2)	69(21.6)	McNemar's	22.909	**<0.001**
Analgesia (Y), n(%)	302	127(42.1)	267(88.4)	McNemar's	125.461	**<0.001**
Gender (Male), n(%)	322	101(31.4)	176(54.7)	McNemar's	33.188	**<0.001**
Apgar (Normal), n(%)	282	277(98.2)	267(94.7)	McNemar's	n/a	**0.041**[a]
Foetal birth weight, mean (*SD*)	318	3172.9 (524.2)	3272.6 (438.0)	Paired T-test	-3.259	**<0.001**
Gestational age, median (IQR)	316	40 (2)	40 (2)	Wilcoxon	-2.473	**0.013**
Weight gain, median (IQR)	280	12 (7)	13 (6)	Wilcoxon	-0.416	0.678
Mode of delivery, n(%)	322			Marginal homogeneity	-2.798	**0.005**
Normal		257(79.8)	229(71.1)			
Vacuum/forceps		43(13.4)	55(17.1)			
CS emergency		22(6.8)	38(11.8)			
Signs of labour, n(%)	318			Marginal homogeneity	-3.316	**<0.001**
Contractions		182(57.2)	161(50.0)			
Amnion rupture		79(24.9)	78(24.2)			
Bleeding		29(9.1)	10(3.1)			
Induction		26(8.2)	68(21.1)			
CS emergency		2(0.6)	5(1.6)			

$p < 0.05$ significance
Bold values indicate statistical significance was reached.
[a] Exact *p*-value calculated with binomial distribution used.

To compare mothers' and daughters' reproductive outcomes, differences in continuous data were analysed using paired t-tests or Wilcoxon signed rank tests as appropriate. An analysis of change in the proportion of each binary outcome was undertaken using McNemar's test. For categorical variables with more than two responses, the marginal homogeneity test was applied, which is a generalisation of McNemar's test. In Table 5.4, test statistics presented are

chi square for McNemar's test, t-statistics for the paired t-test, Z-score for Wilcoxon's signed-rank test and standardised MH statistic for the marginal homogeneity test. For continuous statistically significant results, effect sizes were calculated. Cohen's d effect size for foetal birth weight was d = 0.183, which is between small and medium using Cohen's (1988, 1992) classification; for gestational age, Rosenthal's effect size (Rosenthal, 1991) was small with r = -0.139.

The table includes McNemar's test for gender for differences between mothers and daughters. However, it should be noted that the sample for gender has a selection bias because mothers who had at least one daughter were recruited to the study (since their recruitment was dependent on that of their parous daughter). Mothers who only had male offspring were not eligible.

Analysis of conception methods and abortions showed daughters had 10% less natural conceptions and more than one and a half times the rate of abortions than their mothers prior to their first deliveries.

Comparative analyses of mother-daughter reproductive outcomes for the following seven intrapartum covariates showed differences in mother-daughter associations: induction (p <0.001), use of pain relief in labour binary variable (p <0.001), gestational age (p = 0.013), foetal birth weight (p = 0.001), gender (p <0.001), Apgar (p = 0.041) and mode of delivery (p = 0.005). In the analysis of mother-daughter age at first period, height and weight gain in pregnancy, no associations were found.

5.13.1 Primary Outcome Analysis: Similarity in Length of Labour for Mother and Daughter

Logistic regression analysis of mother-daughter length of labour (≤10hrs/>10hrs) showed that if the mother had had a long labour (>10 hrs), the corresponding odds that the daughter would also have a long labour were almost two-fold [OR 1.91 (95% CI 1.19, 3.05, p = 0.007), unadjusted]. Also, exploratory subgroup analysis was performed for mothers and daughters paired for same gender offspring. Subgroup analysis was performed in 147 cases out of 323 mother-daughter pairs. The odds ratio was increased to above three when mothers and daughters were paired for same baby gender [OR 3.23 (95% CI 1.55, 6.74), p = 0.002]. There is no previous exploratory analysis on whether mother-daughter length of labour is linked to same baby gender in first births, therefore this analysis may be seen as a hypothesis generating approach. However, the subgroup analysis has less statistical power to identify subgroup effects and further studies should be conducted to confirm or refute this finding.

Table 5.5 presents an analysis of the relationships between daughters' length of labour and all potential mother-daughter birth related factors. The reference category is defined within Table 5.5.

Table 5.5: Univariate Logistic Regression
(Dependent Variable Length of Labour Binary Daughter, ≤10hrs, >10hrs)

Independent variable	*p*	OR	95% CI	
Length of labour Binary M (ref.: short labour)	**0.007**	1.91	1.193	3.05
Age 1st Period D	0.709	0.97	0.83	1.14
Age 1st Period M	**0.015**	0.82	0.70	0.96
Education D (ref.: academic)	0.214			
Primary and High school	0.410	0.47	0.08	2.86
Full high school	0.463	0.78	0.39	1.53
Higher education	**0.047**	0.56	0.32	0.99
Education M (ref.: academic)	0.292			
Primary and High school	0.919	1.05	0.41	2.70
Full high school	0.161	0.67	0.39	1.17
Higher education	0.106	0.60	0.32	1.12
Height D	0.203	0.10	0.00	3.53
Height M	0.258	0.13	0.00	4.44
Marital Status D (ref.: married)	0.282			
Single	0.105	3.96	0.84	18.64
Divorced	0.646	1.76	0.16	19.62
Other	0.802	0.88	0.32	2.41
***Marital Status M** (ref.: married)	0.079			
Divorced	0.541	0.79	0.38	1.66
Other	0.748	1.19	0.41	3.45
Weight Gain D	**<0.001**	1.11	1.05	1.16
Weight Gain M	0.593	1.01	0.97	1.05
Age D	**<0.001**	1.09	1.04	1.14
Age at 1st birth M	0.240	1.04	0.98	1.10
Induction D (bin)(ref: no)	0.386	1.27	0.74	2.19
Onset of labour D (ref.: contractions)	0.631			
Fluid rupture	0.862	1.05	0.60	1.83
Bleeding	0.435	0.60	0.16	2.19
Induction	0.344	1.32	0.74	2.36
Onset of labour M (ref.: contractions)	0.885			
Fluid rupture	0.860	0.95	0.56	1.63
Bleeding	0.462	0.74	0.33	1.66
Induction/Elec CS	0.670	0.85	0.39	1.82
Anaesthesia D (ref.: epidural)	**<0.001**			
Spinal	0.403	0.46	0.08	2.82
None	**<0.001**	0.22	0.10	0.47
Anaesthesia D (bin)(ref.: yes)	**<0.001**	0.22	0.10	0.48
Anaesthesia M (ref.: None)	0.912			
Epidural	0.954	0.98	0.52	1.86
Pethidine	0.605	1.17	0.65	2.11
Nitrous oxide	0.411	2.60	0.27	25.54
Spinal	0.499	0.43	0.04	4.88
General	0.775	1.30	0.21	7.99
Augment D (bin) (ref.: none)	**0.040**	2.18	1.04	4.59
Augment M (bin) (ref.: none)	0.526	0.76	0.32	1.80
Foetus body weight kg D	0.137	1.00	1.00	1.00

Foetus body weight kg M	0.079	1.00	1.00	1.00
Gestational Age D	0.053	1.18	1.00	1.40
Gestational Age M	0.086	1.12	0.98	1.27
Gender D (ref.: male)	0.762	1.07	0.68	1.68
Gender M (ref.: male)	0.144	1.44	0.88	2.35
Mode of delivery D (ref.: normal)	0.060			
Vacuum/forceps	0.131	1.59	0.87	2.91
CS Emergency	**0.046**	2.53	1.02	6.28
Mode of delivery M (ref**.** normal)	0.250			
Vacuum/forceps	0.697	0.88	0.46	1.69
CS Emergency	0.116	2.20	0.82	5.84
Length of labour Binary M with M-D gender filter	**0.002**	3.23	1.55	6.74

D = daughter, M = mother
(bin) = binary variable
$p < 0.05$ sig
Bold values indicate statistical significance was reached.
*Marital status M; there were no 'single' data.

5.13.2 Other Potential Underlying Influences on Daughters' Length of Labour

In the analysis of other factors such as marital status, height, age at first period (daughter), and daughters' onset of labour and induction, no association was seen. The univariate logistic regression analysis (see Table 5.5) shows that the daughters' rising age and weight gain appear to independently increase the likelihood of longer labour durations [OR 1.09 (95% CI 1.04, 1.14), p <0.001] and [OR 1.11 (95% CI 1.05, 1.16), p <0.001] respectively. The daughters' gestational age was not significantly associated with length of labour [OR 1.18 (95% CI 1.00, 1.40), p = 0.053]. Shorter labour in daughters was highly significantly associated with non-pharmacological pain relief in labour [OR 0.22 (95% CI 0.10, 0.47), p <0.001], reference category epidural use (p <0.001), as was anaesthesia (binary, reference category 'yes'), i.e. shorter labour for those women not using anaesthesia [OR 0.22 (95% CI 0.10, 0.48), p <0.001]. Daughters' use of augmentation [OR 2.18 (95% CI 1.04, 4.599), p <0.040] showed statistical significance for longer labours (the reasons for this are discussed in section 5.18). Similarly, daughters' mode of delivery by emergency

caesarean section showed statistical significance for longer labours [OR 2.53 (95% CI 1.02, 6.28), *p* <0.046], presumably because the more time nulliparous women spend in labour (and women with epidural anaesthetic have longer labours) the more likely they are to receive Oxytocin augmention, which in turn increases rates of caesarean section (see references in Section 5.18). Finally, mothers' age at first period [OR 0.82 (95% CI 0.70, 0.96), *p* <0.015] and daughters' higher education [OR 0.56 (95% CI 0.32, 0.99), *p* <0.047] were statistically significant; however, with poor clinical relevance.

5.14 Physiological Births

5.14.1 Mother-Daughter Physiological Births Sub-set

Similarities in mother-daughter birth characteristics in physiological labour and birth pairs were assessed for comparison with paired mother-daughter labour and birth characteristics in the full dataset. A physiological birth is defined as a normal vaginal delivery with spontaneous labour onset, with no induction or augmentation of labour or pharmacological pain relief. In the full dataset there were 31 daughters and 154 mothers who had had normal physiological labours and births. However, only 21 mother-daughter pairs were matched for physiological births.

Table 5.6 provides the demographic characteristics and clinical outcomes of the matched mother-daughter physiological birth pairs.

Table 5.6: Characteristics of the Physiological Birth Population (n = 21) and Outcomes

Variable		Daughters		*Mothers' 1st birth*	
		n	***%***	***n***	***%***
Country of birth	Israel	19	*90.5*	10	*47.6*
	Other	2	*9.5*	10	*47.6*
Education	≤ Trade/tech school	3	*14.3*	9	*42.8*
	Academic	18	*85.7*	10	*47.6*
Marital status	Married	21	*100*	15	*71.4*
				5	*23.8*
Signs of labour	Contractions	17	*81*	11	*52.4*
	Amnion rupture	4	*19*	6	*28.6*
	Bleeding	0	*100*	4	*19*
Induction	None	0	*100*	0	*100*
Augmentation	None	0	*100*	0	*100*
Analgesia	None	0	*100*	0	*100*
Mode of delivery	Normal	21	*100*	21	*100*
Gender	Male	11	*52*	7	*33.3*
	Female	10	*48*	14	*66.7*

The fact that numbers do not always add up to n = 21 (100%) is due to missing data.

	Daughters			**Mothers' 1st birth**		
Variable	Mean (SD)	Min	Max	Mean (SD)	Min	Max
Age at Q	30.29 (3.48)	22	38	58.43 (6.77)	43	70
Age 1st birth	30.29 (3.48)	22	38	24.19 (3.36)	20	33
Weight gain kg	12.71 (4.86)	6	23	12.95 (4.71)	8	25
Gestational age	39.9 (1.18)	38	42	39.7 (1.56)	36	42
Foetal birth weight g	3244 (360)	2730	4025	3121 (351)	2300	3650

Comparison between the two datasets, the full dataset (n = 337, depicted in Table 5.7) and the physiological dataset (n = 21, depicted in Table 5.8), showed some similarities and differences between outcomes. In both datasets, the daughters were on average six years older than their mothers at the time of first birth (physiological dataset: daughters' mean age 30 yrs, *SD* 3.48, and mothers' mean age 24 yrs, *SD* 3.36; full dataset daughters' mean age 30 yrs, *SD* 5.46,

and mothers' mean age 24 *SD* 3.70). The daughters gained less weight overall than their mothers in both datasets, however, mother-daughter weight gain was very similar in the physiological dataset (mean weight gain daughters = 12.7 kg; mothers = 12.9 kg).

In the full dataset, the daughters' babies were born on average one week earlier than their mothers'. However, in the physiological dataset, the mother-daughter gestational age was very similar (daughters' mean gestational age = 39.9 weeks; mothers' mean gestational age = 39.7 weeks). The most common sign of labour onset overall was contractions (physiological dataset: daughters' 81% and mothers' 52%; full dataset daughters' 49% and mothers' 56%). In addition, mothers and daughters had ±100g difference in mean foetal birth weights in both datasets (physiological dataset: daughters' mean foetal birth weight = 3,244g and mothers' mean foetal birth weight = 3,121g; full dataset: daughters' mean foetal birth weight = 3,273g and mothers' mean foetal birth weight 3,176g). However, although the mother-daughter maximum birth weights were similar in the full dataset (daughters' maximum birth weight = 4,665g, and mothers' maximum birth weight = 4,700g), in the physiological dataset the daughters' maximum foetal birth weight (4,025g) and the mothers' maximum foetal birth weight (3,650g) were dissimilar. This may be due to the small sample size in the physiological sample or because daughters having physiological births may have resisted intervention. Gender distribution among first born offspring in both datasets revealed that mothers gave birth to over double the number of females than males (physiological dataset mothers' female offspring n = 14, 66.7% and male offspring n = 7, 33.3%; full dataset mothers' female offspring n = 229, 68% and male offspring n = 107, 31.2%), whereas the daughters had a similar gender distribution among their firstborn offspring (physiological dataset: daughters' female offspring n = 10, 48% and male offspring n = 11, 52%; full dataset daughters' female offspring n = 153,

45% and male offspring n = 184, 56%). This phenomenon is explained in section 5.13.

For comparison of length of labour data in three classifications between the full dataset (n = 337 pairs) and the physiological dataset (n = 21 pairs), length of labour for matched mother-daughter pairs in the full and physiological datasets were entered into tables (Tables 5.7 and 5.8). The time intervals were chosen to create etiologically relevant length of labour time periods.

Table 5.7: Matched Mother-Daughter Full Dataset Pairs (n = 337) for Length of Labour in Three Groups

Group	Variable	Daughter Median		n	%	Mother 1st Birth Median		n	%
1	Length of labour in 4 time intervals	4	1. 0-2 hours	4	*1.2*	3	1. 0-2 hours	36	*10.7*
			2. 2-6 hours	42	*12.5*		2. 2-6 hours	107	*31.8*
			3. 6-10 hours	100	*29.7*		3. 6-10 hours	63	*18.7*
			4. >10 hours	169	*50.1*		4. >10 hours	123	*36.5*
			Missing	22	*6.5*		Missing	8	*2.4*
2	Length of labour in 3 time intervals	1	1. 0-12 hours	191	*56.7*	1	1. 0-12 hours	253	*75.1*
			2. 12-18 hours	88	*26.1*		2. 12-18 hours	42	*12.4*
			3. 18+ hours	36	*10.7*		3. 18+ hours	34	*10.1*
			Missing	22	*6.5*		Missing	8	*2.4*
3	Length of labour in binary time intervals	1	1. 0-10 hours	144	*42.7*	1	1. 0-10 hours	206	*61.1*
			2. >10 hours	171	*50.7*		2. >10 hours	123	*36.5*
			Missing	22	*6.5*		Missing	8	*2.4*

Table 5.8: Matched Mother-Daughter Physiological Birth Pairs (n = 21) for Length of Labour in Three Groups

Group	Variable	Daughter Median		n	%	Mother 1st Birth Median		n	%
1	Length of labour in 4 time intervals	4	1. 0-2 hours	2	*9.5*	3	1. 0-2 hours	4	*19*
			2. 2-6 hours	7	*33.3*		2. 2-6 hours	10	*47.6*
			3. 6-10 hours	8	*38.1*		3. 6-10 hours	4	*19*
			4. >10 hours	4	*19.1*		4. >10 hours	3	*14.4*
2	Length of labour in 3 time intervals	1	1. 0-12 hours	18	*85.7*	1	1. 0-12 hours	18	*85.7*
			2. 12-18 hours	2	*9.5*		2. 12-18 hours	2	*9.5*
			3. 18+ hours	1	*4.8*		3. 18+ hours	1	*4.8*
3	Length of labour in binary time intervals	1	1. 0-10 hours	17	*81*	1	1. 0-10 hours	18	*85.7*
			2. >10 hours	4	*19*		2. >10 hours	3	*14.3*

Comparing the two mother-daughter datasets (the full dataset n = 337 and the physiological dataset n = 21) for length of labour, a number of similarities and differences were found.

Overall, more daughters (n = 171, 51%) laboured for over 10 hours than their mothers (n = 123, 36%). However, in the physiological dataset there was an almost equal percentage of mothers and daughters who laboured for less than 10 hours (mothers' n = 18, 86%; daughters' n = 17, 81%). This may be partly explained by the fact that for both generations of women, labours of less than 10 hours were deemed 'normal', so therefore there was less clinical pressure to intervene.

5.15 Analysis of Variance (ANOVA) for Daughters' Continuous Length of Labour

Three assumptions were satisfied to apply one-way analysis of variance (ANOVA). These were normality of distribution, homogeneity of variance and no influential observations (see section 5.17.1). ANOVA was used to evaluate the effect of mothers' length of labour categorical independent variable at three defined time intervals (0-12 hrs, 12-18 hrs, 18+ hrs) on daughters' continuous length of labour outcome variable. The F-ratio (F = 4.08, *p* = .018) indicates that daughters' length of labour (outcome variable) is explained by differences in mothers' length of labour (independent categorical variable).

Table 5.9 depicts the results for ANOVA analysis for mother-daughter length of labour in mothers' three time intervals (0-12 hrs, 12-18 hrs, 18+ hrs) and daughters' continuous length of labour data.

Table 5.9: ANOVA Results of the Mother-Daughter Length of Labour Data

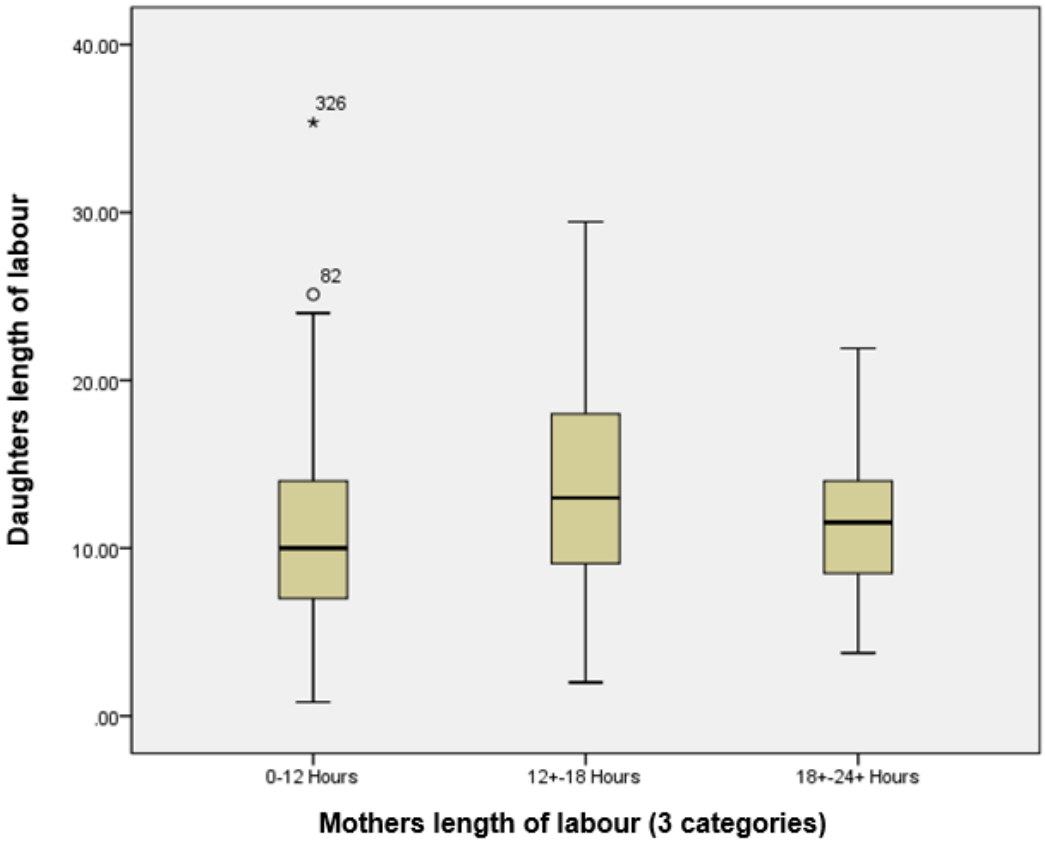
	Sum of squares	df	Mean square	F	Sig.
Between groups	235.054	2	117.527	4.088	.018
Within groups	8711.644	303	28.751		
Total	8946.698	305			

Figure 5.3. depicts box plots showing the distribution of daughters' length of labour highlighting the medians, quartiles and ranges. Mean (SD) of daughters' length of labour categorised according to mothers' long length of labour intervals (0-12 hrs, 12-18 hrs, 18+ hrs) shows that for the first two time intervals, daughters' mean (SD) falls within the same range as the mothers' mean (category 0-12 hrs daughters' mean *SD* = 10.96 *(5.41)*; and category 12-18 hrs daughters' mean *SD* = 13.53 *(5.96)* respectively). For the last and longest time

interval (18+ hrs) daughters' length of labour mean *SD* is outside of the mothers' length of labour range, and is shorter than the mothers' length of labour in this category; mean *(SD)* = 12.00 *(4.25).* One explanation for this may be the lack of universal consensus on the definition of what constitutes delay in labour progress, and lack of criteria for cut-offs for adequate time for longer labours for nulliparous women in this generation. Thus, the frequency of augmentation and caesarean delivery is high for labours longer than 12 hours in this cohort of women, as is the use of epidural analgesia which in itself may prolong labour (Zhang *et al*., 2001) and may result in potentially unnecessary interventions.

Comparison of the three groups' length of labour demonstrates a statistically significant difference in daughters' length of labour between the three groups defined by categorical mothers' length of labour. *Post hoc* testing using Bonferroni correction shows that there is a statistically significant difference in daughters' length of labour between the first (mothers' short labour 0 - 12 hrs) and second (mothers' long labour 12 - 18 hrs) group (p = 0.017, mean difference = 2.53 hrs) but not between the other two groups.

Figure 5.3: Distribution of Daughters' Length of Labour by Mothers' Length of Labour Groups



5.16 Main Results

5.16.1 Results for Logistic Regression Model

Variables that were found to be statistically significant at the 0.1 level in the univariate analysis were explored in a multivariable logistic regression model. A final predictive model for daughters' length of labour included mothers' length of labour (≤10 hours or >10 hours), daughters' age, daughters' weight gain in pregnancy and daughters' use of anaesthesia. The adjusted odds ratio for daughters having a long labour if their mothers also had a long labour was OR = 1.88, 95% CI 1.12, 3.17, p = 0.017. Daughters age and weight gain increased the odds for long length of labour in daughters, while non-use of anaesthesia and spinal anaesthesia decreased the chances of having a long labour

compared to epidural, though spinal anaesthesia was not statistically significant. Women who do not have any analgesia during labour have considerably lower chances of long labour compared to those women who had epidural anaesthesia [OR 0.27 (95% CI 0.12, 0.60), *p* <0.001]. Results for multiple logistic regression are presented in Table 5.10.

Table 5.10: Multivariable Logistic Regression for Daughters' Length of Labour

	B	***p***	**OR**	**95% CI**
(Constant)	-3.27	<0.001		
M length of labour (ref. ≤10hrs)	0.63	0.017	1.88	1.12, 3.17
Age (D)	0.08	0.005	1.08	1.02, 1.14
Analgesia (D) (ref. Epidural)		0.003		
Analgesia (D) (Spinal)	-1.35	0.162	0.26	0.04, 1.72
Analgesia (D) (None)	-1.32	0.001	0. 27	0.12, 0.60
Weight gain (D) (kg)	0.10	<0.001	1.10	1.04, 1.16

The model showed a very good fit with the Hosmer-Lemeshow test: *p* = 0.943, which yielded a predictive value of 66%.

To further provide model fit, a small classification table was created. Two length of labour variables were used to evaluate the model by sensitivity and specificity. Model prediction showed correct classification of long length of labour in 66% of cases (accuracy) with reasonable sensitivity (74%) and specificity (56%). The percentage of daughters who are predicted by the model to have a long labour and will experience long labour is 66% (positive predictive value), and 64% of daughters who are identified by the model as not having a high risk of long labour will have a labour length within 10 hours (negative predictive value).

Sensitivity: A/(A+C) x 100

116/(116+40) = 116/156 = 0.70.743 = 74%

Specificity D/(D+B) x 100

74/(74+59) = 74/133 = 0.556 = 56%

The calculation matrix below shows test indicators and outcome calculations for sensitivity and specificity.

	Longer Length of labour 10+ hrs	**Shorter Length of labour 0-10 hrs**	**%**
Long Length of labour	A True +ve 116	B False +ve 59	55.6 (specificity)
Short Length of labour	C False –ve 40	D True –ve 74	74.3 (sensitivity)

Positive and negative predictive values were calculated according to the following formula:

Positive Predictive Value: A/(A+B) × 100

116/(116+59) = 66%

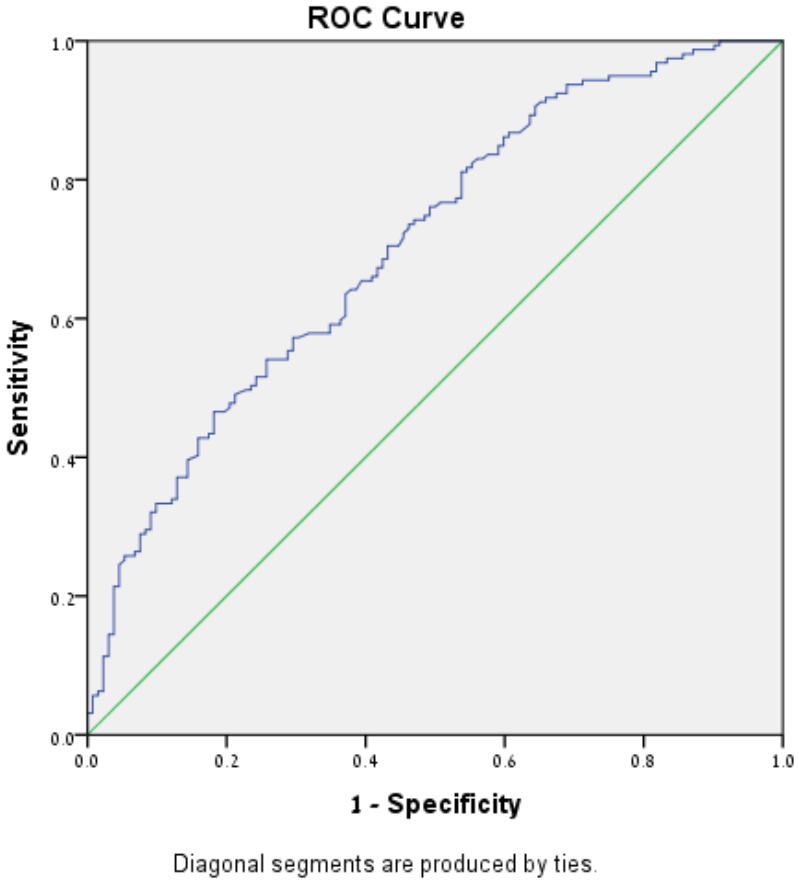
Negative Predictive Value: D/(D+C) × 100

74/(74+40) = 64%

The predictive model was further analysed using a Receiver Operating Characteristic curve (see Figure 5.4). The curve plots the sensitivity against one minus the specificity (false-positive). The area under the curve illustrates the likelihood that the proposed model will determine that mothers' length of labour together with other factors in the model has a high probability of predicting daughters' length of labour. A model with no discrimination will have an area = 0.5, which would produce a straight line. For the mother-daughter logistic regression prediction model, the area under the curve was 0.72 (95% CI 0.60,

0.77), p <0.001) which, according to Hosmer and Lemeshow (2000), falls into the category of being a fair and acceptable level of discrimination.

Figure 5.4: Receiver Operating Characteristic Curve - Graphical Representation of the Prediction Capacity of the Model



5.16.2 Assumptions Check for Logistic Regression

To justify the use of logistic regression modelling, analysis of the cleaned dataset was conducted to observe if the assumptions of logistic regression were met and satisfied. All assumptions were satisfied. The following section provides the details of the assumption check for logistic regression.

5.16.2.1 Linearity of the Logit

One assumption of logistic regression is that the continuous predictors of the model are linear with the logit of the dependent variable. Table 5.11 estimates logits for daughters' age in three-year category age groups.

