UTS UNIVERSITY OF TECHNOLOGY SYDNEY

Gestational surrogacy practice and risk experiences of gestational surrogates in Thailand

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under the supervision of Professor Elizabeth Sullivan and Associate Professor Alex Wang

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Certificate of original authorship

I, Jutharat Attawet, certify that this thesis is submitted in fulfilment of the requirements for the award of Doctor of Philosophy in the Faculty of Health at the University of Technology Sydney. I certify that the work in this thesis has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree, except as fully acknowledged within the text.

I also certify that this submission is my own work, except to the extent that assistance from others in the project's design and conception, and style, presentation and linguistic expression is acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

This research was supported by an Australian Government Research Training Program Scholarship.

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Date 11/01/2021

Supervisor statement

I confirm that, to the best of my knowledge, the work of this PhD thesis represents the original research work of the candidate. She is the first author and responsible for at least 80% of the work of each study (Chapters 4 to 6). The research was carried out and the thesis was prepared under my direct supervision. The contributions made to the research by me, the co-supervisor, and the members of the advisory team were consistent with normal supervisory and advisory practice. Other external contributions to the research are acknowledged.

I confirm that the co-authors of the three studies, Professor Cindy Farquhar, Dr. Vanessa Jordan, Dr. Karin Hammarberg, Dr. Zhuoyang Li, and Chief Executive Officer Louise Johnson have agreed to the submission of the nominated studies as part of this PhD thesis.

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Elizabeth Anne Sullivan

Date…….....

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Statement of contributions for works of joint authorship within this thesis

This thesis by compilation contains published work and work that has been submitted or accepted for publication or is currently under peer review (Chapters Four, Five, and Six). I hereby declare that I have been primarily responsible for determining the research questions, managing data collection, analysing the data, and drafting the manuscripts. The contributions of my supervisors Professor Elizabeth Sullivan and Associate Professor Alex Wang, the advisor Dr. Jane Walker, and co-authors Professor Cindy Farquhar, Dr. Vanessa Jordan, Dr. Karin Hammarberg, Dr. Zhuoyang Li, and Chief Executive Officer Louise Johnson to the three studies was consistent with normal supervisory and advisory practice involving data synthesis, interpretation, and manuscript editing.

I take full responsibility for the accuracy of the information and findings presented in this PhD thesis.

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- Attawet, J., Wang, A. Y., Farquhar, C. M., Jordan, V., Li, Z. & Sullivan, E. A. 2020, 'Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis', *Human Fertility,* vol. 23, no. 2, pp. 1-12, < https://doi.org/10.1080/14647273.2020.1794062>.
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- ‘Womb for work’ was presented in the 3MT, Research Student Forum at UTS in 2018 and submitted to Visualise Your Thesis competition, 2018 at UTS

Signed ……

Jutharat Attawet

Date …….

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Abbreviations

ACT	Australian Capital Territory
ANZARD	Australia and New Zealand Assisted Reproduction Database
ART	Assisted Reproductive Technology
ASRM	American Society for Reproductive Medicine
CARTR	Canadian Assisted Reproductive Technologies Register
CDC	Centers for Disease Control and Prevention
CFAS	Canadian Fertility & Andrology Society
CI	Confidence Interval
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CLBR	Cumulative Live Birth Rate
CREC	Central Research Ethics Committee in Thailand
D&C	Dilation and Curettage
DVT	Deep Vein Thrombosis
ESHRE	European Society of Human Reproduction and Embryology
eSET	Elective Single Embryo Transfer
FET	Frozen-thawed Embryo Transfer
FSA	Fertility Society of Australia
GCP	Good Clinical Practice

GRS	Graduate Research School
HFEA	Human Fertilisation and Embryology Authority
HIV	Human Immunodeficiency Virus
HREC	Human Research Ethics Committees
ICMART	International Committee for Monitoring Assisted Reproductive Technologies
ICSI	Intracytoplasmic Sperm Injection
IFFS	International Federation of Fertility Societies
IVF	In vitro fertilisation
JOINT SOGC	Joint Society of Obstetricians and Gynaecologists of Canada
JSOG	The Japan Society of Obstetrics and Gynaecology
QLD	Queensland
MET	Multiple Embryo Transfer
MeSH	Medical Subject Headings
MOPH	Ministry of Public Health in Thailand
NASS	National ART Surveillance System
NHMRC	National Health and Medical Research Council
NOS	The Newcastle-Ottawa Scale
NPESU	National Perinatal Epidemiology and Statistics Unit
NSW	New South Wales
NT	Northern Territory