Table 5.11: Daughters' Length of Labour Logit (Binary) vs. Daughters' Age in Three-year Categories

Age	n	Over 10 hrs, a	a/n, %	Proportion p=a/n	p/(1-p)	ln(p/(1-p))
18-20	16	6	37.50	0.3750	0.60	-0.51
21-23	42	16	38.10	0.3810	0.62	-0.49
24-26	30	12	40.00	0.4000	0.67	-0.41
27-29	57	34	59.65	0.5965	1.48	0.39
30-32	92	54	58.70	0.5870	1.42	0.35
33-35	42	23	54.76	0.5476	1.21	0.19
36-38	20	12	60.00	0.6000	1.50	0.41
39+	13	13	100.00	1.0000	#DIV/0!	#DIV/0!

The figure below shows the logit transformation of daughters' length of labour (binary) and the continuous age (x) variable divided into three-year categories.

Figure 5.5: Daughters' Length of Labour Logit (Binary) vs. Daughters' Age in Three-year Categories

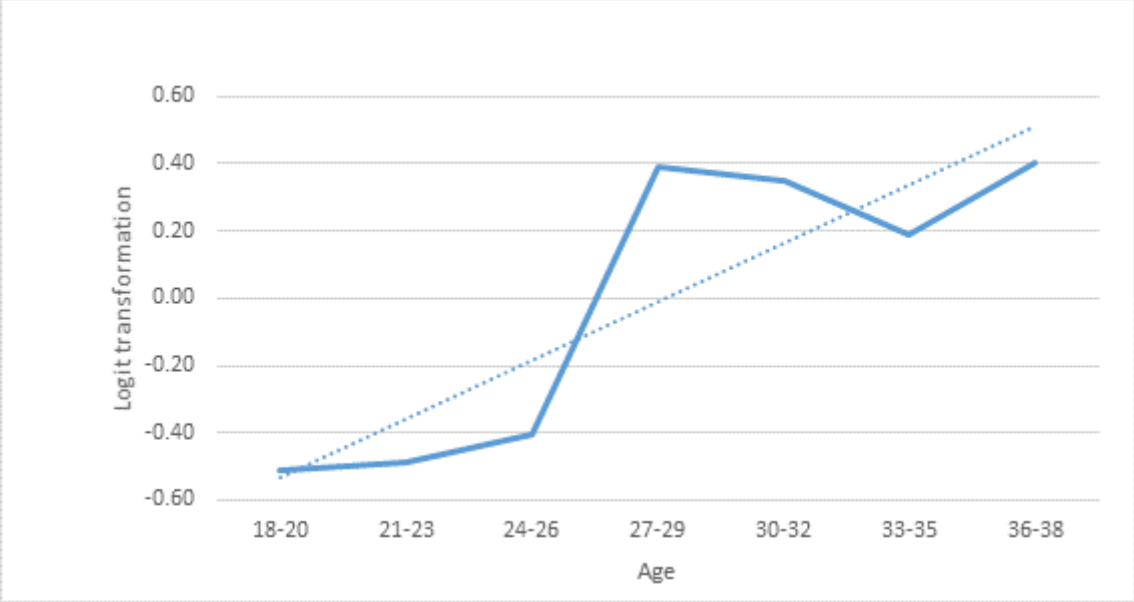


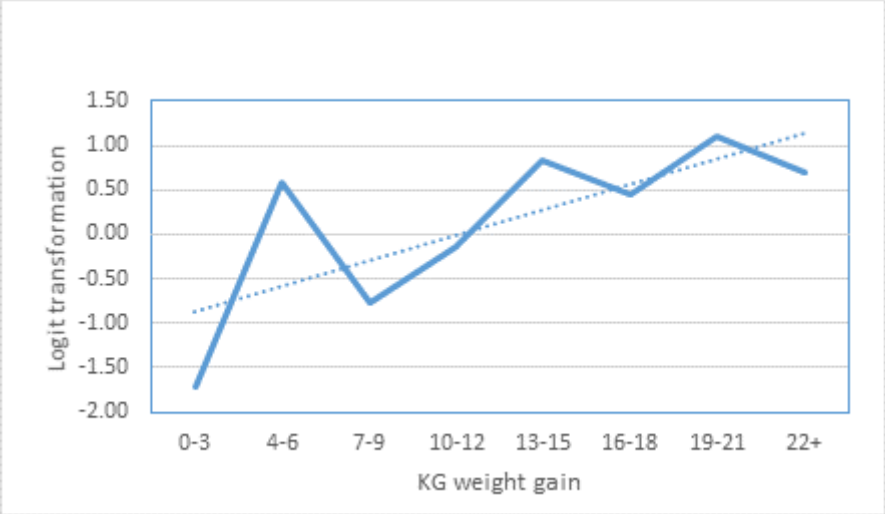
Table 5.12 estimates logits for daughters' weight gain in 3 kg category groups.

Table 5.12: Daughters' Length of Labour Logit (Binary) vs. Weight Gain in Pregnancy in 3 Kg Categories

Kg	n	Over 10 hrs, a	a/n, %	Proportion p=a/n	p/(1-p)	ln(p/(1-p))
0-3	13	2	15.38	0.1538	0.18	-1.70
4-6	14	9	64.29	0.6429	1.80	0.59
7-9	41	13	31.71	0.3171	0.46	-0.77
10-12	84	39	46.43	0.4643	0.87	-0.14
13-15	76	53	69.74	0.6974	2.30	0.83
16-18	31	19	61.29	0.6129	1.58	0.46
19-21	24	18	75.00	0.7500	3.00	1.10
22+	21	14	66.67	0.6667	2.00	0.69

Figure 5.6 shows the logit transformation of daughters' length of labour (binary) and the continuous weight gain kg (x) variable divided into 3 kg categories.

Figure 5.6: Daughters' Length of Labour Logit (Binary) vs. Weight Gain in Pregnancy in 3 Kg Categories



Both graphs (Figures 5.5 & 5.6) show an approximately linear increasing trend. In an effort to avoid the violation of this assumption, Hosmer and Lemeshow (2000) recommend using the Box-Tidwell approach to check for the linearity of the logit (Tabachnick & Fidell, 2013). Using this method, a logistic regression model was created regressing the dependent variable on each of the continuous predictors (daughters' age and weight gain) and their interaction terms, which consists of the continuous predictors and its natural log. To apply the Box-Tidwell test, two new variables were created: the log of daughters' age and the log of daughters' weight gain. Two new interactions were then introduced into the model: daughters' age*log age, and daughters' weight gain*log weight gain. If at least one interaction is significant, then the assumption is violated. The results of the Box-Tidwell test for linearity of the logit showed that the assumptions of linearity were met, age*log age $p = 0.683$ and weight gain*log weight gain $p = 0.655$.

Finally, the continuous variables (daughters' age and weight gain) were converted into categorical variables (for age the five categories were 0-5, 6-10,

11-15, 16-20, 21-25+ years; and for weight gain the five categories were 0-20, 21-25, 26-30, 31-35, 36-40+ kg) and introduced into the model in place of the continuous variables. The Hosmer-Lemeshow test was used to determine if the poor predictions (lack of fit) are significant, which would indicate that there are problems with the model. However, although a slightly poorer Hosmer-Lemeshow fit was achieved (p = 0.956 instead of p = 0.989), the test result indicated a good fit.

5.16.2.2 Absence of Multicollinearity

A limitation of logistic regression is that it is sensitive to variables that have very high correlations with each other. Variables that are highly collinear often produce very large standard errors and inflated regression estimates (Tabachnick & Fidell, 2013). Therefore, the collinearity between the independent variables in the model has to be observed. A standard procedure that allows for this is the calculation of tolerance for each variable. The tolerance statistic is the calculation of the variance of each of the independent variables in the model not explained by all of the other independent variables in the model. A higher tolerance value suggests low levels of collinearity. Menard (2010) suggests that a tolerance of less than 0.2 is alarming. Although logistic regression software does not typically offer a tolerance function, Menard (2010) suggests that the model be run as a linear regression to observe the relationship among independent variables. The variables from the logistic regression (see Appendix 5, Table A5.1) were run as a linear regression to achieve tolerance and variance inflation factor results.

The variance inflation factor (VIF) measures the impact of collinearity among the variables in a regression model.

$VIF = 1/(1-R^2)$

There is no formal variance inflation factor number for determining presence of multicollinearity. However, values of variance inflation factor that exceed 10 are often regarded as indicating multicollinearity, which may destabilise the model. The results are shown in Appendix 5, Table A5.1. No multicollinearity was observed.

5.16.2.3 No Influential Observations

An influential observation is an observation for a statistical calculation whose deletion from the dataset would noticeably change the result of the calculation. In particular, in regression analysis, an influential point is one whose deletion has a large effect on the parameter estimates. Leverage is a measure of how far away the independent variable values of an observation are from those of the other observations.

Figure A5.2 (see Appendix 5) shows a field created from the linear regression diagnostics. Unlike other plots, the patterns are not relevant. Sorted in descending order (i.e., the highest number is 0.6 [<1]), the observation has low leverage and therefore will not have that much influence. The figure shows residuals vs. leverage.

5.16.2.4 Independence of Errors

Logistic regression requires each observation (the error terms - the residuals) to be independent. This is so that the data-points should not be from any dependent samples design (e.g., before-after measurements or matched pairings). The Durbin-Watson statistic is a number that tests for autocorrelation

in the residuals from a statistical regression analysis. The statistic is always between 0 and 4. A value in the range of 1.5 to 2.5 means that there is no autocorrelation in the sample. Figure 5.7 represents a rectangle with all the points being between +3 and -3 on the residual (y axis), and -3 and +3 on the predicted value on the x axis, showing that there is no worrisome level of correlation between the residuals.

Figure 5.7: Durbin-Watson Scatter-plot Showing Predicted Value and Residuals in the Regression Analysis

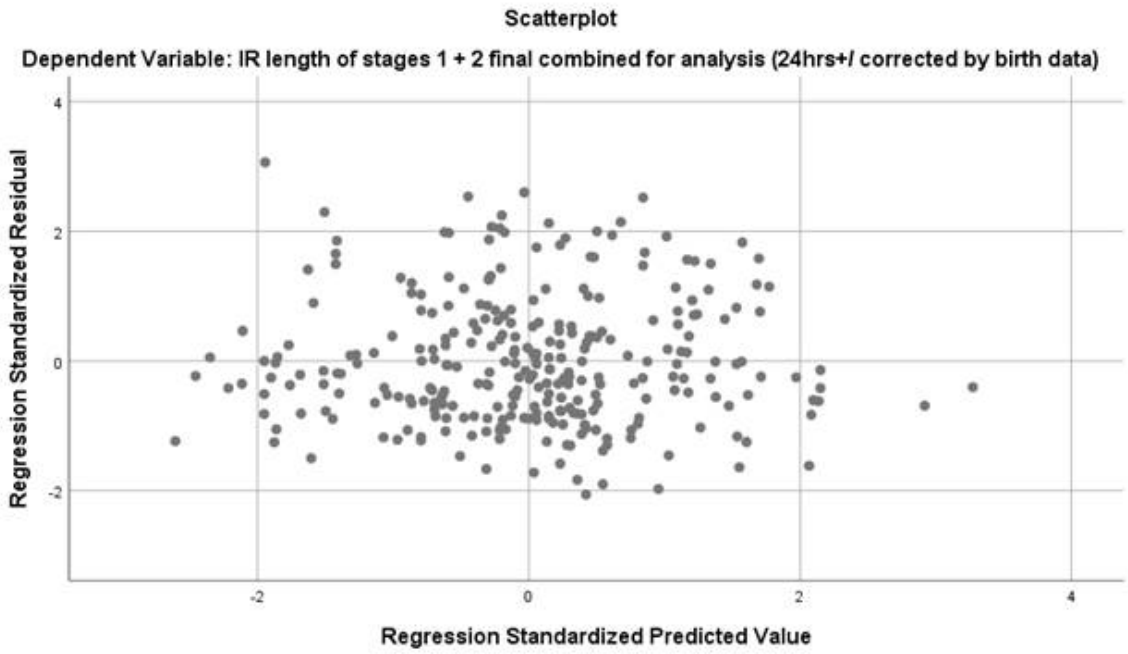


Table 5.13 shows the model summary for the Durbin-Watson test, which gives a statistic value of 1.8.

Table 5.13: Durbin-Watson Test for Independence (Lack of Correlation) of Errors

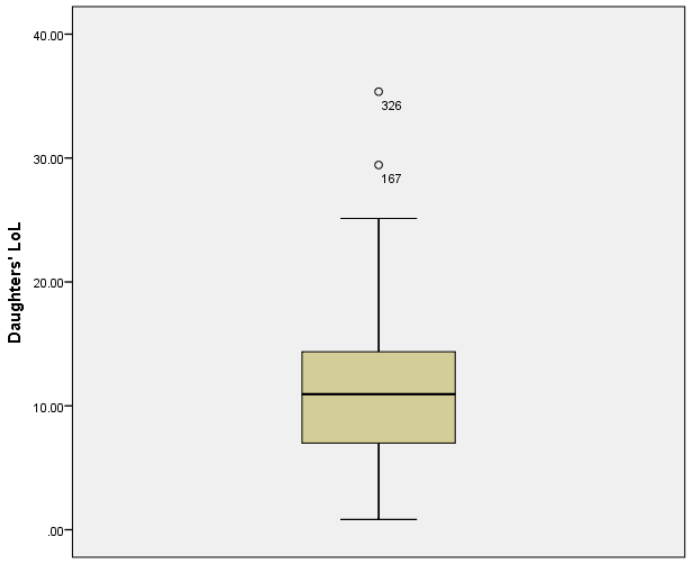
R	R^2	Adjusted R^2	Standard error of the estimate	Durbin-Watson
.334[a]	.112	.096	4.88956	1.864

5.16.2.5 Influential Outliers and Cook's Distance

Cook's distance is used in regression analysis to find influential outliers in a set of predictor values. Data-points with large residuals (outliers) and/or high leverage may distort the outcome and accuracy of a regression. The measurement is a combination of each observation's leverage and residual values. Cook's distance measures the effect of deleting a given observation. Points with a large Cook's distance are considered to merit closer examination in the analysis. An observation with Cook's distance larger than three times the mean Cook's distance might be an outlier.

Figure 5.8 presents a box plot of the data showing outliers. This shows the data in the middle as well as at the ends of the distributions. Cases outside of Cook's distance were not found.

Figure 5.8: Boxplot of the Data Showing Outliers



5.17 Main Results for Linear Regression Model

Linear regression methods follow the same principles and are subject to the same sorts of considerations as multivariable logistic regression. As linear regression assumes all independent variables are continuous or binary, dummy binary variables were created to represent each of the three mothers' length of labour categories.

Linear regression analysis was applied to test the relationship between daughters' length of labour (continuous) and other variables (continuous or categorical).

Variable selection was performed so that only significant independent variables were included. Selection in a step-wise procedure only included variables that improved the model. For daughters' continuously measured length of labour as the dependent variable, linear regression modelling was applied using three categories of mothers' length of labour, by creating a dummy variable for each category for the following time intervals: 0-12 hours, 12-18 hours and 18+ hours (two dummy variables were used in the regression with the 0-12 hour category used as a reference as the largest group), and daughters' age, weight gain in pregnancy and use of anaesthesia (binary) as factors in the model (see Table 5.14). As in the logistic regression, it is important that the assumptions on which the methods depend are also tested. Assumptions were checked and satisfied. They are presented in section 5.17.1

The variables presented in Table 5.14 showed an association with daughters' length of labour. F-test of overall model significance indicates that the relationship is statistically significant ($F(5,285) = 6.75$, $p < 0.001$). The linear regression model with mothers' length of labour and daughters' age, weight

gain in pregnancy, and use of anaesthesia showed that approximately 11% of the variance in the model was explained by these factors ($R^2 = 0.106$).

Table 5.14: Multivariable Linear Regression for Daughters' Continuous Length of Labour with Mothers' Long Length of Labour Categories

	B	p	95% CI
(Constant)	2.42	0.235	
Length of Labour M (12-18 hrs)	2.57	0.004	0.82, 4.33
Length of Labour M (18+ hrs)	0.51	0.602	-1.40, 2.41
Age (D)	0.14	0.021	0.02, 0.27
Weight gain (D) (kg)	0.14	0.019	0.02, 0.26
Analgesia yes/no (D)	3.03	0.001	1.21, 4.86

Table 5.14 describes the relationship between each independent variable and daughters' length of labour. Except for the variable Length of Labour M (18+ hrs), confidence intervals are positive, indicating positive associations between daughters' length of labour and the corresponding variable, and *p*-values (at 5% level) for Length of Labour M, Age (D), Weight gain (D) and Analgesia yes/no (D) show statistically significant relationships.

The same linear regression model was applied using alternative (shorter) time categories for mothers' length of labour taken from the mothers' questionnaire: 0-6 hours, 6-10 hours and 10+ hours. A dummy variable for each category was created (two dummy variables were used in the regression) and used with the daughters' continuously measured length of labour, with 0-6 hours (the first category) as a reference as it was the largest group. F-test of overall significance for this model indicates that the relationship is statistically significant ($F(5,285) = 5.496$, $p < 0.001$). The linear regression model with daughters' age, weight gain in pregnancy and use of anaesthesia showed that

approximately 9% of the variance in the model was explained by these factors ($R^2 = 0.088$).

Table 5.15: Multivariable Linear Regression for Daughters' Continuous Length of Labour with Mothers' Short Length of Labour Categories

	B	*p*	95% CI
(Constant)	2.63	0.202	
Length of Labour M (6-10 hrs)	-0.25	0.773	-1.10, 1.47
Length of Labour M (10+ hrs)	0.93	0.174	-0.42, 2.28
Age (D)	0.14	0.022	0.02, 0.27
Weight gain (D) (kg)	0.15	0.017	0.03, 0.27
Analgesia yes/no (D)	2.81	0.003	0.95, 4.67

Table 5.15 describes the relationship between each independent variable and daughters' length of labour. Age (D), Weight gain (D) and Analgesia yes/no (D) show statistically significant relationships (at 5% level). Mothers' length of labour was not statistically significant in this model; however, the regression coefficients (B) indicate the direction of the relationship with daughters' length of labour, consistent with the previous model: negative (B = -0.25) for the second category of mothers' labour between 6-10 hours, and positive (B = 0.93) for the third category corresponding to mothers' labour over 10 hours.

In both of the regression models (long and short categories) the R^2 values are low ($R^2 = 0.106$ and $R^2 = 0.088$ respectively). This suggests that predictions may be imprecise or unreliable, since 89 - 91% of variation may be explained by the impact of other external factors such as birth environment, social aspects, birth policies and clinical aspects of labour, case mix factors between hospitals, doctor-woman's choice, and other factors relating to peripartum vulnerability.

5.17.1 Results for Assumptions Check for Linear Regression

Five assumptions were tested for the linear regression model:

5.17.1.1 Test for Linear Relationships Between Outcome Variable and the Continuous Independent Variables

The initial judgement of a possible relationship was first made on the basis of scatter plots to show whether relationships were linear. Each of the independent variables reflects the effect on the dependent variable (daughters' continuous length of labour) with the adjusted regression coefficient for daughters' length of labour representing the amount of the effect.

A linear relationship between outcome variable (daughters' length of labour) and independent continuous variables (daughters' age at delivery in years, and daughters' weight gain in pregnancy in kg) is shown in the figures below (Figures 5.9 and 5.10), although the linear trend is rather weak.

Figure 5.9: Scatterplot for Two Variables:
Daughters' Length of Labour and Daughters' Age at Delivery

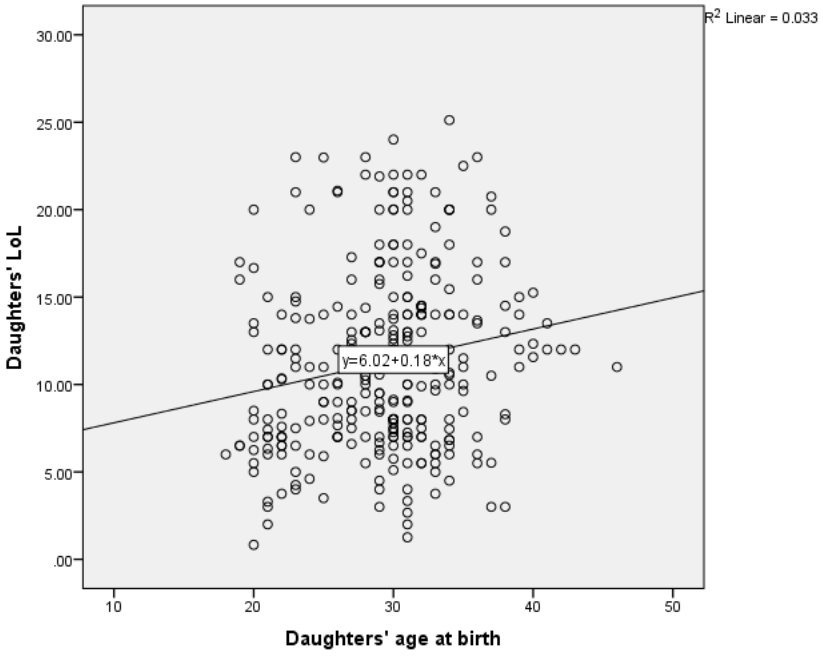
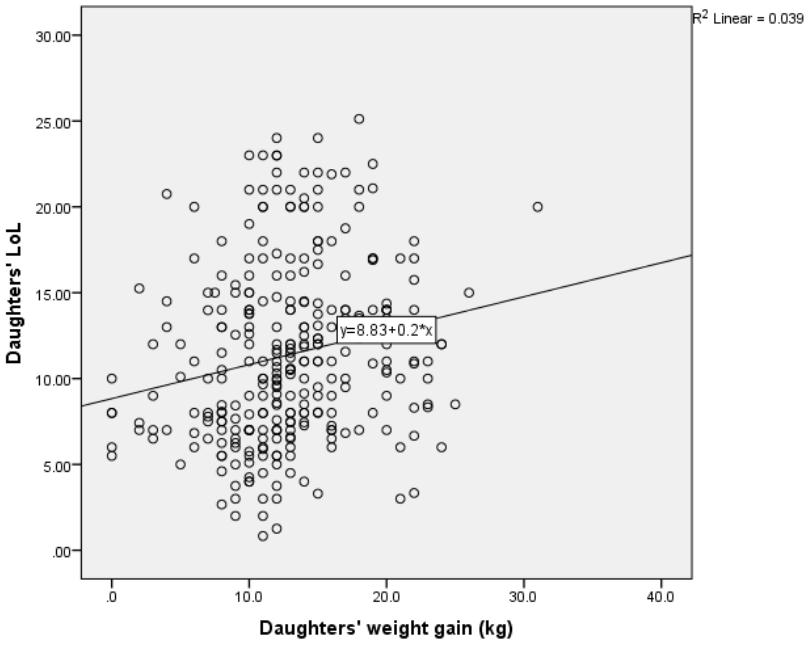


Figure 5.10: Scatterplot for Two Variables:
Daughters' Length of Labour and Daughters' Weight Gain in Pregnancy



5.17.1.2 Tests for Residual Normality

The scatter plot (see Appendix 5, Figure A5.2) shows that the residuals are not distributed in any pattern with the predicted values. The model assumptions are met and homoscedaseity was not violated.

5.17.1.3 Test for Normal Distribution of Residuals

Appendix 5 (Figure A5.3) shows a histogram with residuals on the vertical axis and daughters' length of labour on the horizontal axis. The residuals appear to be normally distributed.

In addition, a P-P plot (also known as normal Q-Q plot) (see Appendix 5, Figure A5.4) shows that the residuals are normally distributed. The example in this figure shows all of the points basically on the reference line, thus the data appear to be normally distributed.

5.17.1.4 Tests for Absence of Multicollinearity

As in logistic regression analysis, the collinearity between the independent variables in the linear regression model had to be observed. The smaller the tolerance of a variable, the more redundant is its contribution to the regression (i.e., it is redundant with the contribution of other independent variables). If the tolerance of any of the variables in the regression equation is equal to zero (or very close to zero), the regression equation cannot be evaluated.

The variance inflation factor measures the impact of collinearity among the variables in a regression model. Although there is no formal variance inflation factor number for determining presence of multicollinearity, a value of 10 is recommended as the minimum level of tolerance (Tabachnick & Fidell, 2013). Values of the variance inflation factor that exceed 10 are often regarded as indicating multicollinearity, which may destabilise the model. Table A5.2 (see Appendix 5) shows that the levels of tolerance and variance inflation factor are within limits which will not affect adversely the results associated with the multiple regression analysis.

5.17.1.5 Test for Influential Observations in Linear Regression

When the chosen model is fitted to the data, the presence of an outlier is not necessarily influential with respect to the fitted model. One way to test the influence of an outlier is to compute the regression equation with and without the outlier. Outliers (values that are outside of the areas of a distribution that would commonly occur) may be influential in linear regression analysis. Two outliers in the dataset (case nos. 167 & 326) were identified as having longer labours (29 hrs and 35 hrs respectively). After checking data information at source no error was detected, and they are assumed to be due to variability in

measurement of length of labour. The two outlier points were first excluded from the analysis and then re-introduced into the analysis and were not found to be influential (Table 5.16).

Table 5.16: Outliers Presented in a Table from SPSS Analysis

Case number	Standard residual	Daughters' Length of Labour, combined stages 1+2	Predicted value	Residual
167	3.39	29.44	11.88	17.56
326	4.42	35.36	12.44	22.91

Figure 5.8 (see section 5.16.2.5) presented a boxplot showing the five-point summary of the data on daughters' length of labour. In addition, cases outside of Cook's distance (i.e., influential to the regression results) were not found. Cook's D is a good measure of the influence of an observation on the regression model. Not all outliers are influential in linear regression analysis. The combination of an observation's leverage and distance determines its influence. Appendix 5 (Table A5.3) shows descriptive statistics from the dataset for Cook's distance. The maximum value of Cook's distance in the sample is .08 (which is less than the value of 1), which thus shows there are no problematic cases in this sample.

5.18 Discussion

This chapter examined mother-daughter similarities in labour and birth characteristics in nulliparous women. To the best of my knowledge, mothers' length of labour has not previously been explored as a predictive determinant of daughters' length of labour. Overall, several interaction effects on the length of labour of nulliparous women were found, one of which was her mother's length of labour. In addition, an important contribution of this study is the assessment of several labour and birth characteristics simultaneously on length of labour.

Age, weight gain in pregnancy and use of anaesthesia are known to have influences on length of labour, and the findings of this study are consistent with earlier studies (Greenberg *et al.*, 2007; Mousa *et al.*, 2012; Yazdani *et al.,* 2012). Other researchers have also confirmed that an older (Sheiner *et al.*, 2002; Timofeev *et al*., 2013) and heavier population (Kominiarek *et al.*, 2011; Kawakita *et al.*, 2016), and different clinical practices such as epidural use (Frigo *et al*., 2011) and directed pushing in the 2nd stage (Anim-Somuah *et al*., 2011) may influence labour length.

Predictors that were expected to influence daughters' length of labour, but did not demonstrate any statistical significance, were induction of labour, foetal birth weight and gestational age. This may be due to other confounders. Medical induction of labour is often more painful than spontaneous labour and produces a greater analgesic requirement than does spontaneous labour (Capogna, 2001). Analgesia may have had an overriding effect as an influential predictor over induction as an independent variable. Although it is known that high infant birth weight significantly influences prolonged first and second stages of labour among primiparas (Högberg & Lekâs Berg, 2000), current policies for induction of labour for suspected foetal macrosomia (Boulvain *et al*., 2016) and elective caesarean section for a predicted infant birth weight of >4000g may have reduced the number of potentially high infant birth weight research outcomes in the daughters' cohort. Finally, longer gestational age as an outcome predictor may have been reduced by current policies of routine induction of labour for pregnancies considered 'post-term' in the daughters' cohort.

The SiLC study showed that if the mother had had a longer labour (>10 hrs), the corresponding odds of a longer labour was almost two-fold for the daughter [OR 1.91 (95% CI 1.19, 3.05), p = 0.007]. Significance was increased to an odds

ratio above three when mothers and daughters were paired for same gender offspring [OR 3.23 (95% CI 1.55, 6.74), p = 0.002]. Modelling analysis showed that mothers' length of labour, daughters' age, daughters' weight gain in pregnancy, and daughters' use of epidural anaesthesia significantly influenced daughters' length of labour.

The length of labour for the whole daughter cohort did not differ from that of the mothers' cohort for babies born at either ≤38 weeks or >38 weeks. However, daughters' length of labour was shorter for babies born ≤3,500g compared to babies born >3500g (mean 11.15 hrs, *SD* 5.32; and mean 12.16 hrs, *SD* 5.58 respectively).

Women who used epidural analgesia in labour increased their likelihood of a longer labour by over four-fold. Daughters' increased age, weight gain, foetal birth weight and gestational age were independently associated with an increased likelihood of longer labour durations.

In the full dataset, more daughters laboured for over 10 hours than their mothers. This is similar to findings by Laughon *et al*. (2012a), who analysed nearly 140,000 births in an intergenerational study and found that nulliparous women took 2.6 hours longer to give birth during the years 2000-2008 than women did 50 years earlier. However, in the physiological dataset, there was an almost equal percentage of mothers and daughters who laboured for less than 10 hours. Although the physiological birth sample is small (n = 21), these findings may be a strong indication that, without intervention, mothers and daughters (up to six years older than their mothers at the time of their first births), are likely to give birth within a similar timeframe.

Similar to findings in the Laughon *et al.* (2012a) study, daughters' babies born in the full dataset and infants born in Laughon's contemporary group (years 2002-2008) were born on average one week earlier than the older generation. This may be due to current policies of routine induction of labour at term (discussed in this section). However, whereas Laughon *et al.* (2012a) found that babies in the contemporary group tended to weigh more at birth than babies born a generation earlier, in this study mother-daughter foetal birth weights were similar. This may be explained by the fact that the daughters gained less weight overall than their mothers, whereas women in Laughon *et al.'s* (2012a) contemporary group tended to weigh more than those who delivered a generation earlier. In a review of the literature, studies have shown a positive correlation between maternal weight gain and gestational weight gain (Monte *et al*., 2011).

Finally, similar to the Laughon *et al.* (2012a) study findings, women in the contemporary cohort and the daughters in this study were six years older than the women from the earlier generation at the time of their delivery. Delayed motherhood seems to have become a trend all around the world, with social and cultural factors responsible for the increasing age of pregnant women (Mills *et al*., 2011).

Among the changes in delivery practices, both this study and the Laughon *et al.* (2012a) study showed increased use of inductions, augmentations and epidural anesthesia for the daughters' cohort compared with the earlier generation.

In the daughters' cohort there were 10% less normal deliveries compared with the mothers' cohort. Vacuum/forceps extractions, elective and emergency caesarean sections were notably more common in the daughters' cohort by a 4%, 2% and 5% increase respectively compared with the mothers' cohort.

There are large variations in rates of obstetric interventions between and within countries (Macfarlane *et al*., 2016), with some factors relating to characteristics of the maternity care systems where women choose to birth (Sandall *et al.*, 2016) and some factors relating to women's choices.

In both the full dataset and the physiological dataset, the daughters were more educated than their mothers. Although there is considerable research on childbirth education impacting women's choices in labour and childbirth, research on women's levels of education as an influence on their decision-making for childbirth is sparsely researched. One study (Regan *et al*., 2013) investigated factors influencing women's decisions on mode of delivery, including caesarean section. In a sample (n = 49) of well-educated (73% had a university degree) low-risk nulliparous women with a mean age of 28.7 years, almost half of the participants claimed that they had decided on what type of birth they wanted before they were pregnant, and over 65% wanted a natural birth. This may indicate that educated women around 29 years of age are likely to formulate opinions and make choices for their own births. However, these highly educated women assumed the use of interventions would reduce the risks of childbirth, indicating that higher levels of education may increase women's acceptance of common interventions even though the evidence shows that the more educated women are, the more they want normal births. In the SiLC study, 64% of the daughters' cohort had a university education, with a mean age of 29.5 years and an increased number of clinical interventions than in the mothers' cohort. This increase in interventions may be related to local hospital practices or women's choices. However, it is unlikely that a higher education level is the main influential factor on women's choices. Other variables are more likely to have influenced rising intervention rates in the daughters' cohort. These have been discussed earlier in this section.

Women in the daughters' generation are exposed to updated knowledge, technology and modern obstetric practices resulting in some women being deadlocked in complex and interventional birth processes (*The Lancet*, 2014). In addition, midwives and clinicians changing shifts in hospital labour wards may interrupt the continuity of care for labouring women (Hildingsson *et al*., 2015). These factors and other influences may have reduced the consistency of management decisions, encouraged multi-individual judgments and choices (including choices made by these birthing women) and led to yet more interventions. Furthermore, clinical knowledge is constantly being refreshed and renewed, making it almost impossible to keep abreast of new developments in the field and to convert those developments into an output of recommendations to represent best practice. All these factors combined make it difficult to determine whether decisions for interventions in the daughters' cohort were based on population thresholds or truly dysfunctional labours.

Decisions for labouring women are often based on routine procedures which are in turn based on population norms (Spong *et al*., 2012; ACOG, 2014). Maternity carers need to give the necessary support, care and advice to women planning normal labours and births (NICE, 2011; RCM, 2011). Where appropriate, a mother's birth history may be directly related to her nulliparous daughter's birth progress. Use of clinical skills for decision-making based on familial birth patterns may be particularly relevant, in determining appropriate countermeasures to contemporary women's unnecessary interventions. Finally, there is a multitude of external barriers (e.g., institutional timeframes, space, time, and staff and financial resources) which will need to be overcome in order to implement personalised care plans for first time birthing mothers.

Labour augmentation occurred in 12% of the daughter cohort (as compared to 7% for the mothers'), with those receiving augmentation having higher odds of a

longer labour [OR 2.18 (95% CI 1.04, 4.59), p = 0.040]. Assuming the indication for augmentation is a prolonged labour, it is logical that those subject to augmentation would have a longer labour overall than those who labour spontaneously. Consistent with prior studies, this study demonstrates that in women treated with oxytocin for labour augmentation it may take many hours to lead to cervical change compared to women who labour spontaneously (Harper *et al*., 2012). Rising augmentation rates indicate lack of consensus in classification of labour dystocia, possibly explaining the increased use of augmentation within the younger generation of women.

Compared with their mothers, the daughters in this study received more interventions, which may reflect a temporal change in obstetric practices across the generations (see section 5.15). Other studies from high resource countries have also identified similar trends (Zhang *et al*., 2010b; Laughon *et al*., 2012b; Betrán *et al*., 2016). The greater mean maternal age in the daughters' cohort may partially account for the increase in labour and delivery intervention rates (Herstad *et al*., 2016) since rates for caesarean sections are known to increase with advancing age in women (Janoudi *et al*., 2015); however, this is likely to only be a partial explanation. A number of studies have demonstrated a wide variation in intervention rates between maternity hospitals and, after controlling for case mix, found that a substantial amount of the variation is likely to be due to local philosophies and norms of practice (Wennberg, 2011; Glantz, 2012; Ham, 2013; Corallo *et al*., 2014).

It is of note that between the mother and daughter generations (1967-1998 and 2015 respectively), changes in the socioeconomic situation, lifestyle norms and medical practices have resulted in the earlier discovery of pregnancy, better access to health services, more engagement with maternity care, and an increased tendency towards abstinence from harmful habits such as alcohol

consumption and smoking. These changes have also resulted in the higher use of IVF and intrapartum interventions.

It appears that physiological length of labour is highly variable, and that population norms, based on widely accepted benchmarks, may not be relevant for clinical decision-making related to particular women in labour. Slow progress of labour, particularly in nulliparous women, is not always pathological and may not require medical intervention. Decisions relating to medical interventions for obstetric issues outside the population norm should ideally include maternal, paternal, inter- and intragenerational and extended familial birth histories (as discussed in Chapter Two).

The statistical models for the SiLC study show sensitivity when applied to long labours. A mother's 'long labour' in her first birth (>10 hours) may predict a slow-but-normal long labour in her nulliparous daughter. Since nulliparity is a known 'risk factor' for long labours, the daughters' success rate of non-instrumental vaginal deliveries in this cohort study was lower than their mothers.

The proposed models may one day be used as an additional tool for understanding the barriers to and for facilitating methods for normal birth practices. The findings of the SiLC study suggest that such data may be useful to inform the development of alternative length of labour predictor models for nulliparous women in labour, but more in-depth studies are needed.

5.19 Strengths and Limitations

The recruitment strategy approaching nulliparous daughters in antenatal clinics was successful, with most women agreeing to participate because they felt the subject was relevant, personal and valuable for future research. Moreover,

mothers who subsequently agreed to participate often recounted their birth stories spontaneously and openly while filling out the birth questionnaire.

The study had a high response rate and retained a high number of participants during the course of the study. Missing or unclear information was accrued by contacting participants by email or telephone. The self-administered questionnaire used to collect the mothers' data was written in easy-to-understand language. The tool made the study feasible and low cost (Bowling, 2005). I ensured that I was available on both sites and contactable by telephone and/or email to answer any queries concerning questions contained in the questionnaire. Statistical analysis was thorough and enabled the building of predictive models for nulliparous women's length of labour. Other influences on daughters' labour length were also identified.

Findings should be considered in light of potential limitations. First, in the mothers' cohort, the primary outcome of interest is based on self-report. Although previous research comparing recall to birth record documentation has been validated within Israeli populations (Seidman *et al*., 1987; Gofin *et al*., 2000, and also the empirical maternal recall study on a sub-set of 101 women from this study described in Chapter Four), accurate continuous data on mothers' length of labour (questionnaire responses were categorised) were lacking. Second, birth/medical records (used for daughters' birth information) are intended for patient care and the data are not systematically recorded for research purposes. This may imply that some birth files included abridged case notes, missing clinical implications. Third, the length of labour data included women who were induced, augmented, had an epidural, were delivered by vacuum/forceps, and/or by emergency caesarean section prior to achieving complete dilation. Interventions may have accelerated physiological labour length (or decelerated labour length as in the case of epidural use), and data

about frequency, duration, intensity, dosage or timing of the medical interventions were not available.

Although the mothers gave birth to over double the number of females than males in their first deliveries compared to their daughters who had a similar gender distribution among their first born offspring, this was taken into consideration by controlled statistical analysis. Finally, while comparative research may provide unique insights into mother-daughter length of labour, the findings need to be tested for practical application using prospective clinical studies.

5.20 Conclusions

One of the primary objectives of this study was to investigate associations in mother-daughter labour and first birth characteristics. Particular emphasis was placed on variables associated with a mother's length of labour as a prediction of her daughter's length of labour.

Despite daughters having more interventions than their mothers, findings indicate that mothers' first birth length of labour may have a predictive value in daughters' first births. In addition, after controlling for variables which may be expected to influence length of labour, stable predictive models for daughters' length of labour were produced. This was particularly true when matched for gender of offspring. Thus, the data may indicate that for daughters having a first delivery with familial characteristics outside the population norm, the mother's first birth history may be particularly relevant for predicting her daughter's length of labour.

5.21 Summary

The data presented in this paper show a strong positive association between mothers' and daughters' length of labour in first births. The association persisted after adjusting for the increased number of interventions in the daughters' cohort. Practitioners could inquire about familial labour patterns as an additional heuristic to guide practice, alongside formal evidence and the signs and symptoms exhibited by the individual woman. Future research could test the efficacy of maternal labour length for decision-making around intervention for labour that is slower than normal, using controlled study designs.

Chapter Six: Discussion, Interpretation and Conclusions

6.1 Introduction

This thesis aimed to explore mother-daughter similarities in first labour and birth characteristics. Intergenerational mother-daughter paired labour length was of particular interest. A systematic review of familial studies in Chapter Two found positive inter- and intragenerational influences on the following pregnancy and birth outcomes: gestational age, preterm birth, prolonged pregnancy, dystocia, caesarean section, infant birth weight, and foetal growth restriction including small for gestational age and intra-uterine growth restriction. No studies were found comparing mother-daughter length of labour.

An empirical study on maternal recall of birth and delivery events (Chapter Four) found that the mothers' recall of first birth events with hospital birth records was remarkably in agreement for the following perinatal factors: labour onset, induction, epidural, birth weight, gestational age and mode of delivery. The reliability of maternal recall for obstetric history accrual supports the empirical rationale for the use of maternal recall even many years after delivery. Results from the SiLC (Similarities in Labour and Childbirth) empirical study (Chapter Five) showed a strong positive association between mothers' and daughters' length of labour in first deliveries. This association persisted after adjusting for the increased number of interventions in the daughters' cohort. Similarities in other mother-daughter birth characteristics included signs of labour onset, infant birth weight, gestational age and normal delivery.

This chapter discusses, interprets and concludes this thesis with an emphasis on the following points:

- The current state of the evidence on inter- and intragenerational influences on pregnancy and birth outcomes.
- Maternal recall of first labour events and the local Israeli population.
- Mother's first birth history as a predictive model for her nulliparous daughter's labour progression.
- Physiological prolonged labour progression and factors enabling or constraining clinical decisions for normal birth.

Each point reflects on material within previous chapters and outlines insights in the light of contemporaneous literature. Finally, individualised maternity care practices evaluating normal birth, and achieving normal birth using a predictive birth model are presented and discussed. Implications and recommendations, future research questions and areas for further research are suggested at the end of the chapter.

6.2 Inter- and Intragenerational Influences on Pregnancy and Birth Outcomes - the Current State of the Evidence

The systematic review of inter- and intragenerational influences on pregnancy and birth outcomes in Chapter Two of this thesis identified a number of birth outcomes transmitted from parents to children, successive recurrence of birth outcomes in the same mother, and birth outcome recurrence between siblings. Despite significant advances in genetic and epigenetic research on pregnancy and birth outcomes, it is still not fully understood which etiological factors contribute to specific birth outcomes (such as birth weight or small for gestational age). This may be due, at least in part, to the fact that most studies focus on risk factors in pregnancy. Yet, findings in the systematic review showed factors linked with birth outcomes are likely rooted in familial processes

and influences. By linking birth outcomes across parents and their children, and within families, this inter- and intragenerational approach revealed striking and persistent similarities in birth outcomes amongst families, such as gestational age and birth weight within mother-daughter pairs, preterm birth with parental influences, a mother-daughter association with dystocia and caesarean section, and prolonged pregnancy with parental and older sister effects, to name a few. It was found that foetal and maternal genetic processes explain a portion (less than half) of the intergenerational similarity (Magnus *et al*., 1993; Lunde *et al.*, 2006). No systematic review in this area has previously been undertaken. Moreover, the present review implemented a comprehensive screening approach for articles on familial characteristics of birth outcomes to include intragenerational influences (sister-brother). Research on within-family associations expanded the knowledge base.

As genetic factors are often unobserved in population-level survey data, the predictive effect of familial associations on birth outcomes may remain unexplained. This systematic review was the first line of enquiry into the intra- and intergenerational birth outcome phenomenon. The second line of enquiry was applied in Chapter Five, where associations of mother-daughter birth outcomes were evaluated.

This systematic review adds to intra- and intergenerational literature on familial birth outcomes by collating important empirical evidence and providing reliable findings. A longer-term (down the generational line) and broader (across and within families) updated investigation of familial birth factors from credible trusted sources would benefit maternity research. The future of women's maternity care lies in improving perinatal care through personalised information. Each woman's unique familial profile may be reflected in her family history.

Future research may wish to focus on familial histories of pregnancy and birth for individualised, personalised maternity care of nulliparous women.

6.3 Maternal Recall of First Labour Events and the Local Israeli Population

Maternity carers often rely on maternal report of perinatal events. A methodical review of 29 articles on maternal recall of birth events (Chapter Three) found varying levels of agreement based on periods of up to one year, 1-10 yrs and ≥10 yrs.

Chapter Four described an empirical study on maternal recall of first birth events by 101 participants, up to 49 years following delivery. This study was the first to investigate maternal recall of eight labour and birth outcomes in one mother-daughter cohort, namely onset of labour, use of pain relief medication, length of labour, delivery outcome, gestational age, infant birth weight, gender and Apgar score. Moreover, to the best of my knowledge, this is the first study to investigate agreement of maternal recall with birth records for induction of labour and labour onset.

As greater attention is paid to familial recurrence of birth events and the development of personalised medicine in obstetrics, accurate historical birth information has become crucial, as seen in longer labours in the daughters' generation compared with their mothers' (empirical study results from SiLC study Chapter Five, and Laughon *et al*., 2012a). Although current cross-sectional data may be useful for identifying population norms, low sensitivity and specificity for individuals limit the precision of decisions made in the clinical management of nulliparous women's labour and delivery.

In summary, predictions for nulliparous daughters' labour length and delivery outcome based on mothers' recalled first birth history and birth outcome characteristics may improve care and management for nulliparous daughters. Identifying pre-specified subgroups of women whose positive perinatal outcomes have a high chance of being predicted based on familial norms may result in a decrease in routine interventions, including caesarean delivery. Sub-groups of such women may include those who would otherwise have been diagnosed with pathologically large babies, prolonged pregnancies or prolonged labour. Less interventions in labour for nulliparous women are likely to reduce the rate of primary caesarean deliveries, which may in turn reduce potential maternal and neonatal complications and the likelihood of a subsequent caesarean section. Longitudinal and intergenerational birth data based on mothers' recall of birth events may ultimately provide a potential diagnostic resource for researchers. Further maternal recall studies are needed to evaluate the validity of mothers' birth history as a predictive model for daughters' normal physiological birth.

Married, well-educated Israeli women showed good agreement between mothers' reports and birth records for most perinatal events. An issue that needs to be addressed is whether to use the mother's recall or birth records in other regions of the world for taking a maternal history. One could use the recorded figures when available, or alternatively use them just when any discrepancy arises. However, in some countries data are weak and there is no way of confirming that recalled or recorded information is correct. This should be taken into account when designing birth studies and may be a topic for future maternal recall research.

6.4 Mother's First Birth History as a Predictive Model for Nulliparous Daughter's Labour Progression

This thesis provides evidence of generational changes in labour management and mode of delivery over the last 50 years. Not only has childbirth become a highly medicalised process, but, in spite of new research showing variability in labour progress for nulliparous women (Oladapo *et al*., 2018), no movement or research has yet succeeded in quantifying the adequacy of labour progress. This finding makes clinical decision-making for slowly progressing women in labour difficult.

Although the daughters' cohort were on average six years older than their mothers at time of first birth, it is unlikely that advanced maternal age is the main contributing factor to the high rates of induction, augmentation, epidural usage, instrumental delivery and caesarean section seen in the daughters' cohort. It is more probable that use of technology in the hospital environment and iatrogenic over-diagnosis of risk have influenced healthcare providers to use interventions that accelerate labour and birth.

Despite the fact that the majority of women entering labour are healthy (WHO, 1996a), rates for normal birth are decreasing. In addition, although physiological labour and birth is associated with lower rates of auto-immune disease for the baby (Dahlen *et al*., 2013; Olza-Fernandez *et al*., 2014; Marin *et al*., 2015), the benefits of vaginal delivery are not widely known.

Results from the SiLC study in this thesis (Chapter Five) show that predictive length of labour regression models for nulliparous daughters may provide important information to inform future studies that seek to develop a new baseline for assessing normal physiological labour progress among first time birthing mothers. The models showed that mothers' first labour length may be a

reliable estimator for daughters' expected length of labour. When matched for the same infant gender in the mother-daughter pairs, the association increased threefold. Although the magnitude of association shown by the odds ratio may lead to unrealistic estimates of non-intervention benefits for daughters with the same infant gender as their mothers having a long labour, it may be used in terms of how much more likely it will be prognostic of outcome. These findings may be a new step forward in facilitating normal births for healthy women and have a potential influence on clinical decisions made for women when delay in progression is suspected.

6.5 Physiological Prolonged Labour Progression and Factors Enabling or Constraining Clinical Decisions for Normal Birth

The new WHO (2018) recommendations for slow-yet-normal cervical dilation are aimed to minimise unnecessary medical interventions. For many women delivering in the hospital setting, however, a labour without intervention may be thwarted by a doctor's or midwife's advice for intervention, such as induction of labour at 41 weeks' post-term. Particularly, nulliparous women, as opposed to women who have given birth before, may not realise that normal labour options are available. Lacking in confidence or knowledge, they may believe that the doctor, midwife or the system is always inherently right.

Persistent rising trends and large variations in caesarean section rates indicate that the current prevalence for intervention have little to do with evidence-based medicine. Three challenging factors are associated with decisions made during labour management: 1) measuring length of labour, 2) population norms and labour progress, and 3) factors enabling or constraining normal birth in the hospital environment.

6.5.1 Measuring Length of Labour and Changes in Rates of Birth Interventions Over Time

In these times of high technology use and standard hospital routines, recommendations regarding measuring length of labour and timing of delivery are founded on balancing maternal and perinatal risks. Yet, healthy low risk nulliparous women who are inherently capable of normal labour progress, but when progressing slowly in labour, are sometimes left with little choice but to comply with a health professional's decision to accelerate labour. For the clinician working in a medical setting, spontaneous but slow progress in labour is not a reason for labour induction or augmentation.

Cervical dilation rates among low-risk nulliparous women (with and without spontaneous labour onset) have been questioned and critiqued since Friedman's research in 1978 (Friedman, 1978). The standard Friedman partogram showed 4 cm as the cervical dilation for transition from the latent to the active phase of labour and a continued progress rate of one centimetre an hour. More recently, in 2013, Boyle *et al*. published a study conducted over a span of six years (2002-2008) in the US on 38,484 women who had delivered their first child by caesarean section. One third (35%) of the women in the overall sample had a caesarean section due to a diagnosis of "failure to progress", or slow progress of labour. More than 40% of the nulliparous women who had a caesarean section for failure to progress had not reached 5 cm dilation of the cervical os.

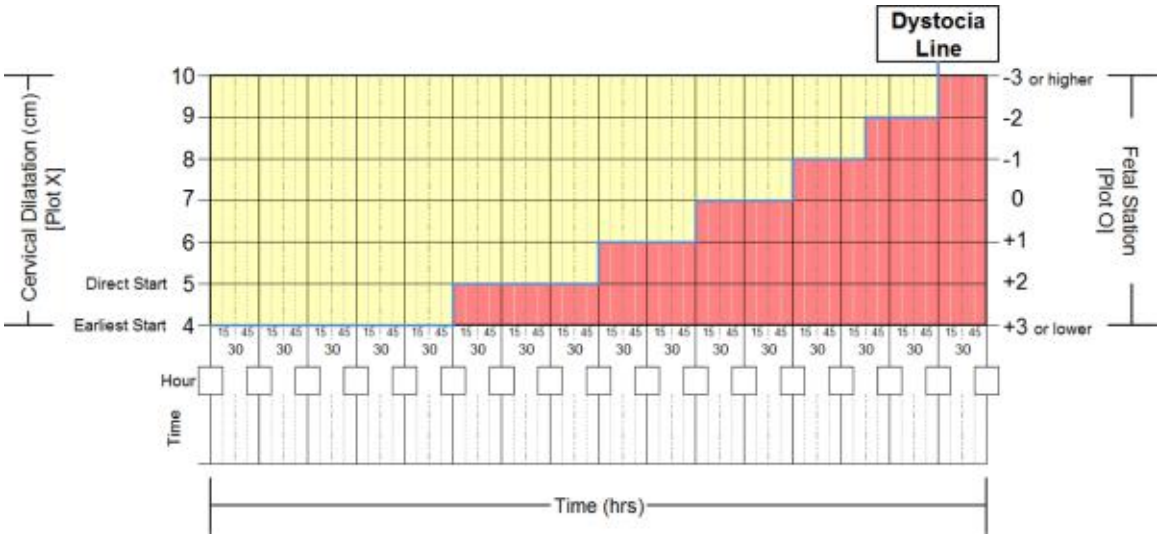
As discussed in Chapter One, 6 cm dilation of the cervical os is now considered the beginning of active labour. Many of the nulliparous women in Boyle *et al.*'s study (2013) were still in the latent phase of labour when taken for a caesarean section, due to slower than normal labour progress (ACOG, 2014). Out of the nulliparous women who reached the second stage of labour, one in three had a

caesarean section within three hours of the active pushing phase. This is of concern because the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) released recommendations in 2012 and 2014 that define ‘arrest of labour’ as longer than three hours of pushing in first-time mothers, or even as longer than four hours for situations such as where an epidural is *in situ* (Spong *et al*., 2012; ACOG, 2014).

Another reason for unplanned caesarean section due to failure to progress is induction of labour. In a 2010 study that included 233,844 mothers who gave birth between 2002 and 2008, it was found that half of the induced women who had a caesarean section due to failure to progress had not reached 6 cm dilation (Zhang *et al.*, 2010b). Not yet in active labour, these induced women were labelled as “failure to progress”.

In an attempt to avoid the increasing rate of unnecessary caesarean sections, Neal and Lowe (2012) proposed a new model for labour progress based on Zhang *et al*.’s (2010b) curves where the increasing rate of cervical change is seen as very gradual (see Figure 6.1). In this partograph for nulliparous women, the alert and action lines are replaced with a ‘dystocia’ line which suggests a cut-off between slow but normal labour and pathological labour which requires intervention.

Figure 6.1: Partograph for Low-risk, Nulliparous Women with Spontaneous Labour Onset



Source: Neal & Lowe (2012).

Yet even Neal and Lowe's (2012) research cannot accurately define boundaries of safety for labour progress in nulliparous women who are having particularly long first stages of labour with slower dilation rates than are traditionally associated with active labour (Neal *et al*., 2010).

To date, dystocia diagnosis is often based on vaguely defined delays in cervical dilation, with much variation in intervention rates between maternity hospitals and local norms and practices (see Wennberg, 2011; Glantz, 2012; Ham, 2013; Corallo *et al*., 2014). This implies that not all obstetric management decisions made for nulliparous women with respect to measuring length of labour are optimal, and do not necessarily safeguard against interventions used to speed up slow but normal labour progress.

Cross-generational studies such as Laughon *et al*. (2012a) show how nulliparous women today labour for longer than women did 50 or so years ago. Reasons for this may include the use of an out-of-date yardstick for measuring normal labour length - especially within the hospital setting, and normal-but-

slow labours being misdiagnosed as dystocic and taken for unnecessary caesarean delivery. Rising caesarean section rates and interventional births may have a lot to do with clinician thresholds and local practices. Lack of agreement on how normal birth without interventions should progress magnifies the problem. Controlling for iatrogenic intervention in cross-generational studies of labour and birth may prevent life threatening unnecessary interventions that often occur due to misclassification of labour progression and medical errors.

6.5.2 Population Norms and Labour Progress – What Predicts Labour Length?

The use of population norms as a tool to set clinical boundaries for the labour progression of all women is problematic. Diagnosis of normality of progression in labour can only be made retrospectively, so it is impossible to predict whether a labouring woman fits under a 'normal' parameter or not. Moreover, cervical assessment over time may not reflect true labour progress or justify interventions for a slowly progressing labour.

To justify appropriate interventions for slowly progressing labours, Neal *et al*. (2015) recommend a '3-point approach' which includes determining active labour onset, identifying atypical labour progress and knowing when an assisted vaginal or caesarean section birth may be justified (earliest point of arrest diagnosis). However, although onset of labour determination, accurate assessment of cervical dilation and effacement, and subsequent progression rates may be criteria for measuring normal labour progress, these criteria are insufficient to measure progress variation among nulliparous women (Oladapo *et al*., 2018).

In an attempt to diagnose dystocic labour, Hamilton *et al*. (2016) used mathematical analyses based on multifactorial models for high discrimination of

labour progression disorders and the need for a caesarean delivery. However, tracking labour progress by bedside computerisation further increased the use of technology.

Time limits, and labour and delivery schedules based on population norms, are factors that encourage the labelling (or mis-labelling) of a woman's labour progress as 'failed'. Both Neal *et al.*'s (2015) 3-point approach and Hamilton *et al.*'s (2016) multifactorial models are attempts to identify and guide policies for labour arrest. However, the lack of an undisputed definition of labour dystocia, and the absence of an accurate method for measuring normal labour progress in healthy labouring nulliparous women, indicates that not even a measurement of labour progress based on population norms is a sound clinical method.

Identifying and guiding policies for labour arrest should be replaced by identifying and guiding policies for normal birth. Normal progress and duration in labour is not universal nor standardised (Oladapo *et al*., 2018). Furthermore, given that there is no defined criteria or cut-off to mark the onset of labour in obstetric practice, evaluation of length of labour is unlikely to be entirely accurate. Thus, identifying safe time limits for labour progression, normal or otherwise, has become even more problematic. Presumably, the SiLC model for assessing labour progress also does not overcome this barrier.

There is no blueprint for ideal or 'normal' birth progress. Evidence on failure to progress is inconclusive and implies that standardisation of labour progress, especially for nulliparous women, is likely not possible or feasible. Any measurement standardisation might result in error standardisation. A caesarean section for a first time birthing mother is a very high price to pay for a labour that has stalled but not arrested. For normal healthy nulliparous women, simple supportive care together with individual unique labour progress expectations -

based on their mothers' first birth history and individual familial norms - may herald fewer perceived 'arrests' and a simultaneous lowering of assisted births and of caesarean section rates.

6.5.3 Factors Enabling or Constraining Normal Birth in the Hospital Environment

Currently, a birth that takes place in the clinical setting must comply to a 'normal' standard by progressing as expected. Any deviation from the norm (based on statistical averages and population norms) renders labour progress as 'abnormal' and warrants intervention to set labour back on its normal path. Judging by the number of rising interventions currently used to expedite labour and birth, it seems almost impossible for an individual woman to remain 'normal' among a larger birthing population.

Maternity care provided within the hospital setting deals almost exclusively with length of gestation and length of labour as a measurable dimension. Yet, as described in earlier sections of this thesis, quantifying labour progress is remarkably difficult because slow but normal labours fall outside of the central tendency and dispersion limits of population norms. Studies that report mean and standard deviations for diagnosis of progression and normality may only do so retrospectively using phases and stages of labour as defined by maternity carers. This method of assessing labour progress may not reflect true labour progression and ignores a woman's own perceptions on when labour starts and progresses (Dixon *et al*., 2013). Rigid limits applied in clinical practice for the assessment of prolonged labours not only constrain normal births but further the use of obstetric interventions. Moreover, the probability of normal birth for nulliparous women in the clinical setting is further reduced by longer than normal (yet normal for them) durations of spontaneous labour.

The central question is how best to facilitate normal birth in the hospital setting? A national prospective cohort study (The Birthplace in England Collaborative Group, 2011) found that the rate of normal birth for healthy low risk women differed depending on the place in which they were giving birth. Normal birth was more likely and achievable in freestanding midwifery units or at home than within obstetric units in hospital. Other factors that support normal birth are non-continuous foetal monitoring, free movement and mobility during labour, and non-supine birthing positions (Miller *et al*., 2015). Continuous one-to-one support (Hodnett *et al*., 2011) and water immersion during labour (Cluett & Burns, 2009) were found to reduce the need for anaesthesia in labour. These factors are modifiable and may be used to inform practice aimed at promoting and supporting normal births for healthy normal nulliparous women in the hospital setting. Other clinical factors that may increase intervention during birth are individual procedures, such as induction of labour or caesarean section. While not a risk factor in and of itself, nulliparity is linked to higher rates of induction (Humphrey & Tucker, 2009; Laughon *et al*., 2012b), epidural use (Jeschke *et al*., 2012) and caesarean section (Janssens *et al*., 2008).

Healthy nulliparous women in a medical environment are classified as healthy women, with no previous birth history and with high probability of achieving a normal birth. The resources required for these women are often minimal and cost-effective so long as unwarranted clinical interventions, new technologies, hospital protocols, trends in maternity care and unsubstantiated variations in clinical practice are resisted.

However, a certain degree of specialisation for normal management of birth for nulliparous women in hospital is required. Because significantly less has been published regarding normal birth for normal healthy women than for high-risk obstetric patients, important indicators and predictors relating to normal birth

may have been overlooked or undervalued. An individualised model of maternity care for normal birth, based on maternal history, can be practised by midwives and doctors. With its focus on minimising technological interventions and providing individualised support, the new SiLC model of care may someday be used as an added measure to assess normal labour progress, although more cohort studies are needed.

6.6 Advancing Normal Birth

In this section, the support for advancing normal birth is summarised, based on the SiLC study findings. The proposed midwifery model of care for low risk nulliparous women is defined and supporting outcomes of the SiLC study are presented.

Prediction models of labour progression for nulliparous women may help to support and promote normal birth in maternity care. They are likely to be useful for maternity clinicians, obstetric healthcare providers and policy-makers who require an individual baseline value for monitoring population variations. Recently published obstetric management research on labour progression in birthing women has been discussed in the earlier chapters of this thesis and in this chapter. In all cases, objective criteria are used to assess labour progress. However, significant variation in pinpointing labour onset differences (Hanley *et al*., 2016) and in dilatation measurements and descent of the foetal presenting part (Neal *et al*., 2015) may make monitoring progress in labour inaccurate and women prone to interventions to expedite seemingly slowly progressing labour. Consistency in *approaches* to measuring labour progress is vital for appropriate clinical decisions to be made - in each individual case and for each individual labouring woman.

The SiLC study evidence may have the potential to support normal birth. While documenting a nulliparous woman's mother's birth history does not guarantee that she will give birth in a similar manner to her mother, recording the mother's birth history may identify those daughters with a higher than usual chance of having a normal (but uncommon for some) birth. Based on familial history, this model may be used in hospitals, birth centres and home birth practices.

There are three factors that often influence measuring progression of normal labour. These are: diagnosing labour onset, early versus late admission, and spontaneous versus other labour onset.

6.6.1 Diagnosing Labour Onset

Although labour onset is an important marker for the start of labour from which point rates of progression are measured, there is weak consensus in the amount of cervical dilatation necessary to indicate that the active phase of labour has begun (Hanley *et al*., 2016). Women admitted to labour wards in the latent (as opposed to the active) phase of labour are at a higher risk of obstetrical interventions (Mikolajczyk *et al*., 2016) to accelerate progress towards a potentially normal labour which has not yet started.

If the SILC model is shown to assist in predicting labour onset in future prospective studies, it may be used to help determine active labour by assessing the signs and symptoms of the individual woman.

6.6.2 Early vs. Late Admission

Studies have shown that caesarean rates are higher among women admitted during the early stages of labour than among those admitted with advanced

cervical dilatation (Boyle *et al*., 2013; Mikolajczyk *et al.*, 2016). While dystocia is often presented as an objective entity, in reality it is an elusive diagnosis to define, particularly within the hospital setting where the system classifies labour progress into risk categories. Thus, obstetricians focusing on diagnosing pathology may pre-empt an otherwise normal labour and delivery by predicting, preventing and treating potential complications (Kjærgaard *et al*., 2009; Kjærgaard *et al*., 2010).

Admission decisions, early or late, affect maternity care in the long run. The nature of the care received and the frequency with which interventions are used may interfere with advancing a normal birth and its benefits. Enemas, IVs, withholding nourishment and water, early rupture of membranes, electronic foetal monitoring, inductions, analgesia, instrumental birth, episiotomy and caesarean births are interventions which may be overused, inappropriately administered and barriers to a normal birth. Generational differences in maternity care over time strengthens this point. In the full dataset, the mothers' cohort had 154 cases of normal physiological labour and birth, while in the daughters' cohort there were 31 cases. In comparing the two cohorts' data, interventions appear to be overused in the daughters' generation. Conceivably, this overuse may be avoided by taking the mother's birth history as preparation for planning individualised, family based, perinatal care.

If the SILC model is shown to accurately predict labour length in future prospective studies, it could be used to determine the optimal time for each woman to be admitted to hospital in labour.

6.6.3 Spontaneous vs. Other Labour Onset

The onset of the active phase of labour is often defined by a cervical dilatation of 3-5 cm in the presence of regular contractions. Contemporary expectations of 'active labour' for nulliparous women are often overly stringent for this population (Neal *et al*., 2010).

The rationale for labour induction policies should be congruent with maternal/foetal medical problems and obstetric pathologies. However, this is not always the case. An aspect not often admitted to by physicians suggesting labour induction to normal healthy women (for criteria such as a post-date pregnancy) is that interventions come with health risks (Jansen *et al*., 2013; Teixeira *et al*., 2013).

This evidence would suggest that there are questions a midwife should ask nulliparous women when induction is advised. The expectant mother who aspires to experience a normal birth should be encouraged to enquire about her familial birth history, information that may be gleaned by interviewing her biological mother. Specific questions about labour onset, rate of labour progress and natural or other methods used to alleviate stress and pain while in labour are of interest. In addition, age of mother at first birth, weight gain in pregnancy and type of delivery, gestational age, infant birth weight and gender should be taken into account when evaluating and predicting length of labour in daughters.

It is within the midwife's professional scope of practice to express opinions on the practices of a specific physician, or standardised hospital protocol. A midwife may advance normal birth by encouraging the expectant mother who is inclined towards a normal birth to write out a preferred birth plan. By engaging in a discussion, the midwife has the opportunity to point out the advantages of having a normal birth. Common definitions of terms used in maternity-centred

care such as ‘natural birth’, ‘normal birth’ and ‘fully-supported birth’ may encourage expectant mothers to ask questions in preparation for normal birth. Care choices may then also incorporate mother’s birth history as a predictive model for the daughter’s individualised normal birth plan.

6.7 Individualised Maternity Care

Personalised medicine is different from person-centred care. Personalised medicine for maternity care attempts to collapse symptoms into a globally perceived measure of pathology. Although this approach may be helpful in some respects, a person-centred care strategy may help to pinpoint key or recurrent familial aggregation to show significant individual variability. Person-centred care is holistic in approach. It lacks the evidence-based structure of modern medical science which turns women into medical objects and offends their morale as human beings. For this reason, person-centred care is a more suitable paradigm for normal birthing women. Today, highly scientific bureaucratic health systems that work on population-level data are over-medicalising many normal labours. Anecdotal accounts of midwives who support normal birth in the hospital environment describe how women and babies achieve physiological labour and birth. These women focus on what they want for themselves, and often question or refuse unnecessary medical interventions which are suggested for problems which likely don’t exist.

Modelling of woman-centred maternity and management options may be based, at least in part, on the findings of the SiLC study. While it may not provide a single, comprehensive, explicit and interpretable plan for all birthing women, a mother’s birth history may be integrated into other midwifery models and used to guide decision-making for optimising women’s choices for normal birth.

Person-centred care is a new field in maternity care and deserves attention and development.

Person-centred care plans for normal childbirth, especially important for nulliparous women, would benefit from a wider range of guidelines. Labour progression diagnosis should include the mother's (and perhaps extended family's) birth history. Although clinical maternity care based on population norms is effective or satisfactory for most women, clinical response to management is mediated by individual differences. It is this inter-individual (between people) variation from the norm which is unpredictable even when having taken a familial history. Consequently, it is surprising that the normative findings reported by Friedman in 1954 influenced maternity management for progress in labour well into the 21st century.

Both personalised medicine and family-based studies represent new territory in clinical care. While research is moving forward in understanding individual variations in health status, generalisations from aggregate data still form the evidence-base for assessing women's progress in labour. Mother's birth history may be collected as an additional measure to be added to the evidence base.

6.8 Evaluating Normal Birth

Until recently, most women in labour were held to the Friedman curve progression standard. If the cervix of a nulliparous woman did not progress from 0 to 10 cm in 14 hours, she may be assigned a diagnosis of failure to progress and taken for a caesarean section. Since individual differences in women's physiological response to labour have been observed, contemporary modifications of labour practices have set wider ranges to quantify parameters for low risk women in labour (Spong *et al.,* 2012; ACOG, 2014). Although new

standards of progress have extended length of labour times to limit intervention during labour and birth, using a mother's birth history may play an additional role in protecting women from early intervention and assisting them to achieve a normal birth.

The recent evidence for observed variability of length of labour among women may be explained, in part, by individual familial differences. Length of labour *per se* is not the factor of interest. Rather, it is familial variation of length of labour that may be contributing to its natural variation in individual women. Although familial variation alone does not provide a comprehensive picture of all the factors present, it may suggest a trajectory for achieving normal birth.

This was the gap in the literature that this thesis aimed to address. The main goal is that nulliparous women will benefit from a predictive normal birth model based on their mothers' normal first birth history. Further research on familial factors and a better understanding of familial interactions may allow for the development of tailored individual normal birth plans. Relevant to recent rising trends in obstetric intervention rates and the influence of contextual factors in the hospital setting, the new action plan primarily considers the possible influence of a mother's labour progress in her first birth.

6.9 Implications for Practice

It would seem that there are three constructs central to the development of effective normal birth strategies based on familial history. Major research challenges still remain. However, the prerequisites for the long-term success of a personalised and predictive normal birth plan for nulliparous women are better today than they have ever been.

The first construct (obstetric risk) is currently conceived of as a dichotomy. A clear division between risk in normal childbirth and no risk in normal childbirth (for example, with regard to a nulliparous woman who carries post-date) supports the use of recommended cut-offs for management or treatment of prolonged gestation. Any predictive model for a normal birth in nulliparous women should be built on the recognition that there are degrees of risk rather than just two extremes (i.e., risk and no risk). As an example, for any particular daughter, the level of risk may be based on her mother's birth history. A straightforward maternity history for a mother's first birth may have an influence on her nulliparous daughter's preferences for labour and mode of delivery. In this particular case, a nulliparous woman may carry post-date (as her mother did) and spontaneously deliver a larger than average baby (as her mother did) with a healthy maternal/foetal outcome (same as her mother). The birth may not have been 'post-date' (within the familial context) and the baby may not have been 'macrosomic' (within the family context) - just larger than average. However, the model is far from refined. Although the SiLC model showed reasonable mother-daughter associations for certain perinatal events, mother's recall is not 100% for all perinatal events (as seen in Chapters Three and Four) and mother's birth history alone may not provide a person-focused birth trajectory.

The predictive quality of the new predictive birth model for nulliparous women may be increased by collecting the following information: maternal age, body mass index and weight gain during pregnancy, gestational age, birth weight, infant gender and mother's first birth history.

To minimise unnecessary interventions, those women who are truly low risk and can have a normal birth must be identified so that they may receive appropriate care and support throughout labour. Equally important is to identify those

women who are truly high risk and need a caesarean section so that they may proceed under optimum conditions.

The second construct is that often only a small percentage of the birthing population is at the extremes of high or low risk. The majority of women fall in the middle of the distribution of risk. For example, the majority of women who have post-term pregnancies are likely to have a normal delivery with no additional risk to their baby. The current preventive approach of relying on population norms for decisions (on, for example, inductions for post-term pregnancies) may bring large benefits to the birthing community in general, but offers little to each individual woman. Incorporating a mother's first birth history into current guidelines for the clinical management of normal labour progress in her daughter's first birth may move the entire distribution of risk to lower levels and may improve maximum likelihood for a normal birth.

The third construct is that a low risk nulliparous woman's likelihood for a normal birth is reflected in the familial birth characteristics of the family to which she belongs. Thus, it may be safe to assume that a nulliparous woman whose healthy mother delivered a larger than average baby (infant birth weight >4 kg) in her first delivery (foetal macrosomia is defined as infant birth weight >4 kg, which is an indication for a nulliparous woman to deliver by caesarean section) may be likely to be able to deliver a larger than average baby in her first birth. Ranges for particular obstetric characteristics such as longer than average pregnancies, longer than average labours or larger than average babies, create subgroups within the general population. These subgroups serve as a useful heuristic to remind us about normal variability in birth characteristics among families.

Clinical obstetric guidelines which are context-specific within families may help guide decisions on normal labour management. Individualised thresholds based on familial birth history may help differentiate between normal birth and births that might benefit from some clinical intervention. The findings of this study could strengthen the capacity for women to experience 'normal' births and to reduce the use of inductions, augmentations and surgical deliveries.

This may be particularly useful in identifying women for whom labour is likely to be (normally) longer than average. There is growing evidence on the complexities of managing the so-called 'early' phase of labour (the time between women identifying the sensations of labour and them entering the active phase) (Eri *et al*., 2015; Hundley *et al.,* 2017; Beake *et al*., 2018; Rota *et al*., 2018). This situation may become more acute as new criteria for diagnosing active labour come into practice, since this sets the active labour point at 6 centimetres of cervical dilation (Zhang *et al*., 2010; ACOG, 2014; Nguyen *et al*., 2014; Chukwudi *et al*., 2018). This means that more women will be told they cannot (yet) enter the hospital, raising concerns about the lack of labour support available to women at this stage (Miller *et al*., 2016). Those with physiologically longer than average early labour characteristics may find this part of labour particularly difficult in terms of morale and pain management. Using the tool to identify women for whom this might be the case means that they and their family as caregivers would be better able to anticipate and prepare for this eventuality.

Other potential applications could include:

- Using maternal birth histories collaboratively to adjust for unique childbearing characteristics within a family. Expansion of this approach could include use of electronic technology for integrating mothers' birth

histories as a clinical decision support function relevant to nulliparous daughters' birth care plans.

- Considering changes in practice according to individual familial birth histories, such as applying flexible and negotiable birth plans instead of adhering to structured labour and birth protocols. Examples include prevention of induction of labour for a post-date pregnancy and avoiding augmentation for a slowly progressing labour.
- Using maternal birth history resources individually by applying unique familial-based information per case to focus on the physical needs of each labouring woman and her baby. A 'checklist' approach may be useful to identify familial patterns, such as mother's weight gain in pregnancy, age at first birth, use of analgesia (yes/no) and length of labour (≤10 hrs/>10 hrs).
- Identifying familial barriers to physiological birth and making clinically relevant decisions for individual women. For example, using mothers' birth histories for clinical decision support relevant to nulliparous women with potential risks, such as mothers' first birth by caesarean section due to dystocia and/or a foetal birth weight >4 kg.
- Improving birth experiences for nulliparous women who have prolonged pregnancies/prolonged labours through supportive care and decision-making based on their mothers' normal first birth at a later gestational age or a longer length of labour than evidence-based consensus determines.
- Pre-designing conditions based on mothers' first labour length to promote effective physiological labour support. For example, healthy nulliparous women presenting in spontaneous labour should delay labour ward admission if their mothers had longer than normal 'normal' labours. For women admitted to the labour ward during the latent first stage, medical interventions to accelerate labour and childbirth should be

avoided, especially for those women whose mothers had longer than normal ‘normal’ labours.

- Redefining ‘dystocia’ (i.e., difficult or abnormally slow progress of labour) in alignment with mothers’ first birth progression of labour may reduce the use of interventions during nulliparous daughters’ labour and birth.

6.10 Strengths and Limitations

6.10.1 Strengths

This research has identified a research gap in labour progression literature. To my knowledge, this is the first attempt to employ statistical methods to assess mother-daughter similarities in labour and birth characteristics in first deliveries. Mothers’ agreement between maternal recall of first birth history and archived birth records was researched prior to conducting the main study of this thesis. The SiLC study included a reasonably large sample size with a high response rate yielding a substantial matched cohort. Detailed statistical modelling accounted for interrelationships of a range of variables, including changes in clinical practice over time. Women who underwent induction in the first stage of labour and augmentation and/or emergency caesarean sections in the first or second stages of labour were also included in the analysis. All women in the sample who had laboured were explored for length of labour.

6.10.2 Limitations

There were some limitations to this study. First, the study was prone to selection bias introduced by the convenience sampling of first time birthing mothers attending the two antenatal clinics where the study was carried out. In addition, findings need to be interpreted within the context of the Israeli hospital

setting. It is highly medicalised in its maternity approach, with the length of labour ‘time’ factor applied as a matter of course.

Widespread use of inductions for ‘post-date’ pregnancies in the daughters’ cohort was observed, though less extensively in the mothers’ cohort. To the same effect, use of interventions for slow labours in the daughters’ cohort seemed unrestrained compared to the mothers’, although the high rates of induction/augmentation in this cohort seemed to bias findings towards longer lengths of labour (the reasons for this are discussed in Chapter Five).

A further limitation of this study is that details of the birth order for the index woman (i.e., the daughter) were not collected. It may be that the relationship between first pregnancies is stronger if the index woman is also the first child. This should be explored in further research on the topic.

Finally, parameters for onset of labour in the two datasets were not defined. This may have caused discrepancies while measuring time in length of labour. In addition, discrepancies may have resulted from gathering information by questionnaires within the mothers’ cohort. Degrees of agreement (substantial or moderate) between mothers’ self-reports and medical records may vary equally with the type of birth event, mothers’ recall of the event and the quality of the hospital records of the event. Although mothers’ recall was shown to have good agreement with hospital birth records for most birth events, women’s recall of medical interventions such as induction was under-estimated. Self-reported information may show a lack of agreement for numerous reasons, including misunderstanding of the diagnosis presented, or the forgetfulness of the individual reporting. Likewise, medical records are not necessarily an accurate source of information. Given the potential sources of error with both methods of

ascertaining information, it is impossible to know which assessment comes closer to the truth.

6.11 Concluding Observations

This chapter has outlined the ways in which normal physiological childbirth is often miscalculated in obstetric practice due to the variability in the distribution of time (latent, first and second stages) needed for women, especially nulliparae, to advance throughout the stages of labour. Current maternity practice may find that utilising mothers' first birth history as a predictor for the upper limits of normal in their daughters' labour progression curves helps set realistic boundaries for familial normality, and personal thresholds for individual women.

As already shown, progress rates in labour differ between women and reflect numerous variables. A predictive model for a nulliparous daughter's progress in labour based on her mother's first labour may help establish suitable principles for practice in each individual situation. Women should have the right to choose normal birth as the mode of delivering their babies. A woman's choice for normal birth may now be supported by her mother's first birth history as an additional heuristic to guide practice and increase precision in the clinical management of nulliparous women's labour and delivery.

Mother's first birth data may be used as an additional tool for planning and calculating a nulliparous daughter's normal labour. It may be used to build personalised birth plans, while allowing for realistic adjustments in a nulliparous daughter's longer than normal length of labour with the anticipation of a normal birth outcome. In addition, healthy nulliparous women whose length of labour stretches past average labour lengths, as derived from population norms, may

choose to continue to labour spontaneously if their mothers also had long labours. Utilising the mother's first birth history as a supplement to clinical decisions made for individual women in labour offers a promising new approach to labour management, may bolster the case for a longer than normal 'normal' labour, may broaden current thresholds for labour progress and encourage safe women-centred normal labour care.

6.12 Recommendations

Research on maternal recall of birth events should include further studies involving longitudinal analytic methods or rigorous meta-analyses to more fully explore the agreement of maternally recalled birth outcomes with hospital birth records. Future research should pay particular attention to outcomes that have been under-researched, such as onset of labour and stages in labour. Cultural differences should be explored by using qualitative studies to examine women's perceptions of birth outcomes and agreement with hospital birth records. A full systematic review including quality criteria may provide a more accurate summary of agreement of maternal recall data and hospital birth record data and provide a more valid pooled estimate of agreement results.

Maternity care providers should recognise the possible consequences and risks of interventions in labour. Because nulliparous women have no birth history, they may be at greater risk for interventions and adverse birth outcomes than multiparous women. Optimising natural processes for childbirth may include using a mother's first birth history as a guide and predictor for length of labour in her daughter's first birth. Personalised medicine is an emerging field where clinicians tailor care to individual people's health needs. Not yet evident within maternity care, the potential of woman centred care is to identify those nulliparous women who are likely to have normal births. A mother's first birth

history may give sufficient maternal information to achieve the best birth outcome for her daughter. Research efforts should focus on developing personalised, individualised normal labour algorithms modelled on the mother's birth history.

6.13 Future Research Questions

Future research questions that could take this work forward are:

- Birthing populations and individuals: how can we identify individual women's needs in childbirth and design person-centred care plans?
- Services and processes: What skills are needed to design maternal care services, and organise providers and settings for normal birth?
- System enablers: How can we rearrange accountability, align incentives, prepare competent maternity carers and promote responsible use of interventions?

6.14 Areas for Further Research

- SiLC research in larger datasets should be conducted to increase the sensitivities and specificities for length of labour in the model and improve potential levels of classification/misclassification for nulliparous women.
- Use of the SiLC model should be tested in prospective studies.
- Examine the potential for consensus on how to define labour onset and progress.
- Future epidemiological research may identify groups with reliable maternal information for specific birth variables, thus making fieldwork cheaper and easier.

- Developing person-centred maternity care models for limiting unnecessary interventions in general.
- Recommendations for labouring women to include individualised care, such as continuous labour support, staying upright and moving around, admission to a labour birth facility in active labour (around 6 centimetres dilation), drinking and eating in labour, leaving membranes intact to break on their own, use of drug-free relief measures, and pushing in the second stage of labour as preferred, should all be tested as a means of limiting labour and birth interventions.

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APPENDICES

APPENDIX 1: UCLAN RESEARCH PROGRAMME APPROVAL AND HELSINKI ETHICS APPROVAL

First draft of SiLC protocol

4/05/2014

Research title:
Inter and intra-generational similarities in labour and childbirth: an observational cohort study
Short title: The SiLC- Similarities in Labour and Childbirth – study

Research tools: Questionnaires

This research study has been suggested to me by Professor Soo Downe (UCLAN) and Professor Ariel Many (Sourasky Medical Center, TA, Israel).

Context and setting

The Lis Maternity Hospital had 11,239 deliveries in 2010. 41.9% of all deliveries were primiparous women (n=4709), which is considerably higher than the national statistic of 31.7% (Israel Central Bureau of Statistics, 2010[21]). Childbirth in Israel generally takes place in a hospital. According to the Israeli Association of Obstetrics and Gynecology, more than 99% of all births occur in hospitals (Kupermintz, 2005[22]).
Thus the chosen "site" is well suited to host the research aims.

AIM

To establish the value and feasibility of constructing a labour and birth prediction model for nulliparous women based on the birth accounts of their mothers and sisters.

OBJECTIVES

1. To establish the degree of association in gestation at onset of labour, length of labour, infants birth-weight, and mode of birth between participating women and their mothers and sisters
2. To establish the congruence between the recall of these birth parameters for the mothers and sisters of nulliparous women, and the data recorded in their clinical case-notes.
3. To explore potential predictive models for these parameters for nulliparous women based on the outcomes of their mothers and sisters.
4. To assess the feasibility of a subsequent multi-site study to validate the models developed in objective 3.

BACKGROUND

Few would dispute the need to intervene in pregnancy and labour when overt pathology occurs. However, most risk scoring systems and indicators in the field have low sensitivity and specificity[1] (p51). In addition to composite scoring systems, researchers have noted an association between specific characteristics between one pregnancy and the next, including prolonged gestation[2, 3] prematurity[4], and low birth weight[5]. However, these observations are not relevant for women having their first baby.

Both induction of labour for uncomplicated postmaturity, and augmentation of labor for dystocia, have generated discussion around risk and benefit. In 2003/4, over 20% of labours were induced[6]. A survey of 956 births termed 'normal' in one regional HA[7] indicated that 21% were induced and 14.2% were augmented.

Prolonged pregnancy is currently diagnosed after 41 completed weeks of gestation[8, 9]. Good quality evidence indicates that for every 3000 otherwise healthy women in whom labour is induced at this gestation two less stillbirths will occur than if spontaneous onset was awaited until 42 weeks gestation, and five less than for women delaying labour onset to 43 weeks gestation[10]. In both cases over 2990 women and babies who are not at risk of stillbirth will experience induced labour. At present, there are no effective tools for differentiating the few babies that will die from the thousands for whom longer pregnancies are, apparently, physiological. One possible variable could be a familial trend for a longer pregnancy.

In the only published study we located in this area[11] prolonged pregnancy was deemed to be ≥42 completed weeks gestation. On this basis, a daughter was more likely to have a prolonged pregnancy if her mother had done so (RR = 1.3; CI :1.0-1.7). The risk in a younger daughter was elevated if her elder sister had had a prolonged pregnancy. The sensitivity of the definition of prolonged pregnancy used in this study was not modelled, so it is not clear if the relative risk would have altered with different cut-off points.

Most authorities accept that the 'normal' progress of labour from the active phase (approximately 4 centimetres of cervical dilation) should be approximately 1 centimetre of cervical dilation per hour. However, Albers and colleagues have demonstrated that this average is closer to 1.5 centimetres per hour for some populations[12 13], and others have reported a wide range of labour progress with no evidence of increased adverse outcome in low risk populations[14,15]. Indeed, a recent ACOG practice bulletin[16] has noted that '*considerable variability exists in the diagnosis, management, and criteria for dystocia that requires intervention'* (p16) and, in relation to the second stage of labour, that *'Intervention is not necessary for all factors solely based on time'* (p17).

Based on retrospective data from the same Swedish database as Mogran and colleagues, two studies have explored the inter- and intra-generational associations related to dystocic labour[17 18]. In both cases, the authors noted the influence of varying protocols between generations and between practitioners on the diagnosis. In the Berg-Lekas study[17], if a mother was diagnosed with dystocia during the birth of her eldest daughter, the daughter had an increased risk during her first childbirth (OR 1.7 CI 1.2-2.4). An increased risk was also found for the younger primiparous sister if her elder sister had dystocia when she was primiparous (OR 2.0 CI 1.5-2.7). The risk of an instrumental birth for dystocia in the younger sibling was more than tripled if the elder sibling had experienced the same outcome (OR 3.5 CI 2.1-5.8). Dystocia was diagnosed in 75% of women whose twin sisters had dystocia, but only in 11% of

those whose twin sister had a normal birth. In the Algovik study, correlations were similarly noted between generations and siblings, and the authors concluded that *'genetic effects accounted for 28% (CI 21-32) of the susceptibility for dystocia'* [18] (p832).

It is not clear if the diagnosis of dystocia used in these studies described labours that were pathological, or only those that crossed conventional time boundaries in the absence or presence of pathology. However it was arrived at, the diagnosis did demonstrate an inter- and intra-generational association.

Implications

It is possible that these cross-generational associations are indicators of true pathology that could be predicted and prevented late in pregnancy or early in labour. Equally, familial tendency may be indicative of a physiological factor that is at the extreme end the range of normal.

All three studies were retrospective, and all analysed data on one database, representing a fairly homogenous White population. The definitions of abnormality used were dichotomized (prolonged/not prolonged, dystocic/not dystocic). In order to assess the potential value of inter and intra familial labour onset and progress for a more diverse population, the optimal approach would be to examine associations based on continuous data for characteristics of labour onset and duration (days of pregnancy, time in active labour) between mother-daughter and mother-sister cohorts, and the outcomes for them and their babies (perinatal mortality and morbidity, mode of birth, birth weight for example).

However, large linked data-sets containing these data are not routinely available in Israel. Professor Ariel Many therefore proposes a prospective investigation of the inter- and intra-generational associations in the variables of interest between women who are currently pregnant, and the historical outcomes for their mothers and sisters. He suggests the collection of data method by recall - using both questionnaires, and medical records where accessible – while attempting to establish firm outcomes such as: week at delivery/time of day at onset of labour, SD/VE/OF/CS, and specific complications such as: revision, post partum use of blood products; and weight of neonate and other recallable variables.

Obtaining accurate historical data.

Labour and birth case notes are only legally retained for 25 years in Israel. Case-notes data are likely to be available for sisters, but, given the increasing age at which women have their first babies, they may not be available for the mothers of women who are now pregnant. In addition, as we have already noted, there is no automatic linkage available between mothers and daughters or between sister's clinical data. On this basis, medical records and personal written stories will be necessary if predictive models are to be used in clinical practice.

There is conflicting evidence about the consistency and accuracy of women's memories of their birth experience [19, 20]. Since there has been much inter-generational immigration of Jews to Israel since the 1950's, it may be necessary to rely on mothers' birthing descriptions and stories (added to the additional space for freehand recollections at the end of the questionnaire), and the accuracy of these accounts will not be verified.

Accounting for the influence of ethnicity

The Israeli population is composed of Jews and non-Jews, who differ not only in their religion but also in their customs. Many of the Jews are immigrants from many parts of the world who still retain many of the habits, customs and lifestyles of the societies they had lived in for many generations. Therefore, oral birthing accounts of mothers from different cultures will require cross-cultural sensitivity and scrutiny.

Data collection procedure and potential participant status

The Lis Maternity Hospital has a maternity day clinic which offers antenatal follow-up for women nearing term, and offers birthing courses to primipara women. Potential participants will be approached by staff who have been recruited and briefed to aid with the distribution of questionnaires. Completed questionnaires will be made traceable for the accessing of postpartum information, and confidentiality will be rigorously maintained with no danger of personal or data disclosure.

The majority of the primipara population attending the Lis Maternity Hospital is a homogenous selection of White, middle-class, educated, secular or traditional, Hebrew-speaking Israeli women, living in the Tel Aviv area, and attending antenatal follow-up at the Lis Maternity Hospital.

Accounting for policies for intervention

As noted above, the natural progression of both pregnancy and labour can be interrupted by management policies, and these may change over time and between practitioners. Due to the close living proximity of all the participants attending the Lis Maternity Hospital Follow-up Day Care Center, it may be insightful to record the lead professional for each index woman, and, as far as possible, for each of her participating relatives. We will also note the policies and practices for induction and augmentation of labour that are currently in operation for the index women, and, as far as possible, that were in operation for their relatives. We will examine the impact of these variables in our model testing.

PLAN OF INVESTIGATION

Design: A cohort study

Participants: All consecutive eligible consenting women over the research period.

Numbers of women who may be available for recruitment

The annual birth rate in the Lis Maternity Hospital was 11,239 in 2010. 4,709 (41.9%) were primiparous deliveries. Based on the power calculations below, I estimate that I need to recruit 1,800 primipara women over a period of two years. I assume that approximately 70% of these women will be eligible (n=approx 1260). I estimate that approximately 70% will demonstrate an initial interest (n= approx 882) and approx 70% of these will give consent (approx 620 index women and 620 mothers). I estimate that half of these index mothers will have at least one parous sister (n=310 sisters). If more than one sister has had a baby before the index woman, data will be collected on all the sisters who consent, and one of them will be selected randomly for the analysis.

Inclusion criteria at the time of seeking consent

Nulliparous women:

- above 32 weeks
- baby is a singleton and a cephalic presentation
- mother and baby have no contraindications to spontaneous onset of labour, labour progress, and birth
- who consent to inclusion
- whose genetic mother and/or sister(s) consent to inclusion

with mothers who:

- are genetically related to the index woman
- consent to inclusion

and/or sisters who:

- are genetically related to the index woman
- have had at least one baby
- consent to inclusion

Procedures

1. The research midwife and colleagues will distribute questionnaires to all eligible nulliparous women attending the follow-up day care center/antenatal birthing course at the Lis Maternity Hospital.
2. If their mothers and any eligible sisters birthed at the Kirya or Lis hospital and are interested in taking part in the study, the index woman will be asked to take questionnaires for the family members. This will be available only in Hebrew.

3. The questionnaires – will be signed for consent - and will be returned to the staff at the follow-up day care center/antanatal birthingcourse at the Lis Maternity Hospital at a subsequent visit.
4. The research midwife will locate and collect data from the mothers and sisters case-notes wherever possible.
5. After the labour and birth of the index mother, the research midwife will collect data from her case-notes.
6. Data analysis will take place.

Analytic strategy

1. Accuracy of recalled data on birth outcomes

The level of agreement between recall and clinical records will be plotted visually on a scatter plot, and then compared using the kappa statistic. Exploratory analysis of possible associations between mothers and sisters data will be undertaken separately. Sub-analysis will stratify the data by the age, parity, ethnicity, and time since first birth of the respondent.

2. Similarity of birth outcomes between relatives, and exploratory modelling

Within pair (participant-mother, participant-sister) comparison of:

a) Completed days of gestation at onset of labour (based on agreed EDD from certain LMP, a dating scan, or, where these are not available, on best estimate)

b) Time in labour from diagnosis of active labour to birth, in hours

c) Infant birth-weight in grammes

d) Mode of birth (normal birth with no intervention vs other)

Scatter plots, descriptive data, and multiple regression analyses will be utlised for analysis of a) to d) above. The independent variables will include the age, ethnicity (White Israeli or other), and Jarman (socio-demographic) score of the index woman and of her relatives. Odds ratios and CI for odds will be calculated.

Note will be made of stillbirths and of perinatal mortality and of abnormality/ severe morbidity in the mother or neonate. It is unlikely that the numbers will be large enough for analysis at this stage, but we will examine these data descriptively for any evident patterns, and for consideration for addition to the models for future testing/calculation of power for future studies. This approach will also be used for the data relating to the lead professional and to extant labour management policies and guidelines.

Power

Sample size calculations were done in NQuery Adviser, using a range of plausible scenarios.
A sample of size 500 should be adequate to produce a 1-sided 95% confidence interval on a kappa statistic (to measure agreement) to a tolerance of 0.05 for a continuous or dichotomised variable (if the prevalence is between 0.3 and 0.5), assuming a kappa of at least 0.8.
A sample size of 500 is adequate to compute a 1-sided 95% confidence interval for a correlation coefficient to a tolerance of 0.07 assuming a correlation of at least 0.2. This sample size should therefore be sufficient to estimate the association between continuous variables (index mother/mother or index mother/sister pairs), and also for a multiple linear regression taking into account the other predictors.

For the dichotomised variable (assuming a prevalence of about 40%), a one-sided 95.0% confidence interval for an expected odds ratio of 1.455 will extend to a lower confidence limit of 1.068 when the sample sizes are 200 and 300, respectively, a total sample size of 500. Although this sample size would not be adequate for odds ratios less than this, the cumulative evidence from each of the analyses should be sufficient to assess the feasibility of a larger study.

Ethical considerations

Data management. All identifiable data will be kept in a locked cabinet in a locked office, accessible only to the research team.
Disclosure. Data will be collected. The names of the participants will be available to the principal investigator and co-investigator and will be available only after coded password and username are allocated to each participant. The file will not be sent electronically without encryption and will not leave the premises.
Confidentiality will be maintained at all times, and names will not be used in any published reports of the study.

Time-frames for the complete study

The intended time frame for the complete study is 3-5 years.
The total number of participants in the complete study, n=500.

Intended schedule includes:

1) Collection of completed questionnaires subject to ethics approval from the Helsinki Ethics Committee of the Sourasky Medical Center and from the UCLAN research study ethics board.
2) Ongoing literature review.
3) Set up “on site” with recruitment of midwives working in the Maternity Day Care Center/ante natal birth courses at the Lis Maternity Hospital.
4) Recruitment of participants, distribution of questionnaires to participants and relatives.

5) Recording births of index women.
6) Review and synopsis of birth records.
7) Recording and synopsis of participants' relatives birth stories.
8) Analysis of recall by questionnaire.
9) Analysis of outcomes
10) Writing up

Research Management

The midwife researcher, Mindy Ebrahimoff, will provide day-to-day coordination and management. Her responsibilities include: continuous liaison with the "site" – the day care center at the Lis Maternity Hospital/ante natal-birthing courses where questionnaires will be distributed and returned, updating Professor A. Many (and DoS Dr. Victoria Hall-Moran, and Prof. Soo Downe – UCLAN) as to progress and findings, data collection, accessing case-notes, primary data entry, analysis, writing up.

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Research Programme Approval Letter, UCLAN 2013.

Date: 11th November 2013

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NW14 1NE

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www.uclan.ac.uk

Dear Mindy,

RESEARCH PROGRAMME APPROVAL FOR THE AWARD OF RESEARCH DEGREE OF THE UNIVERSITY OF CENTRAL LANCASHIRE

I am pleased to inform you that the SWESH Research Degrees Sub-Committee has approved your application for Research Programme Approval on a PART time basis for the degree of Master of Philosophy with possibility of transfer to the degree of Doctor of Philosophy

Title of Programme of Research

Assessing the potential for a personalised model of pregnancy and childbirth based on familial reproductive outcomes and its relevance to clinical practice

Supervisors

Director of Studies:	Dr Victoria Hall Moran School of Health
Second Supervisor 1:	Professor Soo Downe School of Health
Second Supervisor 2:	Professor Ariel Many Sourasky Medical centre, Tel Aviv, Israel

Programme Start Date and Duration

The expected programme length is 72 months if transfer to PhD is sought and approved (part-time) with effect from 1st January 2013, subject to conditions specified in the University Regulations.

The expected date for submission of your final thesis is **31st December 2018**.

If you do not propose to transfer to PhD, the maximum programme length is 60 months (part-time)

Ethical Approval of your Project

Your application for RPA has been approved. However, please note that until you have gained ethical clearance (where you answer "No" to all questions on the Ethics checklist and clearance is confirmed by the ethics committee) or ethical approval (where you answer "Yes" to any question on the Ethics checklist and submit an application for full ethical approval which is subsequently approved by the ethics committee) you are not permitted to do any data collection or fieldwork, or participant surveys. To do so will mean you are uninsured, in breach of the Code of Conduct for Research, and liable for disciplinary action.

P.T.O

Transfer from Master to Doctor of Philosophy

Transfer to PhD should take place between 24 - 36 months (part-time students).

Examination Arrangements

a) The arrangements for examining you on your programme of work.
b) The external and internal examiners to be appointed.

These arrangements should be submitted no later than 4 months before you propose to submit your thesis for examination. Please note that you will not be able to submit your thesis until examination arrangements have been approved.

Please feel free to contact me about any aspect of your research programme or with any other queries you may have.

Yours sincerely

Clare Wiggans
Senior Administrative Officer (Research)
Research Student Registry

On behalf of the SWESH Research Degrees Sub-Committee

Copies: Victoria Hall Moran
Soo Downe
Ariel Many
Rob Monks

Lis Maternity Hospital Helsinki ethics approval

Helsinki ethics approval from the Lis Maternity Hospital, Sourasky Medical Center, TA, Israel. Form 4, form 5, and personal letter of authorization from Prof. Many.

Form 4

Approval of the Helsinki sub-committee for research which does not involve medical trials

Date: 19 June 2014

For the attention of: Professor Ariel Many

We are convinced that the research, the details of which appear below, does not involve medical trials involving humans, and stands by the detailed terms of the protocol in Approved medical research trials that do not involve humans.

Name of the Principal Investigator: Professor Ariel Many
Title of research: Intergenerational characteristics of mother-daughter birth outcomes
Protocol No. :0039-14 Version 2 Date: 12 June 2014
Informed consent No. :Version 2 Date: 12 June 2014
Questionnaires for parturients / mothers/ sisters Version 1 Date: 4 May 2014

Approval number in the NIH trials database: N/A

B. Validity of the Approval one year from the day of the director of the medical institution permission.

C. Conditions and restrictions:
None

Name of the Chairman of the Helsinki Committee	Signature of the Chairman of the Helsinki Committee	Date	Date of the discussion of the Helsinki committee
Professor Marcel Tupilski	Prof. Marcel Topilsky Chairman of the Ethics Committee (Helsinki) Sourasky Medical Center Tel-Aviv	19/6/2014	30/5/2014

Form 5

Approval of the Director of the Medical Institute/qualified person

Date: 19 June 2014

For the attention of: Professor Ariel Many

Subject: Approval to perform research that does not involve trials with humans

According to your request dated:4 May 2014 the following approval number has been allocated: 0039-14-TLV, in order to perform the research according to the research protocol included with the request.

Name of the Principal Investigator: Professor Ariel Many
Title of research: Intergenerational characteristics of mother-daughter birth outcomes
Protocol No. :0039-14-TLV Version 2 Date: 12 June 2014
Informed consent No. : Version 2 Date: 12 June 2014
Questionnaires for parturients / mothers/ sisters Version 1 Date: 4 May 2014

Approval number in the NIH trials database: N/A

According to my authority by memorandum of the managing director 15/2006 to give permission to arrange research which does not involve trials with humans, in the Tel Aviv Sourasky Medical Center, after the approved request by the institutional Helsinki subcommittee dated:30 May 2014 and after being convinced that the stated research is according to the principles of the Helsinki declaration and regulated research approval for performing research trials that do not involve humans, I hereby approve the performance of research subject to the following terms:

Terms of the Approval

1. The research will be performed according to the principles of the Helsinki declaration and according to the procedural demands to approve research not involving trials with humans, and the up-to-date international requirement of guidelines.

2. The research will be performed only after providing a good explanation to the participant or to their legal representative and after their signature on the form of approval has been attached to the request.

3. Every change, additional or deviating from the research program, must have written approval of the medical institute's Helsinki sub-committee.

4. The Principal Investigator involved in the research is obligated to notify the medical institute's Helsinki committee on cessation of the research.

5. Extending the research expiration date: Two months before changing the approved period to perform the research, the Principal Investigator is obligated to transfer an advancement report regarding the research period to the medical institute's Helsinki committee. The committee will inform the Director of the medical institute of its decision regarding the continuation of the research period. The director will issue a new approval for the research.

6. Upon termination of the research, the Principal Investigator will provide a concluding report to the Helsinki committee regarding the research period and the results.

7. The approval is given to the Principal Investigator and to the specifically mentioned medical institute only and cannot be transferred elsewhere.

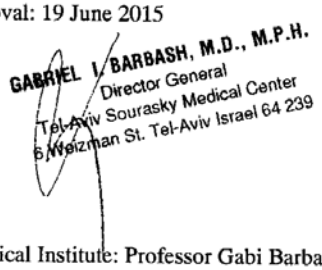
8. Additional Restrictions:

NONE.....
.....
.....

9. Validity of the Approval: 19 June 2015

GOOD LUCK!

With much respect,



The Director of the Medical Institute: Professor Gabi Barbash

Copy: Chairman of the Institutional Helsinki Committee: Professor Marcel Tupilski
.....

THE STATE OF ISRAEL
MINISTRY OF HEALTH
TEL AVIV SOURASKY MEDICAL CENTER
Affiliated to the Tel-Aviv University
Sackler Faculty of Medicine
Municipality of Tel Aviv-Yaffo

LIS MATERNITY HOSPITAL

מדינת ישראל
משרד הבריאות
המרכז הרפואי תל-אביב ע"ש סוראסקי
מסונף לפקולטה לרפואה ע"ש סאקלר
באוניברסיטת תל-אביב
עיריית תל-אביב-יפו

בית חולים "ליס" ליולדות

15/7/2014

To whom it may concern
The UCLAN Ethics Committee

re. MPhil/PhD student Mindy Ebrahimoff, UCLAN ID:G20487845
Midwifery & Women's Health; UCLAN
Research project approval, Helsinki, Sourasky Medical Center, Tel Aviv, Israel

The following research study has received Helsinki Ethics Committee approval (see forms 4 & 5 attached): **Intergenerational characteristics of mother-daughter birth outcomes.** Protocol No. 0039-14-TLV; date 12/6/2014.

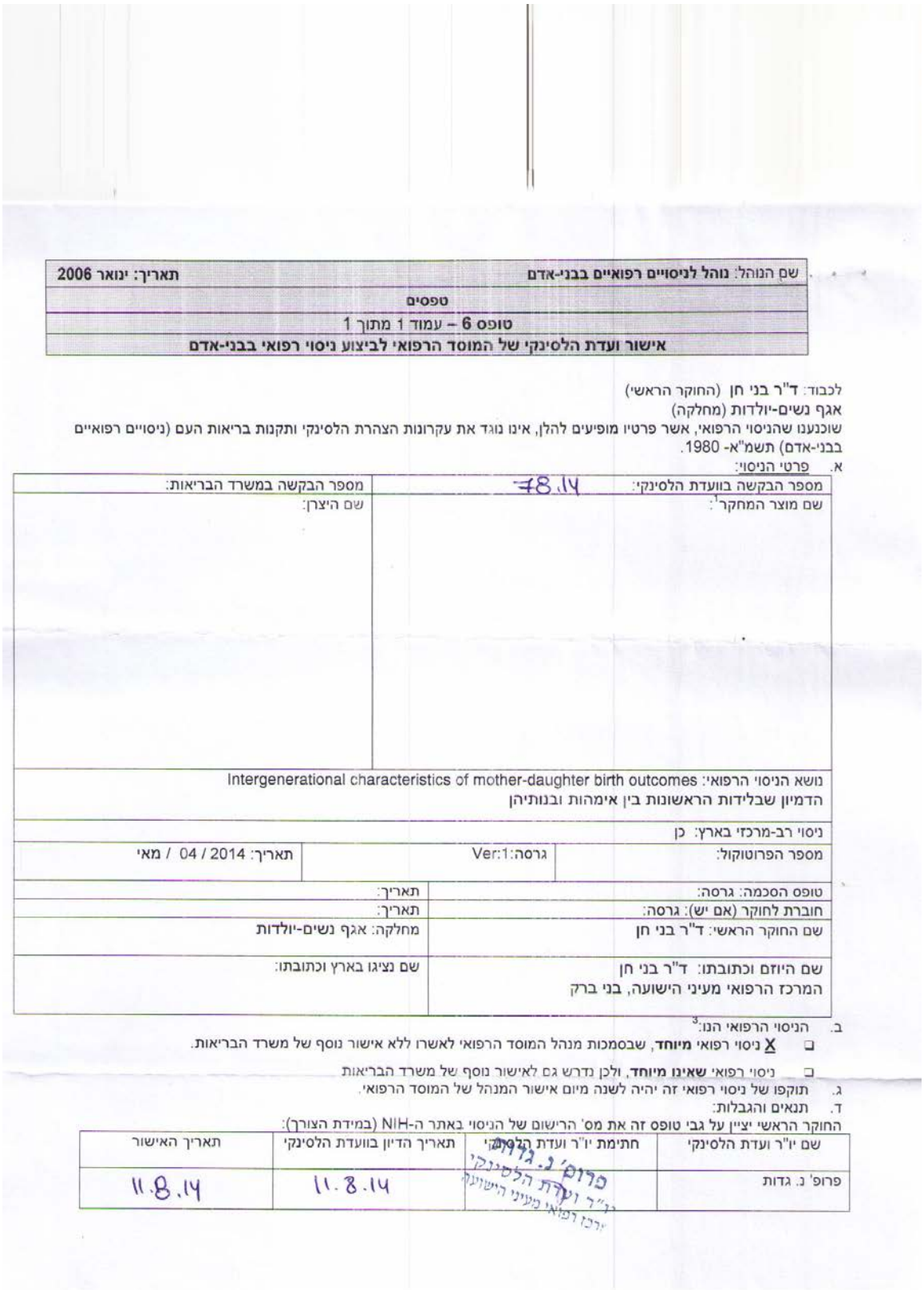
I, Professor Ariel Many - the principal investigator – together with the Helsinki Ethics Committee, Sourasky Medical Center, provide authorization and approval for Mindy Ebrahimoff to carry out research as the co-investigator.
The study is being conducted at the Sourasky Medical Center. Questionnaires are to be distributed in the ante-natal follow-up day clinic to prima-gravidas nearing term. Mothers and sisters of primi-gravidas will receive questionnaires via daughter/sister or by post. Birth records of parturients, mothers and sisters will be accessed via the hospital archives wherever possible. Information obtained during the research will be protected from disclosure.
The Helsinki Ethics Committee at the Souraski Medical Center agrees that standards are in compliance with Helsinki regulations for the Protection of Human Subjects. There are no known risks associated with this research. Any information obtained during this study that could identify participants will be kept strictly confidential. The results obtained from the research will be published in a dissertation, and may be published in medical journals or presented at professional meetings.
The research will continue until enough participants have been recruited for the assessment and analysis of significant results.

Please don't hesitate to contact me for any further information.
Yours sincerely,

Professor Ariel Many
Head of Labour and Delivery
Lis Maternity Hospital
Sourasky Medical Center, Tel Aviv.

6, Weizman St., Tel-Aviv 64239 Tel. 972-3-6974444 Fax. 972-3-5469580 פקס. 03-6974444 :רח' ויצמן 6, תל-אביב 64239 טל'
www.tasmc.org.il/lis

Ma’ayney Maternity Hospital Helsinki ethics approval



שם הנוהל: **נוהל לניסויים רפואיים בבני-אדם**	**תאריך: ינואר 2006**
טפסים	
טופס 6 – עמוד 1 מתוך 1	
אישור ועדת הלסינקי של המוסד הרפואי לביצוע ניסוי רפואי בבני-אדם	

לכבוד: ד"ר בני חן (החוקר הראשי)
אגף נשים-יולדות (מחלקה)
שוכנענו שהניסוי הרפואי, אשר פרטיו מופיעים להלן, אינו נוגד את עקרונות הצהרת הלסינקי ותקנות בריאות העם (ניסויים רפואיים בבני-אדם) תשמ"א- 1980.

א. פרטי הניסוי:

מספר הבקשה בוועדת הלסינקי: 78.14	מספר הבקשה במשרד הבריאות:
שם מוצר המחקר[1]:	שם היצרן:
נושא הניסוי הרפואי: Intergenerational characteristics of mother-daughter birth outcomes הדמיון שבלידות הראשונות בין אימהות ובנותיהן	
ניסוי רב-מרכזי בארץ: כן	
מספר הפרוטוקול:	גרסה: Ver:1 תאריך: 04 / 2014 / מאי
טופס הסכמה: גרסה:	תאריך:
חוברת לחוקר (אם יש): גרסה:	תאריך:
שם החוקר הראשי: ד"ר בני חן	מחלקה: אגף נשים-יולדות
שם היוזם וכתובתו: ד"ר בני חן המרכז הרפואי מעיני הישועה, בני ברק	שם נציגו בארץ וכתובתו:

ב. הניסוי הרפואי הנו:[3]
☐ X ניסוי רפואי **מיוחד**, שבסמכות מנהל המוסד הרפואי לאשרו ללא אישור נוסף של משרד הבריאות.
☐ ניסוי רפואי **שאינו מיוחד**, ולכן נדרש גם לאישור נוסף של משרד הבריאות.

ג. תוקפו של ניסוי רפואי זה יהיה לשנה מיום אישור המנהל של המוסד הרפואי.

ד. תנאים והגבלות:
החוקר הראשי יציין על גבי טופס זה את מס' הרישום של הניסוי באתר ה-NIH (במידת הצורך):

שם יו"ר ועדת הלסינקי	חתימת יו"ר ועדת הלסינקי	תאריך הדיון בוועדת הלסינקי	תאריך האישור
פרופ' נ. גדות	פרופ' נ. גדות יו"ר ועדת הלסינקי המרכז הרפואי מעיני הישועה	11.8.14	11.8.14

שם הנוהל: **נוהל לניסויים רפואיים בבני-אדם**	**תאריך: ינואר 2006**
טפסים	
טופס 7 - עמוד 1 מתוך 2	
אישור מנהל המוסד הרפואי לביצוע ניסוי רפואי בבני-אדם	

תאריך: ~~30.07.2014~~ 11.8.14

לכבוד:

ד"ר בני חן _____ (החוקר הראשי)

אגף נשים-יולדות _____ (מחלקה)

פרופ'/ד"ר נכבד/ה,

הנדון: **אישור לביצוע ניסוי רפואי בבני-אדם**

מספר הבקשה בוועדת הלסינקי: 72.14	מספר הבקשה במשרד הבריאות:	מספר הרישום באתר ה-NIH: ניסוי קוסמטי-אין צורך
נושא הניסוי הרפואי: Intergenerational characteristics of mother-daughter birth outcomes הדמיון שבלידות הראשונות בין אימהות ובנותיהן		
שם מוצר המחקר[1]:	שם היצרן:	
מספר הפרוטוקול:	גרסה:	תאריך:
טופס הסכמה: גרסה: Ver 1	תאריך: 2014 / 04 / מאי	
חוברת לחוקר (אם יש): גרסה:	תאריך:	
שם החוקר הראשי: ד"ר בני חן	מחלקה: אגף נשים-יולדות	
שם היוזם וכתובתו: : ד"ר בני חן המרכז הרפואי מעיני הישועה, בני ברק	שם נציגו בארץ וכתובתו:	

בהתאם לבקשתך מיום: 30.7.14 ניתן בזה אישור מספר: 72.14, לביצוע הניסוי הרפואי לפי פרוטוקול הניסוי שצורף לבקשה.

בתוקף ההסמכה שקיבלתי מהמנהל הכללי של משרד הבריאות, לתת אישור כ"מנהל" לעשיית ניסוי רפואי בבני-אדם, במוסד הרפואי מעיני הישועה, לאחר שהבקשה אושרה על-ידי ועדת הלסינקי המוסדית בתאריך: 11.8.14 ולאחר שהבקשה אושרה על-ידי משרד הבריאות בתאריך: _____[2], ולאחר ששוכנעתי כי הניסוי הרפואי הנו בהתאם לעקרונות של הצהרת הלסינקי ותקנות בריאות העם (ניסויים רפואיים בבני-אדם) תשמ"א-1980, וכי חוזה ההתקשרות בין היוזם, החוקר הראשי והמוסד הרפואי עומד בדרישות הנוהל לניסויים רפואיים בבני אדם, הנני מאשר את ביצוע הניסוי בכפוף לתנאים הבאים

[1] מלא את הפרטים בהתאם לסוג מוצר המחקר; אם מדובר באמ"ר, יש לציין את שם האמ"ר והדגם.
[2] מחק את המיותר

שם הנוהל: **נוהל לניסויים רפואיים בבני-אדם**	**תאריך: ינואר 2006**
טפסים	
טופס 7 - עמוד 1 מתוך 2	
אישור מנהל המוסד הרפואי לביצוע ניסוי רפואי בבני-אדם	

תנאי האישור:

1) הניסוי הרפואי יבוצע לפי העקרונות של הצהרת הלסינקי ועל-פי דרישות הנוהל של ניסויים רפואיים בבני אדם בישראל (2005) ודרישות הנהלים הבין-לאומיים העדכניים.

2) הטיפול יינתן רק לאחר מתן הסבר למטופל/ת או לנציגו/ה החוקי והחתמתו/ה על טופס ההסכמה מדעת שצורף לבקשה.

3) כל שינוי, תוספת או סטייה מפרוטוקול הניסוי הרפואי, טעון אישור בכתב של ועדת הלסינקי של המוסד הרפואי ו/או של משרד הבריאות.

4) על החוקר הראשי בניסוי הרפואי לדווח לוועדת הלסינקי של המוסד הרפואי וליוזם על כל אירוע חריג רציני (SAE) שארע במהלך הניסוי הרפואי (כמפורט בסעיף 15.1.1 בנוהל), או על הפסקת הניסוי. ועדת הלסינקי המוסדית תבדוק את הדיווח ותעביר את חוות-דעתה למשרד הבריאות.

5) הארכת תוקף הניסוי הרפואי: **חודשיים בטרם חלוף התקופה המאושרת לניסוי הרפואי**, חובה על החוקר הראשי להעביר דו"ח **התקדמות** על מהלך הניסוי לוועדת הלסינקי של המוסד הרפואי. הוועדה תודיע על החלטתה לגבי המשך הניסוי למנהל המוסד הרפואי. המנהל ינפיק אישור חדש לניסוי הרפואי.

6) בתום הניסוי הרפואי יגיש החוקר הראשי, לוועדת הלסינקי דו"ח מסכם על מהלך הניסוי ותוצאותיו.

7) האישור ניתן לחוקר הראשי ולמוסד הרפואי המצוינים לעיל ואינו ניתן להעברה לאחר.

8) בניסויים רפואיים הכרוכים במתן שירותים: ביצוע בדיקות רפואיות או באספקת אביזרים, תכשירים רפואיים או משתלים, חובה על החוקר הראשי להודיע לרופא המטפל בחולה בקהילה על השתתפותו בניסוי.

9) אין לפרסם כל מידע אודות הניסוי הרפואי באמצעי התקשורת ההמוניים, כגון עיתונות, רדיו, טלוויזיה, אינטרנט, למעט פרסום בעיתונות מדעית או בכנסים מדעיים, ולמעט פרסום לצורך גיוס המשתתפים בניסוי.

10) אספקת מוצר המחקר (**Investigational Product – IP**) או האמ"ר למוסד הרפואי בו נערך הניסוי הרפואי היא באחריות יוזם הניסוי. אחסונו וניפוקו של מוצר המחקר למטופלים הם באחריות החוקר הראשי. במקרים של תכשירים רפואיים, פעולות אלו יבוצעו באמצעות בית המרקחת המוסדי, אלא אם כן ועדת הלסינקי החליטה אחרת.

11) אספקת תכשירים רפואיים הרשומים בישראל תעשה באמצעות בית-המרקחת המוסדי.

12) שמירת מסמכים: יש לשמור את כל מסמכי הבקשה, האישורים וכל המסמכים הנאספים במהלך הניסוי הרפואי **לפחות 15 שנים מתום הניסוי**.

13) הגבלות נוספות: _____

_____

_____

14) תוקף האישור: _____

בהצלחה!

בכבוד רב,
מנהל המוסד הרפואי

העתק: יו"ר ועדת הלסינקי המוסדית: פרופ' נ. גדות
מנהל/ת בית המרקחת של המוסד הרפואי: ד"ר חגי רדוצקי
היוזם/נציגו בארץ (באמצעות החוקר): שם היצרן:

University of Central Lancashire

UNIVERSITY OF CENTRAL LANCASHIRE
Ethics Committee Application Form

PLEASE NOTE THAT ONLY ELECTRONIC SUBMISSION IS ACCEPTED

This application form is to be used to seek approval from one of the three University Ethics Committees (BAHSS; PSYSOC & STEMH). Where this document refers to 'Ethics Committee' this denotes BAHSS; PSYSOC & STEMH (see Appendix 1 for list of Schools associated with each ethics committee). These Ethics Committees deal with all staff and postgraduate research student project. Taught (undergraduate and MSc dissertation projects) will normally be dealt with via School process / committee.

If you are unsure whether your activity requires ethical approval please complete an UCLan Ethics Checklist. If the proposed activity involves animals, you should not use this form. Please contact the Research Development and Support Team within Research & Innovation Office – roffice@uclan.ac.uk – for further details.

Please read the Guidance Notes before completing the form. Please provide all information requested and justify where appropriate. Use as much space as you need – the sections expand as you type. Click on box or circle to select relevant option (e.g. type or Yes/No) and click on 'grey oblong shape' to start typing for the free text entry questions. Each question on this form has instructions on how to answer that particular question. In addition links to relevant documents (e.g. templates, examples, etc.) and further guidelines are available in the Guidance Notes which can also be access from the question by clicking on appropriate question number. It is the applicant's responsibility to ensure that an English translation of any supporting documentation is a faithful translation of the copy being used with participants.

Your application needs to be filled in electronically and emailed to roffice@uclan.ac.uk. Please insert in the subject line of your email the acronym of the committee that needs to deal with your application. Committee acronyms are BAHSS, PSYSOC or STEMH – see Appendix 1, at the back of this form, for list of Schools associated with each ethics committee.

PLEASE NOTE – ethical approval can be granted in **phases**. If you have a project that is likely to evolve, or has subsequent phases determined by initial results – you can apply for Phase One approval, and then come back for Phases Two, Three or even more as your research progresses.

If this application relates to an activity which has previously been approved by one of the UCLan Ethics Committees, please supply the corresponding reference number(s) from your decision letter(s).

Section 1
DETAILS OF PROJECT

All applicants must complete Section 1

1.1 **Project Type:**		
☐ Staff Research ☐ Commercial Project	☐ Master by Research ☑ MPhil Research ☑ PhD Research ☐ Professional Doctorate	☐ Taught MSc/MA Research ☐ Undergrad Research ☐ Internship
1.2 **Principal Investigator:**		
Name: Dr. Victoria Hall-Moran (DoS)	School: Health UCLAN	Email: VLMoran@uclan.ac.uk
	Choose an item.	
1.3 **Other Researchers / Student:**		
Name: Mindy Ebrahimoff	School : Health	Email: mindyebb@gmail.com
Prof. Soo Downe (advisor)	Health	SDowne@uclan.ac.uk
	Choose an item.	
	Choose an item.	
Prof. Ariel Many (on site investigator)	Sourasky Medical Center, Tel Aviv, Israel,	arielm@tasmc.health.gov.il

1.4 **Project Title: Inter and intra-generational similarities in labour and childbirth: an observational cohort study**		
Intergenerational characteristics of mother-daughter birth outcomes		
1.5 **Anticipated Start Date:**		
10/08/2014		
1.6 **Anticipated End Date:**		
10/08/2016		
1.7 **Is this project in receipt of any external funding** (including donations of samples, equipment etc.)?		
○ Yes ◉ No		
If Yes, *please provide details of sources of the funding and what part it plays in the current proposal.*		
1.8 **Project Description** (in lay's terms) including the aim(s) and justification of the project (max 300 words)		
PURPOSE To explore physiological birthing inheritance through examination of intergenerational associations between biological mother/daughter and sisters - first birth experiences. **AIM** To establish the value and feasibility of constructing a labour and birth prediction model for nulliparous women based on the birth accounts of their mothers and sisters.		

OBJECTIVES

5. To establish the degree of association in gestation at onset of labour, length of labour, infants birth-weight, and mode of birth between participating women and their mothers and sisters
6. To establish the congruence between the recall of these birth parameters for the mothers and sisters of nulliparous women, and the data recorded in their clinical case-notes.
7. To explore potential predictive models for these parameters for nulliparous women based on the outcomes of their mothers and sisters.
8. To assess the feasibility of a subsequent multi-site study to validate the models developed in objective 3.

CONTEXT AND SETTING

The Lis Maternity Hospital had 11,239 deliveries in 2010. 41.9% of all deliveries were primiparous women (n=4709), which is considerably higher than the national statistic of 31.7% (Israel Central Bureau of Statistics, 2010). According to the Israeli Association of Obstetrics and Gynecology, more than 99% of all births in Israel occur in hospitals (Kupermintz, 2005).
Thus the chosen "site" is well suited to host the research aims.

PHASES

This study will be conducted in two phases:

1) A systematic review of the literature on the maternal recall (MR) of birth events will be supported by a current research survey of the MR of mothers of index women. Memories of their birth experiences will be compared to hospital records.
2) Exploration of inter-generational mother/daughter patterns of labour and delivery. Index women (and their sisters if relevant) will have their first birthing outcomes compared with their mothers' first birth outcomes.

1.9 **Methodology** Please be specific

Design: A cohort study

Participants: All consecutive eligible consenting women over the research period.

Number of women who may be available for recruitment

The annual birth rate in the Lis Maternity Hospital was 11,239 in 2010. 4,709 (41.9%) were primiparous deliveries. Based on the power calculations below, I estimate that I need to recruit 1,800 primipara women over a period of two years. I assume that approximately 70% of these women will be eligible (n=approx 1260). I estimate that approximately 70% will demonstrate an initial interest (n= approx 882) and approx 70% of these will give consent (approx 620 index women and 620 mothers). I estimate that half of these index mothers will have at least one parous sister (n=310 sisters). If more than one sister has had a baby before the index woman, data will be collected on all the sisters who consent, and one of them will be selected randomly for the analysis.

Inclusion criteria at the time of seeking consent

Nulliparous women:

- **above 32 weeks**
- **baby is a singleton and a cephalic presentation**
- **mother and baby have no contraindications to spontaneous onset of labour, labour progress, and birth**
- **who consent to inclusion**
- **whose genetic mother and/or sister(s) consent to inclusion**

with mothers who:

- **are genetically related to the index woman**
- **consent to inclusion**

and/or sisters who:

- **are genetically related to the index woman**
- **have had at least one baby**
- **consent to inclusion**

Procedures

7. The research midwife (RM) will approach all eligible nulliparous women attending the follow-up day care center at the Lis Maternity Hospital. The nulliparous woman who agrees to take part in the study will be known as the “index woman”.
8. If the index woman has a biological mother (and also a biological sister/s) who she thinks will be keen to participate in the study, the RM will record the date, index woman’s name, phone number and email address on a prepared log sheet, in order to keep track of potential participants and non-returns.
9. Recruitment of index women is not dependent on consent from the mothers/sisters at this point.
10. The RM will enquire whether the index woman or her mother/sister need help

understanding Hebrew. The RM (mother tongue – English) will offer verbal aid with translation of questionnaires into English (on site) if necessary. Any other language difficulty will exclude the index woman and her family members from the study.

11. The index woman will be given an information sheet about the study and will be asked to complete a consent form and questionnaire on site/or at home (available only in Hebrew), and will be asked to distribute questionnaires to her mother/sister (available only in Hebrew). Participating mothers/sisters will find an explanation about the study and a request for signed consent to participate - prior to completing the questionnaire.
9. Questionnaires will be returned in the sealed envelopes provided, either at a subsequent visit by the index woman to the ante-natal follow-up day care center at the Lis Maternity Hospital, or by freepost. Return – together with signed consent - will be deemed to be consent for inclusion in that element of the study.
10. The research midwife will follow up non-returns by phone/email using contact information from the log sheet three weeks after initial contact.
11. The RM may later contact the participant/s by phone or email in the event that handwriting is illegible and there is a need to clarify information.
12. The RM will offer verbal aid with translation of questionnaires into English for mothers/sisters (visit/call).
13. The questionnaire data will be double entered on to the database, and accuracy checks will be undertaken on a 10% sample.
14. The research midwife will locate and collect data from the mothers and sisters case-notes wherever possible, and these will also be double entered, and checked for accuracy.
15. After the labour and birth of the index mother, the research midwife will collect data from her case-notes, and these data will also be double entered and checked for accuracy.
16. Data analysis will take place

Analytic strategy

1. Accuracy of recalled data on birth outcomes

The level of agreement between recall and clinical records will be plotted visually on a scatter plot, and then compared using the kappa statistic. Exploratory analysis of possible associations between mothers and sisters data will be undertaken separately. Sub-analysis will stratify the data by the age, parity, ethnicity, and time since first birth of the respondent.

2. Similarity of birth outcomes between relatives, and exploratory modelling

Within pair (participant-mother, participant-sister) comparison of:

a) Completed days of gestation at onset of labour (based on agreed EDD from certain LMP, a dating scan, or, where these are not available, on best estimate)

b) Time in labour from diagnosis of active labour to birth, in hours

c) Infant birth-weight in grammes

d) Mode of birth (normal birth with no intervention vs other)

Scatter plots, descriptive data, and multiple regression analyses will be utlised for analysis of a) to d) above. The independent variables will include the age, ethnicity (White Israeli or other), and Jarman (socio-demographic) score of the index woman and of her relatives. Odds ratios and CI for odds will be calculated.

Note will be made of stillbirths and of perinatal mortality and of abnormality/ severe morbidity in the mother or neonate. It is unlikely that the numbers will be large enough for analysis at this stage, but we will examine these data descriptively for any evident patterns, and for consideration for addition to the models for future testing/calculation of power for future studies. This approach will also be used for the data relating to the lead professional and to extant labour management policies and guidelines.

Power

Sample size calculations were done in NQuery Adviser, using a range of plausible scenarios.
A sample of size 500 should be adequate to produce a 1-sided 95% confidence interval on a kappa statistic (to measure agreement) to a tolerance of 0.05 for a continuous or dichotomised variable (if the prevalence is between 0.3 and 0.5), assuming a kappa of at least 0.8.
A sample size of 500 is adequate to compute a 1-sided 95% confidence interval for a correlation coefficient to a tolerance of 0.07 assuming a correlation of at least 0.2. This sample size should therefore be sufficient to estimate the association between continuous variables (index mother/mother or index mother/sister pairs), and also for a multiple linear regression taking into account the other predictors.

For the dichotomised variable (assuming a prevalence of about 40%), a one-sided 95.0% confidence interval for an expected odds ratio of 1.455 will extend to a lower confidence limit of 1.068 when the sample sizes are 200 and 300, respectively, a total sample size of 500. Although this sample size would not be adequate for odds ratios less than this, the cumulative evidence from each of the analyses should be sufficient to assess the feasibility of a larger study.

Ethical considerations

Official registration of this research will be subject to ethics approval from the institutional Helsinki Ethics Committee of the Tel Aviv Sourasky Medical Center - Israel, and the UCLan Ethics Committee of the School of Health, UK.
Participants will receive an information sheet prior to completing the questionnaire, asking them to sign consent and ensuring confidentiality by the use of a coding system.
All identifiable data (paper) will be kept in a locked cabinet in a locked office, accessible only to the research team with a password allowing access to electronic data.
Disclosure: **Data will be collected. The names of the participants will be available to the principal investigator and co-investigator and will be made available for use only after a coded password and username is allocated to each participant. The data file will not be sent electronically without encryption and will not leave the premises. The results obtained from**

the research will be published in a dissertation, and may be published in medical journals or presented at professional meetings.

1.10 **Has the quality of the activity been assessed**? (select all that apply)

- [x] Independent external review
- [ ] Internal review (e.g. involving colleagues, academic supervisor, School Board
- [x] Through Research Degrees Sub-Committee (BAHSS, STEM or SWESH)
- [ ] None
- [ ] Other

Independent external review:

Signed templates in English attached from the Helsinkli Ethics Committee – The Sourasky Medical Center, TA, Israel (the intended research site), and a supporting letter from the principal investigator Prof. A. Many.

1.11 **Please provide details as to the storage and protection for your data for the next 5 years** – as per UCLan requirements

The principal investigator will ensure that data will be stored using appropriate security measures (a locked cabinet in a locked office) according to the data protection protocols of the Helsinki Ethics Committee, The Sourasky Medical Center, TA, Israel. The records will be retained for at least 5 years after the completion of the research and disposed of according to data disposal protocols.

The names of the participants will be available to the principal investigator and co-investigator and will be made available for use only after a coded password and username is allocated to each participant. The data file will not be sent electronically without encryption and will not leave the premises. The data will be processed on a Sourasky Medical Center password protected computer. The reason for this is that statistical analysis of large data sets held remotely is likely to be prohibitively slow.

1.12 **How is it intended the results of the study will be reported and disseminated**?

(select all that apply)

☑ Peer reviewed journal

☐ Internal report

☑ Conference presentation

☑ Other publication

☐ Written feedback to research participants

☐ Presentation to participants or releveant community groups

☑ Dissertation/Thesis

☐ Other

If other, please give details

1.13 **Will the activity involve any external organisation for which separate and specific ethics clearance is required** (e.g. NHS; school; any criminal justice agencies including the Police, Crown Prosecution Service, Prison Service, Probation Service or successor organisation)?

◉ Yes ○ No

If Yes, please provided details of the external organisation / ethics committee and attached letter of approval

NB – external ethical approval **must** be obtained before submitting to UCLan ethics.

Principles for clinical investigations

The Tel Aviv Sourasky Medical Center Institutional Review Board (Helsinki Committee) complies with the following regulations:

- Ministry of Israel public health regulations (Medical Experiments in Human Subjects of 1980) including the most recent additions and amendments through 2006
- The Pharmacological Unit of the Ministry of Health regulations for conducting medical trials on Humans of 1999.
- The provisions of the current International Conference on Harmonization Guidelines for Good Clinical Practice (ICH-GCP). For the formal ICH-GCP declaration

Sourasky Medical Center Helsinki Ethics committee, TA, Israel. Signed English templates attached.

1.14 **The nature of this project is most appropriately described as research involving:-** (more than one may apply)

- ☐ Behavioural observation
- ☑ Self-report questionnaire(s)
- ☐ Interview(s)
- ☐ Qualitative methodologies (e.g. focus groups)
- ☐ Psychological experiments
- ☐ Epidemiological studies
- ☐ Data linkage studies
- ☐ Psychiatric or clinical psychology studies
- ☐ Human physiological investigation(s)
- ☐ Biomechanical devices(s)
- ☐ Human tissue
- ☐ Human genetic analysis
- ☐ A clinical trial of drug(s) or device(s)
- ☐ Lab-based experiment
- ☐ Archaeological excavation/fieldwork
- ☐ Re-analysis of archaeological finds/ancient artefacts
- ☐ Human remains analysis
- ☑ Other (please specific in the box below)

If 'Other' please provide details

:Labour and birth hospital records

Please read all the following questions carefully and if you respond 'Yes' then you should provide all relevant details and documentation (including risk assessments), and justify where appropriate.

Section 2
HUMAN PARTICIPANTS, DATA OR MATERIAL

2.1 **Are you using human participants (including use of their data), tissues or remains**?	
(please select the appropriate box)	
☑ Participants [proceed to question 2.2]	Click here for Q2.20
☑ Data [proceed to question 2.20]	
☐ Tissues / Fluids / DNA Samples [proceed to question 2.20]	Click here for Q2.24
☐ Remains [proceed to question 2.24]	
☐ No [proceed to Section 3]	Click here for Section 3

2.2 **Will the participants be from any of the following groups:**
(tick as many as applicable)
☐ Students or staff of this University
☐ Children/legal minors (anyone under the age of 18 years)
☐ Patients or clients of professionals
☐ Those with learning disability
☐ Those who are unconscious, severely ill, or have a terminal illness
☐ Those in emergency situations
☐ Those with mental illness (particularly if detained under Mental Health Legislation)
☐ People with dementia
☐ Prisoners

☐ Young Offenders

☐ Adults who are unable to consent for themselves

☐ Any other person whose capacity to consent may be compromised

☐ A member of an organisation where another individual may also need to give consent

☐ Those who could be considered to have a particularly dependent relationship with the investigator, e.g. those in care homes, medical students

☑ Other vulnerable groups (please list)

2.2a **Justify their inclusion**

Other: pregnant and birthing women, their sisters/mothers

In order to establish whether labour and birth characteristics are repeated in families

I, the research midwife (RM) am the sole distributor of questionnaires and information. Any woman incapable of consent will not be approached /included.

There are no other vulnerable groups other than index women, and their mothers/sisters. Any included women index/mother/sister – MUST sign independent consent forms to participate. If any one participant (in the family) has not signed consent, the entire family group will be excluded.

2.2b **Is a** DBS **– Disclosure and Barring Service (formerly CRB – Criminal Records Bureau) check required?**

Certain activities and/or groups of individuals require DBS (formerly CRB) clearance.

○ Yes ○ No

If Yes, please advise status of DBS clearance (e.g. gained; in process; etc)

2.3 **Please indicate exactly how participants in the study will be (i) identified, (ii) approached and (iii) recruited**?

N.B if a recruitment advertisement is to be used, please attach

State how you will identify, approach and recruit participants including how you will ensure no coercion will be used in your recruitment.

1. The research midwife (RM) will approach eligible nulliparous women attending the follow-up day care center at the Lis Maternity Hospital, and give a short explanation about the nature of the research.

2. If the index woman is interested in taking part and has a biological mother (and an eligible sister/s) who she thinks will be keen to participate, she will be asked to complete a questionnaire (either on site or at

home).

3. The index woman will be asked to distribute the labour and birth history questionnaire to her mother and, if relevant – sister/s.

4. The questionnaire/s will be returned in the sealed envelope provided to the follow-up day care center at the Lis Maternity Hospital at a subsequent visit or by freepost.

5. The RM may later contact the participants by phone or email to follow up non returns and/or in the event that handwriting is illegible and there is a need to clarify information.

2.4 **Will consent be sought from the participants and how will this be obtained**?

YES

Participants – index women/mothers/sisters - will be asked to sign a consent form. This precedes the questionnaire (sample below).

(Consent form and Questionnaires attached)

A standard consent form, authorised by Helsinki Ethics Committee/Sourasky Medical Centre TA, precedes the questionnaire and includes the details listed below:

A short description of what will be required of the participants (see PIS & questionnaire attached), and the following statements:

1) which addresses confidentiality and security of information, 2) details of who will have access to personal information, 3) a statement that participation in the research is completely voluntary, 4) a statement about any potential risks, harms and benefits to participants, 5) the contact details (mobile phone number) of the investigator/s and supervisor should the participant require further information.

Title of project	Intergenerational characteristics of mother-daughter birth outcomes
Aims of the project	To establish whether labour and birth characteristics are repeated in families
Name of researcher Contact details (phone number and email address)	Mindy Ebrahimoff 0545-401090 mindyebb@gmail.com
Statements of confirmation by the participant	I have been informed of and understand the purposes of the study
	I have been given an opportunity to ask

	questions
	I understand I can withdraw at any time without prejudice
	Any information which might potentially identify me will not be used in published material
	I agree to participate in the study as outlined to me

Name of participant.....

Signature.....

Date.....

(A copy of the consent form and participant information sheet is retained by the research participant. Signed consent forms will be stored securely by the researcher).

2.5 **What information will be provided at recruitment and briefing to ensure that consent is informed**?

Please see attached consent forms and questionnaires

2.6 **How long will the participants have to decide whether to take part in the research**?

A follow-up ante natal visit can take anything from 45 minutes to two or three hours during which time the participant will decide. She may take the questionnaire home for completion and return it at a later ante natal follow-up visit, or not return it at all.

2.7 **What arrangements have been made for participants who might not adequately understand verbal explanations or written information given in English, or who have special communication needs**?

Gives details of what arrangements have been made (e.g. translation, use of interpreters, etc).

Questionnaires are in Hebrew (for use in Israel only). No official/funded translation service into other languages will be available. The RM (mother tongue – English) will offer verbal aid with

translation of questionnaires into English (on site for index women). The RM will offer verbal aid (via the index woman) with translation of questionnaires into English for mothers/sisters (visit/call).

2.8 **Payment or incentives: Do you propose to pay or reward participants**?

○ Yes ◉ No

If Yes, please provided details

2.9 **Does the activity involve conducting a survey, interviews, questionnaire, observational study, experiment, focus group or other research protocol**?

◉ Yes ○ No

If Yes, please provide details and attach copy of what you will be using

Give details of the specific procedures/activities being used and indicate where documentation (i.e. questionnaire or agendas) will be developed as part of the project. Also include what is the experience of those administering the procedures

Questionnaires have been developed and approved by the principal investigator and co-investigator , DoS and advisor. Attached - copy of questionnaires

2.10 **Will deception of the participant be necessary during the activity**?

○ Yes ◉ No

If Yes, please provide justification

Gives details of the deception and explain why the deception is necessary.

2.11 **Does the activity (e.g. Art) aim to shock or offend**?

○ Yes ◉ No

If yes, please explain

Give details, justify and what measures are in place to mitigate.

2.12 **Does your activity involve the potential imbalance of power/authority/status, particularly those which might compromise a participant giving informed consent**?

○ Yes ◉ No

If Yes, please detail including how this will mitigated

Describe the relationship and the steps to be taken by the investigator to ensure that the participant's participation is purely voluntary and not influenced by the relationship in any way.

2.13 **Does the procedure involve any possible distress, discomfort or harm (or offense) to participants or researchers** (including physical, social, emotional, psychological)?

○ Yes ◉ No

No more than minimal risk - the probability and magnitude of harm or discomfort anticipated due to the research questionnaire are not greater than those ordinarily encountered during performance of routine physical or psychological examination tests e.g. annual gynaecological exam. However, in the introductory letter to the mother/sister questionnaire – provision for free women's mental health services has been supplied.

2.14 **Does the activity involve any information pertaining to illegal activities or materials or the disclosure thereof**?

○ Yes ◉ No

If Yes, please detail

2.15 **What mechanism is there for participants to withdraw from the investigation and how is this communicated to the participants**?

*Describe exactly how, and when, participants may withdraw if they change their minds about taking part including how participants **know** they have the right to withdraw.*

A standard consent form, authorised by Helsinki Ethics Committee/Sourasky Medical Centre TA, precedes the questionnaire and includes the details listed below:

A short description of what will be required of the participants (see PIS & questionnaire attached), and the following statements:

1) which addresses confidentiality and security of information, 2) details of who will have access to personal information, 3) a statement that participation in the research is completely voluntary, 4) a statement about any potential risks, harms and benefits to participants, 5) the contact details (mobile phone number) of the investigator/s and supervisor should the participant require further information.

Title of project	Intergenerational characteristics of mother-daughter birth outcomes
Aims of the project	To establish whether labour and birth characteristics are repeated in families
Name of researcher Contact details (phone number and email address)	Mindy Ebrahimoff 0545-401090 mindyebb@gmail.com
Statements of confirmation by the participant	I have been informed of and understand the purposes of the study
	I have been given an opportunity to ask questions
	I understand I can withdraw at any time without prejudice
	Any information which might potentially identify me will not be used in published material
	I agree to participate in the study as outlined to me

Name of participant.....

Signature.....

Date.....

(A copy of the consent form and participant information sheet is retained by the research participant. Signed consent forms will be stored securely by the researcher).

2.16 **What is the potential for benefit**?

To explore the genetic effects of a first childbirth. It is possible that cross-generational associations in labour and childbirth are indicators of true pathology that could be predicted and prevented late in pregnancy or early in labour. Equally, familial tendency may be indicative of a physiological factor that is at the extreme end the range of normal.

2.17 **What arrangements are in place to ensure participants receive any information that becomes available during the course of the activity that may be relevant to their continued participation**?

Describe how participants will be made aware of relevant information that was not available when they started.

N/A

2.18 **Debriefing, Support and/or Feedback to participants**

Describe any debriefing, support or feedback that participants will received following the study and when.

N/A

2.19 **Adverse / Unexpected Outcomes**

Please describe what measures you have in place in the event of any unexpected outcomes or adverse effects to participants arising from their involvement in the project

N/A

2.20 **Will the activity involve access to confidential information about people without their permission**?

○ Yes ◉ No

If yes, please explain and justify

State what information will be sought, from which organisations and the requirement for this information.

2.21 **Does the activity involve human tissue?** See Human Tissue Act (HTA) Supplementary list of Materials to check what is classified as human tissue.

○ Yes ◉ No

If no, please skip to question 2.22

If yes, please detail and answer questions 2.21a & 2.21b

Clearly state the source of the material (a tissue bank governed by its own HTA licence such as Brain Tumour North West, or purchased from overseas, etc.)

2.21a **Will the human tissue be stored at UCLan?**

○ Yes ○ No

If yes, please state how long and in what form - cellular or acellular (DNA extracted)

Please note – if human tissue is only kept for the purpose of DNA extraction rendering it acellular the HTA storage regulations may not apply. If holding for DNA extraction, please state the length of time the tissue would be stored pre-extraction.

2.21b **Is the human tissue being used for an activity listed as a 'scheduled purpose' under Schedule 1 Parts 1 and 2 of the Human Tissue Act 2004?** *(click here to see list of HTA 'scheduled purpose' activities)*

○ Yes ○ No

2.22 **Confidentiality/Anonymity** - Will the activity involve:

	Yes	No
a. non-anonymisation of participants (i.e. researchers may or will know the identity of participants and be able to return responses)?	◉	○
b. de-identified samples or data (i.e. a reversible process in which the identifiers are removed and replaced by a code. Those handling the data subsequently do so using the code. If necessary, it is possible to link the code to the original identifiers and identify the individual to whom the sample or information relates)?	◉	○
c. participants having the consented option of being identified in any publication arising from the research?	○	◉

d. the use of personal data (i.e. anything that may identify them – e.g. institutional role – see DP checklist for further guidance)?	◉	○

*If **yes to any** proceed to question below*

*If **no to all**, please skip to question 2.24*

2.23 **Which of the following methods of assuring confidentiality of data will be implemented**? (Please select all relevant options)

N.B. Please attach completed DP Checklist (click here to see further DP advice)

☑ data and codes and all identifying information to be kept in separate locked filling cabinets

☑ access to computer files to be available by password only

☐ other

CHECK LIST

Participants are aware of:

1) The uses of the information gathered

2)Disclosures

3) Reasons for consent

4) Purpose for which the information is kept

5) Security provisions/ data protection/confidentiality

6) Clear statement on how long Information will be retained

7) Deletion/disposal of data after completion of the research

8) Project co-ordinator contact details supplied for queries or complaints

2.24 **Does the activity involve excavation and study of human remains**?

○ Yes ◉ No

If yes, please give details

Discuss the provisions for examination of the remains and the management of any community/public concerns, legal requirement etc.

Section 3
BIOLOGICAL ORGANISMS/ENVIRONMENT

3.1 **Does the activity involve micro-organisms, genetic modification or collection of rare plants**?
○ Yes ○ No
If yes please provide further details below *State the type and source of the samples to be used in the project and include compliance with relevant legislation.* *If no please continue section 4*

Section 4
HAZARDOUS SUBSTANCES

4.1 **Does the activity involve any hazardous substances**?
○ Yes ○ No
If yes please continue *If no please continue to section 5*
4.2 **Does the activity involve igniting, exploding, heating or freezing substances**?
○ Yes ○ No
4.3 **Does the activity involve substances injurious to human or animal health or to the environment**?
○ Yes ○ No
4.4 **Are you using hazardous chemicals**?
○ Yes ○ No
*If **Yes to any** please attach all relevant COSHH (single substance OR multi/complex substance) and/or risk assessment forms* N.B. Please address issues of quantity involved, disposal and potential interactions as well as a thorough evaluation of minimisation of risk

Section 5
OTHER HAZARDS

5.1 **Does the activity relate to military equipment, weapons or the defence industry**?
○ Yes ○ No
If yes please provide details and attach relevant permissions and risk assessments. Describe the hazard, clearly explaining the risks associated and specify how you will minimise these *If no please continue*
5.2 **Does the activity relate to the excavation of modern battlefields, military installations etc**?
○ Yes ○ No
If yes please provide details and attach relevant permissions and risk assessments. Discuss the provisions for examination and the management of any community/public concerns, legal requirement, associated risks, etc. *If no please continue*

Section 6
FIELDWORK/TRAVEL

6.1 **Does the activity involve field work, lone working or travel to unfamiliar places**?
○ Yes ○ No
If yes, answer the following questions *If no, go to Section 7*
6.2 **Where will the activity be undertaken**?
N.B. If your work involves field work or travel to unfamiliar places (e.g. outside the UK) please attach a risk assessment specific to that place *Give location(s) details (e.g. UCLan campus only)*
6.3 **Does the activity involve lone working**?
○ Yes ○ No
If yes please provide further details below and attach a completed risk assessment form *Describe the lone working element, clearly explaining the risks associated and specify how you will minimise these*
6.4 **Does the activity involve children visiting from schools**?
○ Yes ○ No

If yes please provide further details below and attach a completed risk assessment form *Describe the nature of the visit, clearly explaining the risks associated and specify how you will minimise these*

Section 7
ETHICAL AND POLITICAL CONCERNS

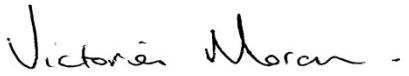
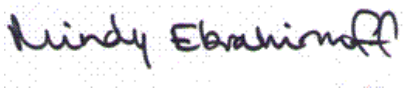
7.1 **Are you aware of any potential ethical and/or Political concerns that may arise from either the conduct or dissemination of this activity** (e.g. results of research being used for political gain by others; potential for liability to the University from your research)?
○ Yes ◉ No
If yes please provide details below *If no please continue*
7.2 **Are you aware of any ethical concerns about collaborator company / organisation** (e.g. its product has a harmful effect on humans, animals or the environment; it has a record of supporting repressive regimes; does it have ethical practices for its workers and for the safe disposal of products)?
○ Yes ◉ No
If yes please provide details below *If no please continue*
7.3 **Are there any other ethical issues which may arise with the proposed study and what steps will be taken to address these**?
○ Yes ◉ No
If yes please provide details below *If no please continue*

Section 8
DECLARATION

This section needs to be signed by the Principal Investigator (PI), and the student where the study relates to a student project (for research student projects PI is Director of Studies and for Taught or Undergrad project the PI is the Supervisor). Electronic submission of the form is required to roffice@uclan.ac.uk. Where available insert electronic signature, if not a signed version of the submitted application form should be retained by the Principal Investigator.

Declaration of the:
◉ Principal Investigator
OR
◉ Director of Studies/Supervisor and Student Investigators
(please check as appropriate)
• The information in this form is accurate to the best of my knowledge and belief, and I take full responsibility for it.
• I have read and understand the University Ethical Principles for Teaching, Research, Knowledge Transfer, Consultancy and Related Activities.
• I undertake to abide by the ethical principles underlying the Declaration of Helsinki and the University Code of Conduct for Research, together with the codes of practice laid down by any relevant professional or learned society.
• If the activity is approved, I undertake to adhere to the study plan, the terms of the full application of which the Ethics Committee* has given a favourable opinion and any conditions of the Ethics Committee in giving its favourable opinion.
• I undertake to seek an ethical opinion from the Ethics Committee before implementing substantial amendments to the study plan or to the terms of the full application of which the Ethics Committee has given a favourable opinion.
• I understand that I am responsible for monitoring the research at all times.
• If there are any serious adverse events, I understand that I am responsible for immediately stopping the research and alerting the Ethics Committee within 24 hours of the occurrence, via roffice@uclan.ac.uk.
• I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of personal data.
• I understand that research records/data may be subject to inspection for audit purposes if required in future.
• I understand that personal data about me as a researcher in this application will be held by the University and that this will be managed according to the principles established in the Data Protection Act.
• I understand that the information contained in this application, any supporting documentation and all correspondence with the Research Ethics Committee relating to the application, will be subject to the provisions of the Freedom of Information Acts. The information may be disclosed in response to requests made under the Acts except where statutory exemptions

* Ethics Committee refers to either BBAHSSS, PSYSOC or STEMH

apply.	
• I understand that all conditions apply to any co-applicants and researchers involved in the study, and that it is my responsibility to ensure that they abide by them.	
• **For Supervisors/Director of Studies:** I understand my responsibilities as Supervisor/Director of Studies, and will ensure, to the best of my abilities, that the student investigator abides by the University's Policy on Research Ethics at all times.	
• **For the Student Investigator**: I understand my responsibilities to work within a set of safety, ethical and other guidelines as agreed in advance with my Supervisor/Director of Studies and understand that I must comply with the University's regulations and any other applicable code of ethics at all times.	
○ **Signature of Principal Investigator:** **or** ◉ **Supervisor or Director of Studies:**	
Print Name:	**Victoria Hall Moran**
Date:	**15/07/2014**
Signature of Student Investigator: Mindy Ebrahimoff UCLAN ID: G20487845	
Print Name: Mindy Ebrahimoff	
Date:	**15/07/2014**

9th September 2014

Victoria Moran and Mindy Ebrahimoff
School of Health
University of Central Lancashire

Dear Victoria & Mindy

Re: STEMH Ethics Committee Application
Unique reference Number: STEMH 255

The STEMH ethics committee has granted approval of your proposal application 'Intergenerational characteristics of mother-daughter birth outcomes'. Approval is granted up to the end of project date* or for 5 years from the date of this letter, whichever is the longer. It is your responsibility to ensure that

- the project is carried out in line with the information provided in the forms you have submitted
- you regularly re-consider the ethical issues that may be raised in generating and analysing your data
- any proposed amendments/changes to the project are raised with, and approved, by Committee
- you notify roffice@uclan.ac.uk if the end date changes or the project does not start
- serious adverse events that occur from the project are reported to Committee
- a closure report is submitted to complete the ethics governance procedures (Existing paperwork can be used for this purposes e.g. funder's end of grant report; abstract for student award or NRES final report. If none of these are available use e-Ethics Closure Report Proforma).

Please also note that it is the responsibility of the applicant to ensure that the ethics committee that has already approved this application is either run under the auspices of the National Research Ethics Service or is a fully constituted ethics committee, including at least one member independent of the organisation or professional group.

Yours sincerely

Gill Thomson

Vice Chair

STEMH Ethics Committee

* for research degree students this will be the final lapse date

NB - Ethical approval is contingent on any health and safety checklists having been completed, and necessary approvals as a result of gained.

Section 9
ACCOMPANYING DOCUMENTATION

Please indicate here what documentation you have included with your application:
☐ Proposal / protocol ☐ RDSC2 form – Application to Register for a Research Degree / Application for Research Programme Approval ☑ External ethics approval letter ☐ Letter of permission ☐ Participant consent form(s) ☐ Participant information sheet(s) ☐ Interview or observation schedule ☑ Questionnaire(s) ☐ Advert(s) ☐ Debrief sheet(s) ☐ DP checklist ☐ Risk Assessment ☐ COSHH ☑ Other
If 'Other' please list/describe Templates in English from the Helsinki Ethics Committee,Sourasky Medical Center, TA, Israel

Appendix 1
BREAKDOWN OF SCHOOLS TO ETHICS COMMITTEES

The Ethics Committee for **Business, Arts, Humanities and Social Science (BAHSS)** has responsibilities for the following Schools:

- Art, Design & Performance
- Education & Social Science
- Journalism & Digital Communication
- Languages, Literature & International Studies (including iSLanDs)
- Lancashire Law School
- Lancashire Business School
- Forensic & Investigative Sciences (Archaeology only)
- GB School of Architecture, Construction & Environment (Architecture/Construction only)
- Sport, Tourism & The Outdoors (Social Science areas)

The Ethics Committee for **Science, Technology, Engineering, Medicine and Health (STEMH)** has responsibilities for the following Schools:

- Computing, Engineering and Physical Sciences
- Forensic and Investigative Sciences (except Archaeology)
- Pharmacy and Biomedical Sciences
- Medicine and Dentistry
- GB School of Architecture, Construction & Environment (Environment only)
- Health
- Sport, Tourism and the Outdoors (Allied Health Research Unit – AHRU; Sport Exercise and Nutritional Science – SENS and Centre for Applied Sport and Exercise Sciences - CASES)

The Ethics Committee for **Psychology & Social Work (PSYSOC)** has responsibilities for the following Schools:

- Psychology
- Social Work

Appendix 2
GUIDANCE NOTES

Forms will only be considered if they are typed in to the ethics application pro-forma. Do not attach these guidance notes in your submission.
The form should be completed in such a way as to be accessible to a lay person, i.e. in plain English with all parts of the protocol clearly outlined. Please explain any abbreviations or acronyms used in the application.
The application form contains nine sections with each section requiring at least an initial question to be answered then depending on the nature of your study; further questions may also need to be completed. This guidance mirrors the application form and is designed to help you to complete the form to a high standard. In order to grant ethical approval, the Ethics Committee needs sufficient detail to be able to judge the ethical issues presented by, and addressed in, the design of the study.
To return to the application form – click on the relevant question number or Section header.

Section 1 – Project Details
All questions in this section must be completed.

Q1.2 This should be the name of the person who takes responsibility for the research from a UCLan perspective. It should therefore be a member of UCLan staff (not an hourly-paid lecturer). In the case of student research, their Main Supervisor or Director of Studies should be named here and the application will be viewed as a joint application and the responsibility of both the student and their principal supervisor (Director of Studies for a research student project and main supervisor for taught or undergrad student projects) . Otherwise, all UCLan supervisors should be listed under Q,1.3 'Other Researcher / Student'. We strongly recommend that all supervisors review the documentation prior to submission for ethical approval.

Q1.4 Where your activity involves participants, the title provided should normally be the same title you use on study documentation for participants (information sheets, consent forms, etc).

Q1.6 Note that Ethics Committee approval is normally deemed to expire **five years** form the approval date unless otherwise requested.

Q1.7 If the project is externally funded i.e. not funded by UCLan, it should be stated here. Give details of the specific funding of the project - for example to buy equipment, pay participants, pay for a research assistant, etc.

Q1.8 The basic summary should indicate broadly what the project is about and what you are interested in finding out. There should be a short rationale for the validity of

the project however extensive background and research literature is not necessary, neither are extensive reference lists, although one or two key relevant studies might be detailed (for example, if your study is following up another, or is perhaps testing a theory presented in another).

Q1.9 Indicate how the research question(s) outlined in the answer to Q1.8 will be addressed. This section might include information about an experimental design for example, indicating the factors that will be investigated. If the project includes any procedure which is beyond established and accepted techniques please include a description of it.

Q1.10 If relevant, describe the review process and outcome. If the review has been undertaken but not seen by the investigator, give details of the body which has undertaken the review.

Q1.11 See UCLan Code of Conduct for Research; UCLan Data protection checklist and LIS IT Security Policy.

Q1.13 If your project has been approved by an external ethics committee (e.g. NHS Research Ethics Committee or properly-constituted ethics committee at another UK University or at another organisation) include a copy of the letter of approval. A properly-constituted ethics committee is one in which has terms of reference, membership with appropriate expertise and which includes lay members (i.e. at least one member independent of the organisation). Ethics committees in other Universities or organisations may or may not be properly constituted. It is the applicant's responsibility to check these details. If you are unsure, you are recommended to contact the Research Development & Support Team for advice or simply to respond 'No' here.

If you have been informed that you need not apply to an NHS REC (usually because your research is classed as audit or service evaluation by the NHS), this is not the same as having received their ethical approval, so you should not select the box indicating approval by an NHS Research Ethics Committee. However, you are recommended to include such communication amongst the documentation submitted (and to list this under 'Other'). Please note that this does not mean that your project may not be managed as research by this committee.

If you have been granted exemption from obtaining explicit patient consent for your research via the Department of Health Patient Information Advisory Group (PIAG) under Section 251 of the NHS Act 2006 (originally enacted under Section 60 of the Health and Social Care Act 2001), please provide details and a copy of the notification. Please note that in such cases application to the Ethics Committee should only be submitted once external approval has been obtained.

Section 2 – Human Participants, Data or Material

Q2.1 Select the appropriate box and then proceed to the question as directed.

Q2.2 Tick as many boxes as applicable and then describe the reason for their inclusion and any relevant exclusion factors, any equality and diversity factors must be explained here. Explain who the proposed participants will be (e.g. student population, members of the Preston Women's Institute, hospital out-patients, etc) and, if appropriate, what age ranges you anticipate they will have. One common error in providing information about participants is that extensive detail is provided about participants in an experimental condition, but detail about a control population is glossed over. If you are using people in the creation of research materials (e.g. video or audio recordings) then these people should be considered participants too, and given briefing/debriefing information accordingly.

Q2.2b Certain activities and/or potential participant groups (e.g. children or vulnerable adults) may require researcher(s) to gain a DBS (Disclosure and Barring Service) certificate. Full information, including guidance on completing a DBS application form, is available at Disclosure and Barring Service (formerly Criminal Records Bureau – CRB) website. If you need a DBS application form please contact roffice@uclan.ac.uk.

Q2.3 Indicate how participants will be approached and what sort of advertising will be used to get people interested. Particular attention should be paid to whether the approach is ethical in terms of enticements to participate or whether participants feel pressured to take part; this is of particular importance in such relationships as therapist/patient and student/tutor etc. In some circumstances some thought may be needed as to whether the approach method is appropriate given the topic of study. For example, approaching couples in the street and asking about partner violence would be considered unacceptable.
If you are mailing to or phoning people, please explain how you have obtained or will obtain their names and contact details.

Q2.4 Confirm how consent is to be obtained, and whether there are any special problems in obtaining informed consent. Indicate whether consent is provided verbally or in written form. If written consent of the participants is not being sought, the investigator must provide justification as to why such consent is unnecessary, impractical or inappropriate or why a non-written method of consent is being used. When postal questionnaires are used to collect the research data, it is usually deemed unnecessary to require formal consent for questionnaires containing no personal, sensitive or identifiable data as the return of the questionnaire will usually suffice to provide implicit consent. Whichever form of consent you use, you should keep appropriate records of the consent (e.g. written witnessed consent, taped verbal consent) for audit purposes.

Where it is expected that participants will not be able to provide informed consent, indicate who will give consent on their behalf. In research with infants and children under the age of 18, informed consent should normally be obtained from a parent or someone with legal responsibility for the child. In addition, children who are deemed competent to make their own decisions about participating in the project should also give their agreement (assent). Exceptionally, and only with clear justification as to why research would be unethical (or perhaps impossible to carry out) if consent from parents or those with legal responsibility for the child were required, the research may proceed using consent/assent only from a competent child. Consent involving adults unable to consent for themselves should follow the guidance of the Mental Capacity Act using the consultee approach.
Obtaining consent for observational research is particularly problematic: unless those observed give their consent to being observed, observational research is only acceptable in situations where those observed would expect to be observed by strangers. Additionally, particular account should be taken of local cultural values and of the possibility of intruding upon the privacy of individuals who, even while in a normally public space, may believe they are unobserved.
Where a written consent form is being used - the Consent Form should, ideally, include a list of statements to indicate to what the participants have consented with each item being initialled by the participant before giving witnessed written consent to the whole form. If a written consent form needs to be in another language, it is the applicant's responsibility to ensure that a faithful translation of the copy being used with participants is provided as part of the submission.

Q2.5 In virtually all studies with human participants, the participants should be given some kind of information sheet to keep, this could either be a briefing or debriefing sheet. Within the information sheet, it should be clear to the study participants what will be the potential risks and benefits to all involved in the research should they choose to participate in the research project. The Information Sheet will normally include: contact details for the researcher, some information about the purpose of the study and why they are being asked to take part, what taking part involves for them, any risks or benefits to taking part, information about confidentiality/ anonymity and how the data will be used, as well as details of right to withdraw, all in a jargon free accessible manner. In cases where distress is possible, it may also contain advice about possible sources of help and support. Where an information sheet is required in another language, it is the applicant's responsibility to ensure that a faithful translation of the copy being used with participants is provided as part of the submission.

Q2.6 The proposed participants must be given time to think through the implications of volunteering/participating. They should be able to ask questions and reflect. Participants should not be rushed into decisions. There are no fixed guidelines and each project should be considered on its own merits, the more burdensome studies will require a longer time for deliberation. However it is good practice for it to be a minimum of 24 hours after receiving full details of the project exceptions being time

critical medical trials etc. There will be cases, such as responding to questionnaire or a website link, where the length of time is determined by the potential recruit.

Q2.7 If applicable, include here a description of how you will make information accessible to small children/adults with disabilities. Describe use of translation services where applicable.

Q2.8 If people taking part in your project are to be offered any payment or incentive to do so over and above appropriate expenses, you must explain. Any form of payment or incentive to take part will need to be clearly justified. It is permissible to pay out of pocket expenses or recompense time and effort, but not any proposal that amounts to an inducement to take a risk which is against the interests of the participants (i.e. it is inappropriate to offer participants excessive payments which might induce them to participant in a project against their better judgement).
If names need to be taken to acknowledge payment, please consider whether this compromises anonymity.

Q2.9 Procedures to be undertaken include all other forms of intervention, so this includes assessment focused questionnaires, and psychological or educational tests. Give details of any invasive procedure and any samples or measurements to be taken. Attach the questionnaire/test, etc. and provide details and supporting evidence of staff experience/expertise administering them.
Questionnaires and/or interview schedules and/or focus group agendas should normally be submitted with the application. If these are to be developed as part of the project, please ensure that this is clearly stated. In such cases, approval will only be granted subject to later approval of the questionnaire(s) and/or interview schedule(s) and/or focus group agenda. Such later approval will normally be considered by Chair's Action. For researchers undertaking qualitative interviews or focus groups where a predetermined schedule or agenda is inappropriate, the researcher should indicate the opening question (or topic) and where possible¬ identify key areas that could be covered. If it is methodologically inappropriate to identify potential areas then the researcher should state this and provide a brief (a few sentences) explanation as to why this is the case. If you are planning to use other data collection methods (e.g. observation, taking tissue/blood samples), please provide clear details of these, either within your proposal or in a separate document.

Q2.10 Deception is allowable in studies where alternative methodologies are not available. Participants should be given an opportunity to remove their data from the study after being informed of any deception.

Q2.11 Art can sometimes deliberately shock and offend. This is legitimate but consideration must be given to likely effects and possible safeguards (e.g. warnings, age restrictions).

Q2.12 Research involving persons in dependent or unequal relationships (for instance, teacher/student) may compromise a participant's ability to give consent which is free from any form of pressure (real or implied) arising from this unequal power relationship. Therefore it is recommended that, where possible, investigators choose participant cohorts where no dependent relationship exists. If, after due consideration, the investigator believes that research involving people in dependent relationships is purposeful and defensible, then please provide additional information setting out the case and detailing how risks inherent in the dependent relationship will be managed. You will also need to provide reassurance that refusal to participate will not result in any discrimination or penalty.

Q2.13 Identify, as far as possible, all potential risks to participants (e.g. physical, psychology, social, legal or economic) associated with the proposed activity/research. Please consider all possible causes of distress carefully, including likely reactions to the subject matter, debriefing, deception or burdens imposed and any preparatory requirements (e.g. special diet, exercise). If there is **any** possibility of distress, please give details and say what steps are to be taken to protect the participants. Details should also be given of any potential risks to investigators (e.g. are there any specific risks to investigators that are greater than those encountered in normal day to day life?).

Q2.14 Before starting a project that will involve research with persons engaged in potentially illegal activities you need to consider under what circumstances you might be legally required to divulged information about your research participants. You need specifically to consider when you anonymise your research data. You also need to consider under what circumstances you might become implicated in the illegal activities and how you will ensure that this does not happen.

Q2.15 How exactly do participants withdraw if they change their minds about taking part? Make sure in your instructions that participants **know** they have the right to withdraw. Please also specify exactly **when** participants may withdraw: for example, can they contact you later to have their data withdrawn, or is withdrawal only possible until the end of the research session (e.g. until they hand in the questionnaire, or finish the experiment)? Consider whether withdrawing from the data collection session poses any risks to the participants health or well-being – for example, will it mean that they miss the debrief or don't have sufficient time to recover from a physiological effect brought on within the research session – and put safeguards in place if necessary.

Q2.16 A lot of projects result in no direct benefit to the participant at the time and it is acceptable to write 'no direct benefit'. However, any project that involves an intervention may result in an immediate direct benefit and this should be stated e.g. gains in reading skills from a literacy intervention for poor readers.

Q2.17 Although this may be an unusual occurrence in a non-medical situation, it is an ethical principle that participants should be made aware of relevant information that was not available when they started. You need to state that if any information, pertinent to the study, becomes available as the study progresses then participants will be informed immediately and that participants will be reminded that their participation is voluntary and they are free to withdraw at any time.

Q2.18 A debriefing of participants may be appropriate in some investigations, for example to enable participants to express how they felt during an investigation, to offer counselling, or to communicate views on the whole process that they were not able to do previously, possibly to explain a study which involved deception. For any project where participants are entitled to full debriefing, this means explaining any deception and why it was necessary, making sure that any negative feelings aroused by participation are nullified, and giving participants enough information to complete their understanding of the nature of the project.
Other feedback, includes how will the results of the project be made available to the participants? It is only courteous, wherever practicable, that participants should have access to any report. It is appropriate for research participants to be able to receive feedback on project they have been involved in, in an appropriate format, where this is possible. You should consider the issue of informing the participants of the results of the project or where they may be able to get access to information (although participants may not be able to be given their individual results).

Q2.19 Describe the measures in place in the event of any unexpected outcomes or adverse effects to participants arising from their involvement in the project. An adverse event may be defined as one which is 'related' (i.e. it can be attributed to the research procedure) and 'unexpected' (i.e. not listed in the protocol as an expected occurrence, or its manifestation was more severe than expected). For example, how will any problems identified by the investigator during the study be referred onwards or dealt with (e.g. helpline numbers given, counsellor available)?

Q2.20 If the project involves access to personal and/or confidential data (including student, patient or client data) without the participant's specific consent provide details of the information being sought, from which organisation (include any relevant), any legal requirements/conditions of access and justification for use of this information.

Q2.21 Please provide details on how the medical research will be undertaken, including confirmation that all human tissue samples and/or body fluids used will be obtained lawfully and with appropriate consent, and be handled and used sensitively and responsibly by investigators. Further Guidance is available from Human Tissues Authority (HTA).

Q2.22 Generally, it will be necessary to say more than 'all your data will be confidential' and we would advise against these kinds of statements in participant

information sheets. One of the reasons for this is that, in everyday understandings of the word 'confidential' it could be taken to mean that none of the information that participants give will be passed on to any other person. Clearly, in a research context, this is not the case. We would also advise that researchers think very carefully before promising participants that only certain, named, individuals will see their information. The first difficulty with this is that it may actually not be legally or practically possible to follow through with this promise. What if you want to reanalyse the data later with a different colleague and they need to see it in order to work with you? You could kick yourself for promising participants that "nobody but myself and my supervisor" will see the information you provide. Also, you might consider that providing information (even in statistical form) to the media or in papers, publications or presentations does actually constitute somebody seeing 'their information' – especially in interview or observational studies.

Sometimes, it might be in the best interests of the research and the participants if you say something more general that you know you will actually be able to stick to and that really does give genuine information about how the information will be used and stored. So, you might say something like "only people with a legitimate professional need will see your actual completed questionnaire" and then go on to explain in what form(s) you will use and pass on the information they give. For example, you might say that "the information you provide will be used to write reports and may be seen publicly" whilst reassuring them that "at no point will you be identified in these reports because the information we give will be numerical and will be information about the group of participants to which you belong, rather than about you personally". You could then even add that "the information you provide will be anonymous; that is, your name will not be recorded anywhere and we will not reveal any personal information about you individually from which you could be identified". Obviously, what you actually say will depend upon who your potential participants are and on what your research procedures will be. It often helps to use examples, if you are concerned that participants will not understand your descriptions of how the data will be stored and used. However, this is the kind of thing that we will expect to see – rather than the relatively uninformative "all data is confidential".

If you are using the School's participant pool in your project that is otherwise intended to be anonymous, you will need to ensure that you have a system that keeps their names (which you may need to give them participant points later) separate from their anonymous research data. People often use tear-off slips for this that can then be placed in separate sealed envelopes.

You also need to think about the role of identifying information when you give participants information about confidentiality and anonymity. This issue most often applies to things like interview data – where, for example, it would be normal to use excerpts from interviews in publications. You may not even know yourself how likely it is that a person might be identified from what you repeat. If the information is highly sensitive or personal and the population is one that is small and very easy to identify (e.g., Vice Chancellors of UK Universities, Heads of Primary Schools in isolated parts of the Scottish Islands) you may even need to consider letting participants see the transcripts and look themselves for identifying information. However, it is important

to remember that survey information and questionnaire data can lead to these kinds of problems with identifying information and so you need to think about these possibilities at the design stages of your project and within your ethics submission. That is, don't fall into the trap of glibly saying 'all data is confidential and anonymous' without thinking through all the ramifications of this and how you will ensure that it can be ensured.

Q2.23 See UCLan DP checklist and LIS IT Security Policy.

Q2.24 Before carrying out any work on the objects, people or other remains of the past, all investigators must consider the ethical implications of their work. There are particular issues surrounding the study of human remains or access to archaeological sites, landscape and artefacts within different countries. All of the major archaeological associations have published codes of conduct and many professional bodies have guidance on how to handle human remains or artefacts.

Study of human remains

For handling human remains please see the BABAO code of conduct, and the Institute for Archaeologists guidance documents. If your project involves the destructive sampling of human remains or objects please outline how the research objectives outweigh the negative implications of intrusive sampling and how damage is to be limited or mitigated against. Do you have permission to conduct intrusive sampling and how will this be documented?

If applicable please outline where your research collection is housed, i.e. in a museum, at UCLan, or as yet to be excavated. Is it subject to any legal conditions? If part of an on-going excavation within the UK does that project have an active Ministry of Justice Licence and what are the conditions of that licence (only applies to sites excavated after 2008). If they are within an existing museum collection please refer to the museums own published codes of conduct and rules where applicable.

Access to Archaeological Materials and Landscapes

All studies must be conducted within the boundaries of the Law, in the UK these laws focus on scheduled monument consent, and the excavation of human remains (other laws may also be implicated for example the Treasures Act, and the Museums Act). Please outline which of these apply, if any, and how the project will meet the criteria of those laws. In other countries archaeological excavation may require a licence, or be affected by local laws and procedures which should be described and addressed. Archaeological field work or museums work will require permission from collection managers or land owners, it may not always be possible to document this (Museums are often too understaffed to provide formal documentation and others will be reluctant to issue written, and so legal documents, should they wish to withdraw permission at any point). However, you should state how permissions will be sought and outline how you will keep track of any emails, phone calls or physical evidence in a project archive.

Section 3 – Biological Organisms / Environment

Q3.1 Health & safety issues are carefully regulated (Containment; Special attention to pregnant women and the immunologically compromised; MOs can be mutated forms, unable to replicate outside the lab). The ethical issue is usually whether or not the risks can be justified by the potential benefits. Environment considerations are minimum disruption to natural environments unless purpose is improvement and respect rights of landowners. Study of rare species must be approved by appropriate bodies (e.g. English Nature). Follow guidelines for archaeology (see Q2.24 guidance).

N.B. If your project requires UCLan Biological Safety Committee (BSC) approval, please use their application form and only once BSC approval has been gained should submission be made to Ethics Committee.

Section 4 – Hazardous Substances

Health & safety issues are carefully regulated – see UCLan guidance notes on hazardous substances and risk assessment. The ethical issue is usually whether or not the risks can be justified by the potential benefits. If the project involves the use of hazardous substances (chemicals, fire, etc.), what detail is needed in the relevant COSHH forms and Risk Assessment forms. What is most important to provide is a list of the potential hazards of the work you propose to do, and not just a list of how you will minimise the risks. For example, you may be working with two chemicals. Neither one on its own is a particular problem, but if the two are accidentally combined – they explode.

Section 5 – Other Hazards

Research related to defence and arms industries may contradict general ethical principles (e.g. avoidance of harm). Approval of such work must involve University Senior Management.

Section 6 – Fieldwork/Travel

Q6.2 The location, or locations, of the investigation should be given. These should be places suitable for the type of investigation to be undertaken and where both participants and investigators are safely able to carry out the work. If this is not apparent then please outline the risks / hazards and specify how you will or intend to minimise these. If your project requires travel away from the university, you will need to submit a Travel Risk Assessment form – UK/Overseas. See UCLan guidance on field work / travel to unfamiliar places.

Q6.3 See UCLan guidance on lone working.

Q6.4 See UCLan guidance on School visits to UCLan.

Section 7 – Ethical and Political Concerns

Please use this section to identify, as far as possible, all potential concerns – ethical / political/ collaborator or any other not raised elsewhere on the form.

Section 8 – Declaration

This section needs to be signed by the Principal Investigator and the student where the study relates to a student project. Electronic submission of the form is required to roffice@uclan.ac.uk. Where available insert electronic signature, if not a signed version of the submitted application form should be retained by the Principal Investigator.

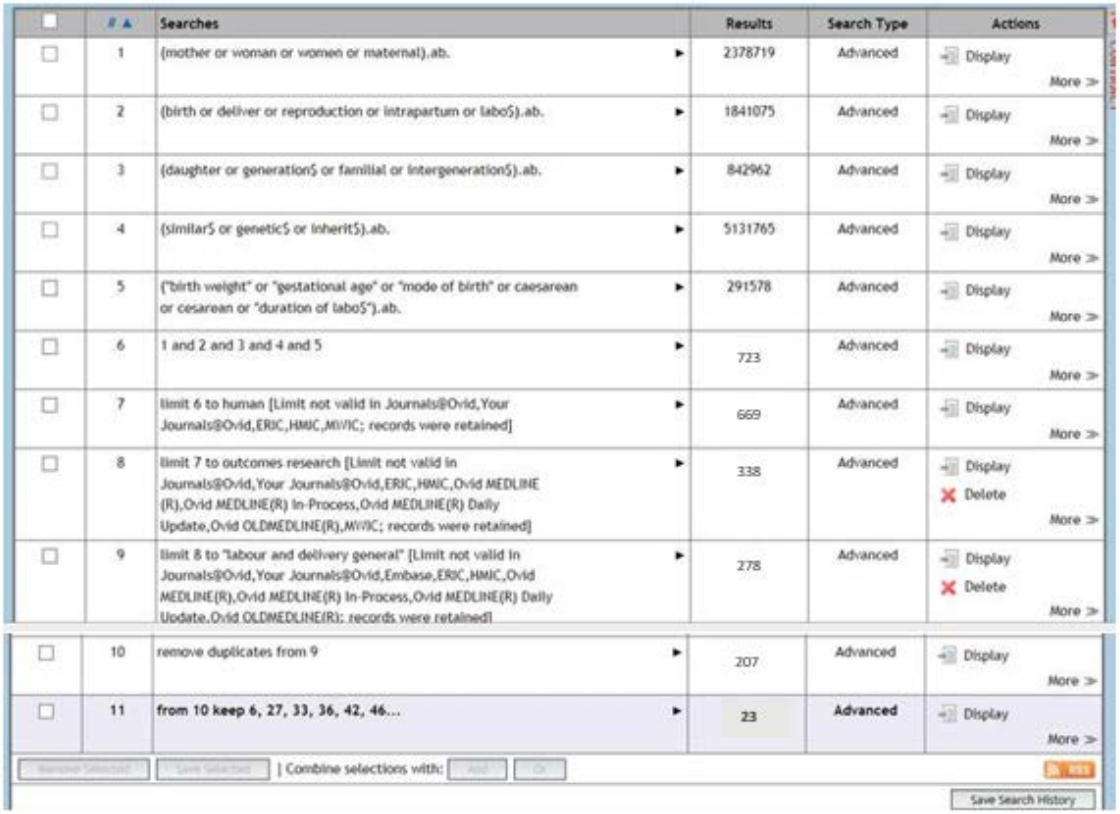
Section 9 – Accompanying Documentation

Use this checklist for enclosure of relevant supporting documentation.

APPENDIX 2: SYSTEMATIC REVIEW (INTERGEN) ARTICLE SEARCH

SR intergen: Final search strategy and results

OVID platform



#	Searches	Results	Search Type	Actions
1	(mother or woman or women or maternal).ab.	2378719	Advanced	Display, More
2	(birth or deliver or reproduction or intrapartum or labo$).ab.	1841075	Advanced	Display, More
3	(daughter or generation$ or familial or intergeneration$).ab.	842962	Advanced	Display, More
4	(similar$ or genetic$ or inherit$).ab.	5131765	Advanced	Display, More
5	("birth weight" or "gestational age" or "mode of birth" or caesarean or cesarean or "duration of labo$").ab.	291578	Advanced	Display, More
6	1 and 2 and 3 and 4 and 5	723	Advanced	Display, More
7	limit 6 to human [Limit not valid in Journals@Ovid,Your Journals@Ovid,ERIC,HMIC,MIVIC; records were retained]	669	Advanced	Display, More
8	limit 7 to outcomes research [Limit not valid in Journals@Ovid,Your Journals@Ovid,ERIC,HMIC,Ovid MEDLINE (R),Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Daily Update,Ovid OLDMEDLINE(R),MYIIC; records were retained]	338	Advanced	Display, Delete, More
9	limit 8 to "labour and delivery general" [Limit not valid in Journals@Ovid,Your Journals@Ovid,Embase,ERIC,HMIC,Ovid MEDLINE(R),Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Daily Update,Ovid OLDMEDLINE(R); records were retained]	278	Advanced	Display, Delete, More
10	remove duplicates from 9	207	Advanced	Display, More
11	**from 10 keep 6, 27, 33, 36, 42, 46...**	23	**Advanced**	Display, More

Combine selections with:	Save Search History

For flow chart of search strategy, see Figure 2.2 in main thesis text.

APPENDIX 3: MOTHER-DAUGHTER INFORMATION SHEET, QUESTIONNAIRES AND CONSENT FORM

The information sheet and questionnaires were written in Hebrew for use in an Israeli survey. (Translation was validated by Professor Many, one of the PhD advisors. Head of L & D, Lis Maternity Hospital).

Q1) For mothers participating in the MR study, and for mothers participating in the SiLC study

Q2) For nulliparae participating in the SiLC study

THE QUESTIONNAIRES APPEAR ON LETTER HEADED PAPER
THE SOURASKY MEDICAL CENTER

(Q1) For biological mothers of women expecting their first child

Dear Participant,

You are being invited take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully, and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

My name is Mindy Ebrahimoff, and I'm a senior midwife at the Lis Maternity Hospital, Tel Aviv. I am a doctoral student at the University of Central Lancashire (UCLAN) in the UK, and I am conducting a study to compare the length of pregnancy till labour begins, length of labour and mode of delivery between participating women and their biological mothers – in their first birth experiences. I will be approaching approximately 300 women to take part in this study.

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason, up until final data analysis has been undertaken – which may take up to 24 months. If you decide to withdraw from the study, your information will be securely disposed of.

All information which is collected about you during the course of the research will be kept strictly confidential. This includes birth information taken from hospital records. You will be identified by an ID number, and any information about you will have your name and address removed so that you cannot be recognised from it. Information from the study will be disposed of securely after five years.

Whilst there are no direct benefits to your participation, your involvement in this research is of benefit to the study of how to enrich first time mothers' birth experiences and improve infant health.

This short questionnaire asks you to respond to a series of statements and questions about **your first birth** experience. The questionnaire will take up approximately 7-10 minutes of your time. Please return the completed questionnaire within 4 weeks.

Completed questionnaires should be sealed in the envelope provided and may be returned by your daughter at her next ante-natal follow up at the hospital, or sent by Freepost to Mindy Ebrahimoff, in the envelope provided.

Should you experience anxiety or distress following memories of a difficult or traumatic childbirth and wish to discuss your feelings or seek emotional support, please contact the Women's Mental Health Services, Sourasky Medical Center T A, located in the rehab building on the ground floor. Consultations are free of charge. For appointments call: 03-6974707.

You may contact me with queries at 0545-401090.

We are very grateful for your participation in this study.

The research team,

Mindy Ebrahimoff, MSc, CNM, senior midwife and clinical tutor, Lis Maternity Hospital, Tel Aviv.

Dr. Victoria Hall-Moran, Director of Studies and supervisor - UCLAN, UK.

Professor Soo Downe, investigator and supervisor - UCLAN, UK.

Professor Ariel Many, research supervisor, Head of Labour and Delivery, Lis Maternity Hospital, Tel Aviv.

Dr. Benny Chayen, Head of Labour and Delivery, Ma'aynei Hayeshua Hospital, Tel Aviv.

<u>This questionnaire is for the biological mothers of first time mothers' only</u>

For the purposes of post-birth follow-up please complete the following:

First name_____ **Family name**_____

ID no. _____

Telephone no._____

Email _____

Age _____ Height_____

Name of the expectant woman (your daughter/sister):

First name_____ Family name_____

What is your relationship with the expectant woman? Mother / Sister

The following questions provide important information and report on the type of person making up the population sample in the study.

Country of origin: Israel, other_____

Date of emigration if applicable _____

Father's country of origin_____

Mother's country of origin_____

Do you currently smoke? Yes / No
If yes, how many cigarettes per day _____

Do you currently consume any alcoholic drinks? Yes / No
If yes, how many units per week? _____

Education:

A) Primary school
B) Secondary school until age 16
C) Secondary school until age 18
D) Further vocational education
E) Academic status: BA or BSc / MA or MSc / PhD

How would you define yourself in relation to religion?

A) Non-religious
B) Traditional
C) Religious
D) Ultra orthodox
E) Other _____

Marital status:

A) Single
B) Married or living with a partner
C) Divorced
D) Widowed
E) Other_____

The following questions refer to your health and first birth only. Please complete them to the best of your ability.

1) At what age did you get your first period? _____/don't remember
2) Did you use fertility treatments to get pregnant? Yes / No
3) Did you have a history of any of the following before your first birth?

   A miscarriage? Yes / No

   A termination of pregnancy? Yes / No

   A Still birth? Yes / No

4) At what age did you deliver your first child? _____
5) Was your baby born early / on time / late?

   Your infant arrived at: _____ weeks, or _____months / don't remember

6) If you gave birth in Israel, hospital name:_____
7) How much weight did you gain in your first pregnancy?_____ / don't remember
8) Was your first pregnancy normal? Yes / No. If not, give details:

   _____

   _____

9) Whilst pregnant, did you suffer from:

   1) high blood pressure
   2) diabetes

   Other problem, give details_____

10) How did your labour begin?

   1) Contractions
   2) Waters breaking
   3) Bleeding
   4) Induction, if yes give reasons_____
   5) Don't remember

11) Did you take pain relief in your first labour?

1) No
2) Epidural
3) Pethidine
4) Gas & Air
5) Other_____
6) Don't remember

12) How much time were you in labour

1) Less than 2 hours
2) 2 - 6 hours
3) 6 - 10 hours
4) More than 10 hours, please give the number of hours: _____

13) How did you deliver your first baby?

1) Vaginal birth
2) Vacuum or forceps
3) Elective cesarean section
4) Emergency caesarean section

Give details_____

14) How did your baby present at delivery?

1) Head
2) Breech
3) Other _____

15) Baby's sex: Male / Female

16) Baby's weight at delivery_____

17) Apgar score normal? Yes /No / Don't remember

18) Was your placenta delivered spontaneously and whole? Yes / No

If no - was it removed in the labour ward? Yes / No

Or in the operating theatre? Yes / No

19) After your birth, did you have abnormal vaginal bleeding that required medical treatment? Yes / No

Did you receive blood transfusions? Yes / No. Other treatment, give details _____

20) Please use this space to describe your first birth in your own words

_____
_____
_____
_____
_____

THANK YOU FOR ANSWERING OUR QUESTIONS!

(Q2) For nulliparae participating in the SiLC study

For women expecting their first baby, who are between 32 weeks pregnant and full term, intending to give birth at the Lis Hospital or Ma'aynei Hayeshua Hospital, and have a (biological) mother who is willing to join in a research study – please read on.

Dear Participant,

You are being invited take part in a research study. Before you decide whether or not to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully, and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

My name is Mindy Ebrahimoff, and I'm a senior midwife at the Lis Maternity Hospital, Tel Aviv. I am a doctoral student at the University of Central Lancashire (UCLAN) in the UK, and I am conducting a study to compare the length of pregnancy till labour begins, length of labour and mode of delivery between participating women and their biological mothers – in their first birth experiences. I will be approaching approximately 300 women to take part in this study.

It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason, up until final data analysis has been undertaken – which may take up to 24 months. If you decide to withdraw from the study, your information will be securely disposed of.

All information which is collected about you during the course of the research will be kept strictly confidential. This includes birth information taken from hospital records. You will be identified by an ID number, and any information about you will have your name and address removed so that you cannot be recognised from it. Information from the study will be disposed of securely after five years.

Whilst there are no direct benefits to your participation, your involvement in this research is of benefit to the study of how to enrich first time mothers' birth experiences and improve infant health.

This short questionnaire asks you to respond to a series of statements and questions. The questionnaire will take up approximately 5-7 minutes of your time. Please return the completed questionnaire within 4 weeks.

Completed questionnaires should be sealed in the envelope provided and posted into the 'research box' at maternity admissions. Your mother's completed questionnaires should be sealed in the envelope provided and can be returned by you at your next ante-natal follow up at the hospital, or sent by Freepost to Mindy Ebrahimoff, in the envelope provided.

You may contact me with queries at 0545-401090.

We are very grateful for your participation in this study.

The research team,

Mindy Ebrahimoff, MSc, CNM, senior midwife and clinical tutor, Lis Maternity Hospital, Tel Aviv.

Dr. Victoria Hall-Moran, Director of Studies and supervisor - UCLAN, UK.

Professor Soo Downe, investigator and supervisor - UCLAN, UK.

Professor Ariel Many, research supervisor, Head of Labour and Delivery, Lis Maternity Hospital, Tel Aviv.

Dr. Benny Chayen, Head of Labour and Delivery, Ma'aynei Hayeshua Hospital, Tel Aviv.

<u>This questionnaire is for first time mothers' only</u>

For the purposes of post-birth follow-up please complete the following:

First name_____ **Family name**_____

ID no. _____

Telephone no._____

Email _____

Mother's first name _____Family name_____

Sister's first name _____Family name_____

I am _____ weeks pregnant today

Your expected date of delivery _____

Where do you intend to give birth? Lis / Ma'aynei Hayeshua

Please complete the following:

Age _____Height_____

At what age did you get your first period? _____/don't remember

Weight before pregnancy _____Weight today_____

The following questions provide important information and report on the type of person making up the population sample in the study.

Country of origin: Israel, other_____

Date of emigration if applicable _____

Father's country of origin_____

Mother's country of origin_____

Do you currently smoke? Yes / No
If yes, how many cigarettes per day _____

Do you currently consume any alcoholic drinks? Yes / No
If yes, how many units per week? _____
Did you use fertility treatments to get pregnant? Yes / No

Do you have any pregnancy related health issues? Yes / No

If yes, give details:

_____

_____

Do you have any general health issues or are you taking any medication which is unrelated to your pregnancy? Yes / No

If yes, give details: _____
_____

Education:

A) Primary school
B) Secondary school until age 16
C) Secondary school until age 18
D) Further vocational education
E) Academic status: BA or BSc / MA or MSc / PhD

How would you define yourself in relation to religion?

A) Non-religious
B) Traditional
C) Religious
D) Ultra orthodox
E) Other _____

Marital status:

A) Single
B) Married or living with a partner
C) Divorced
D) Widowed
E) Other_____

THANK YOU FOR ANSWERING OUR QUESTIONS!

****

Mothers' MR and mother-daughter SiLC Questionnaire Consent Form

The original consent form (information sheet and questionnaires) were written in Hebrew for use in an Israeli survey. (Translation was validated by Professor Many, one of the PhD advisors. Head of L & D, Lis Maternity Hospital).

Each participant received a copy of this consent form.

Mothers MR and mother-daughter SiLC Questionnaire Consent Form

I, _____ (participant's name), understand that I am being asked to participate in a survey/questionnaire that forms part of Mindy Ebrahimoff's PhD research study. This questionnaire has been designed to gather information about maternal recall (for mothers) of first birth outcomes and first birth outcomes in daughters.

I have been given some general information about this research. I understand that the questionnaire requires self-reported answers and Mindy may phone or email to verify responses. The questionnaire will take approximately 7-10 minutes of my time to complete.

I understand that my participation in this project is completely voluntary and that I am free to decline to participate, without consequence, at any time prior to or at any point during the activity. I understand that any information I provide will be kept confidential, used only for the purposes of completing this assignment, and will not be used in any way that can identify me. All survey/questionnaire responses, notes, and records will be kept in a secured environment.

I understand that the results of this research study will be used exclusively for Mindy's research.

I also understand that there are no risks involved in participating in this research.

I have read the information above. By signing below and returning this form, I am consenting to participate in this research.

Participant name (please print): _____

Signature: _____

Date: _____

Please keep a copy of this consent form for your records. If you have other questions concerning your participation in this project, please contact me at:

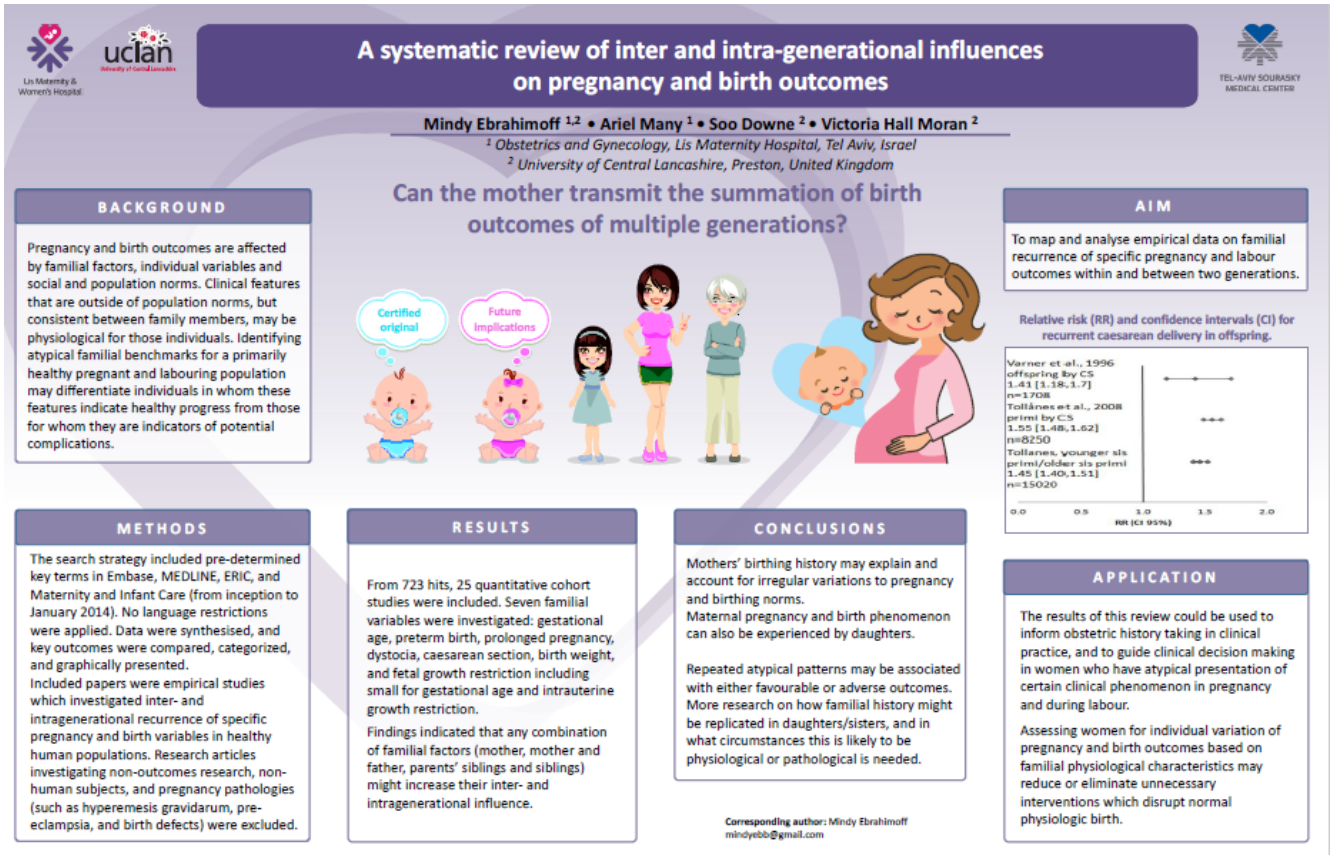
Student name: Mindy

+972545401090 email address:mindyebb@gmail.com

Thank you for agreeing to participate in my project.

APPENDIX 4: POSTER PRESENTATIONS MR + SR

Systematic review of inter and intra-generational influences on pregnancy and birth outcomes study poster presented at the 31st ICM Triennial Congress 18-22 June 2017.



Maternal recall empirical study poster presented at the 31st ICM Triennial Congress 18-22 June 2017.

Agreement between maternal recall of distant first birth events with hospital birth records: A cohort study

Mindy Ebrahimoff [1,2] • Ariel Many [1] • Soo Downe [2] • Svetlana Tishkovskaya [2] • Victoria Hall Moran [2]

[1] Obstetrics and Gynecology, Lis Maternity Hospital, Tel Aviv, Israel

[2] University of Central Lancashire, Preston, United Kingdom

BACKGROUND

Childbirth is a memorable event in women's lives. Birth outcomes, such as mode of delivery, birthweight (BW) and gestational age (GA), are frequently obtained from maternal self-report.

Mothers' recall of previous births is generally assumed to be medically accurate and is often relied upon for clinical decisions.

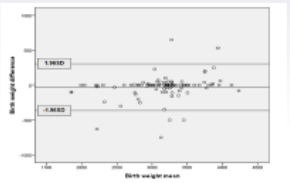
This study compares distant maternal intrapartum recall of first births with hospital birth records.

Is maternal recall a reliable source of perinatal information ?

OBJECTIVE

To determine agreement of maternal recall of gravidity, onset of labour, use of pain relief, delivery outcome, BW, and GA with hospital birth records.

Agreement between recalled and recorded BW with 95% limits of agreement



METHODS

Detailed questionnaire information on delivery events of first-borns births between 1967 and 1997 was collected from a cohort of 101 Israeli women.
At the time of interview women were aged 37-70 and had varied levels of education.
These maternally recalled birth events, 17-49 years postpartum, were compared to hospital birth records. Agreement between the two sources was evaluated by Bland-Altman's plots and Kappa coefficients.
Logistic regression modelling was used to assess predictors of inaccurate reporting.

RESULTS

Levels of agreement

Mode of delivery (almost perfect agreement, K .919; *p .001*)
BW (categorised: almost perfect agreement, K .83; *p .001*)
GA (categorised: moderate agreement, k .568; *p .001*)
Onset of labour (substantial agreement, K .790; *p .001*)
General pain relief (substantial agreement K .618; *p .001*)

Mode of delivery: Women who were older at 1st birth had less agreement than women who were younger.
BW: Women with lower education had less agreement than better educated women.
Onset of labour: Women who were older at 1st delivery had less agreement than women who were younger.
General pain relief: Women with more years elapsed since delivery had less agreement than women with less years.

KEY FINDINGS

Agreement between maternally recalled first pregnancy and first birth events was high ± 33 years post-partum.

- Findings suggest that women reliably self-report their first birth perinatal outcomes even 17- 49 years after delivery.

This was consistent with findings from other studies who noted that pregnancy and birth events are found to be more memorable to mothers expecting their first child.

(Catov et al., 2005; Hopkins et al., 2007; Poulsen et al., 2011; Seidman et al., 1987; Sou et al., 2006)

APPLICATIONS

This empirical study confirms that maternal reporting of certain perinatal outcomes is highly reliable and may be used as a substitute for, or even in preference to, hospital birth records.
Furthermore, maternally recalled birth data may be used when the research question requires more depth beyond what is available within administrative datasets.

Corresponding author: Mindy Ebrahimoff
mindyebb@gmail.com

APPENDIX 5: STATISTICAL TABLES AND FIGURES EXCLUDED FROM THE MAIN TEXT

Table A5.1: Mothers' Self-reported Maternity History and Pregnancy Complications

		Mothers Recall N	%
Pregnancy problems	None	89	88.1
	Appendectomy	1	1.0
	Edema	1	1.0
	Hyperemesis	2	2.0
	PIH	1	1.0
	PMC	3	3.0
	Toxemia 38W	1	1.0
	Triplets - HRP	1	1.0
	Uterine prolapse	1	1.0
	HRP care	1	1.0
Other problems	None	96	95.0
	Back pain	1	1.0
	MTHFR Clexane	1	1.0
	Ritodrine	1	1.0
	Gestational diabetes	1	1.0
	Hypertension	1	1.0
Previous abortions	Yes	9	8.9
	No	92	91.1
TOP - Termination of pregnancy	Yes	4	4.0
	No	95	94.1
	Missing	2	2.0
IUFD = Intra uterine fetal death	Yes	3	3.0
	No	97	96.0
	Missing	1	1.0
Spontaneous conception	Yes	92	91.0
	IUI	3	3.0
	Hormones	1	1.0
	Ikaclomin	3	3.0
	Following tubal cannulation	1	1.0
	Following hysterosalpingography	1	1.0

Table A5.2: Mothers' Frequencies of Multiple Deliveries, Birth Weight and Gestational Age

		Mothers Recall	Hospital Records
BW g (including multiple deliveries)*	N	104	101
	Minimum	1400	1680
	Maximum	4200	4270
	Mean	3093.46	3127.13
	SD	561.914	501.704
GA weeks (including multiple deliveries)*	N	103	74
	Minimum	32	34
	Maximum	42	42
	Mean	39.17	39.18
	SD	2.020	1.808

* Multiple births included one set of triplets and three sets of twins, n=106.

Table A5.3: Levels of Tolerance and Variance Inflation Factor for Mothers' Length of Labour, daughters' Age at Delivery, Daughters' Use of Analgesia and Daughters' Weight Gain

Linear regression	**Collinearity tolerance**	**VIF**
M LoL	0.97	1.03
D age at delivery	0.94	1.06
D analgesis	0.97	1.03
D weight gain (kg) (	0.95	1.04

M=Mother
D=Daughter

Table A5.4: SPSS Output Showing Levels of Tolerance and VIF

Linear regression	**Collinearity tolerance**	**VIF**
M LoL binary dummy 3 cats	0.61	1.64
M LoL binary dummy 3 cat3	0.61	1.65
D age at delivery	0.93	1.07
D weight gain (kg)	0.95	1.05
D analgesia (binary)	0.98	1.02

M = mother
D = daughter
LoL = length of labour

Table A5.5: Diagnostics Summary of Cook's Distance and Leverage Values in Regression

	Minimum	Maximum	Mean	SD	N
Cook's Distance	0.00	0.08	0.01	0.01	291
Centered Leverage Value	0.02	0.06	0.02	0.02	291

Figure A5.1: Residuals vs. Leverage for Checking Cases Influential to the Regression Results

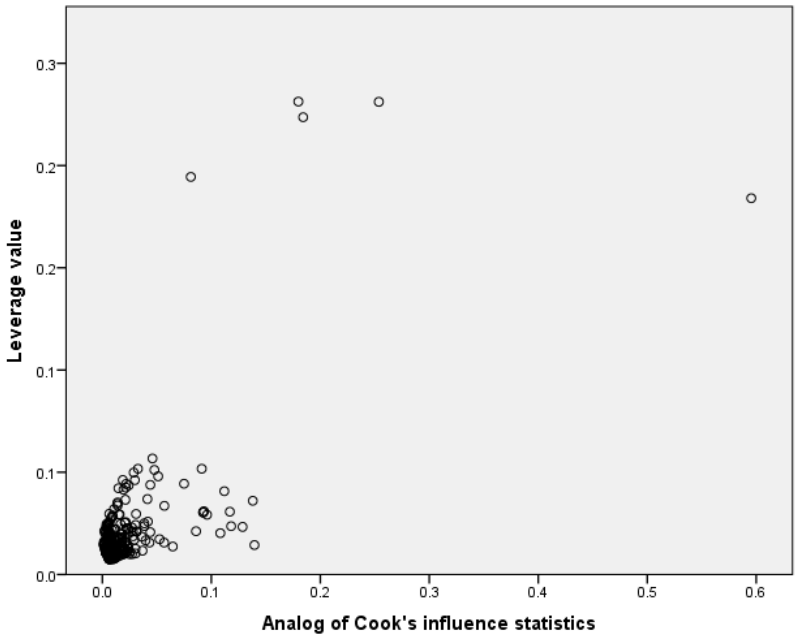


Figure A5.2: Normal P-P Plot of Regression Standardised Residual for Daughters' Length of Labour

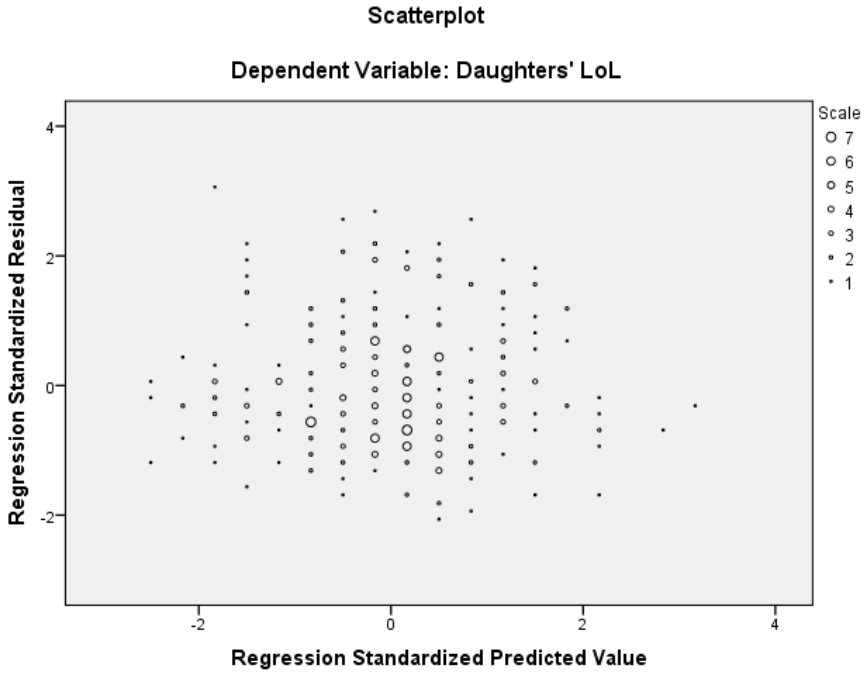


Figure A5.3. Histogram of Standardised Residuals of Daughters' Length of Labour

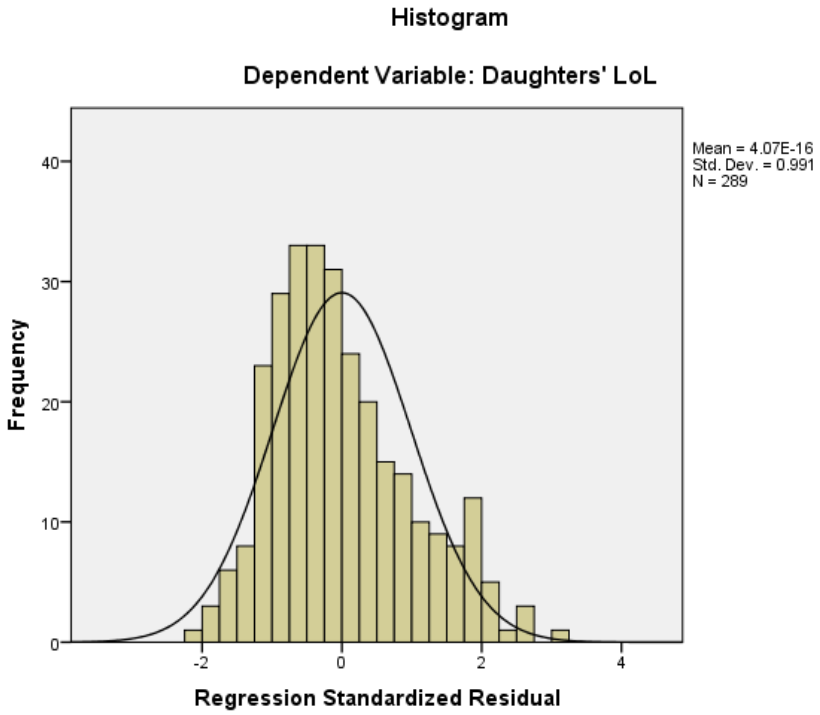


Figure A5.4: Quantile-normal Plot for Daughters' Length of Labour