PGS	Preimplantation Genetic Screening
PGT	Preimplantation Genetic Testing
PGT-A	Preimplantation Genetic Testing for Aneuploidy
PICO	Population, Intervention, Comparison and Outcome
RANZOG	The Royal Australian and New Zealand College of Obstetricians and Gynaecologists
RevMan	Review Manager
RR	Risk Ratio
RTCOG	The Royal Thai College of Obstetricians and Gynaecologists
SA	South Australia
SART	Society for Assisted Reproductive Technology
SET	Single Embryo Transfer
TAS	Tasmania
UK	United Kingdom
US	United States
UTS	University of Technology Sydney
VARTA	Victorian Assisted Reproductive Treatment Authority
VIC	Victoria
WA	Western Australia
WHO	World Health Organization

Abstract

Background: Gestational surrogacy is an assisted reproductive technology (ART) treatment available to help infertile or childless couples, gay couples, individuals, and people in later life to have children. Gestational surrogacy arrangements have become popular, although the treatment is controversial, particularly because of the risks to gestational surrogates, especially those involved in commercial surrogacy. The objective of this PhD thesis is to provide evidence to inform the development of surrogacy practices, policies, and regulations by investigating gestational surrogates' risk experiences, and advocate for practices promoting their health and safety.

Materials and methods: The thesis comprises three exhaustive studies utilising multiple methods to answer research questions from different perspectives. Data were collected as interviews with previous Thai gestational surrogates, a review of published articles, and extractions from the Victorian Assisted Reproductive Treatment Authority (VARTA).

Results: The findings show that commercial surrogacy is an adaptive enterprise with business thriving in many locations, while gestational surrogates face risks involving transnational gestational surrogacy, and incentives for multiple embryo transfer (MET) and higher risk procedures such as embryo transfer from Human Immunodeficiency Virus (HIV) positive couples, posing risks such as multiple births or communicable disease transmission, and unsupportive pregnancies. The thesis findings advocate for single embryo transfer (SET) and altruistic surrogacy practices for gestational surrogates to promote their health and optimise ART outcomes. The findings indicated that MET in gestational surrogacy cases had a much higher multiple birth rate than SET in altruistic surrogacy practice. Additionally, SET in altruistic surrogacy practice showed cumulative live birth rates (CLBRs) up to 50% in six cycles, reflecting the successful rate of ART.

Conclusions: From a public health perspective, SET practice should be universally regulated in surrogacy practice and altruistic surrogacy should be promoted to safeguard surrogates' health along with maximising overall ART outcomes. Commercial surrogacy regulations, especially in Thailand, should also be (re)considered/(re)framed to protect gestational surrogates against the risks from the current business model. The health of gestational surrogates should be promoted by implementing an educational programme for potential gestational surrogates as a part of the surrogacy process to improve their understanding, and their rights in surrogacy treatment should be advocated.

Chapter 1: Introduction

1.1 Background

Assisted reproductive technology (ART) includes medical procedures to treat infertility by collecting oocytes from ovaries and fertilising them in the laboratory with a man's sperm. ART enables infertile different-sex couples, single parents, and gay couples to have children, including their own biological children, using surrogacy arrangements. In a surrogacy arrangement, a woman, known as a surrogate, commits to carrying a foetus and giving birth to a child on behalf of another person or couple, who are known as the intended parents (Armour 2012; Wang et al. 2016). Surrogacy arrangements take two main forms: traditional surrogacy and gestational surrogacy (Jadva et al. 2003; Söderström-Anttila et al. 2016). In traditional surrogacy, the treatment uses the oocytes of the surrogate and inseminates them with either the sperm of the intended father or donated sperm (Armour 2012; Bhatia et al. 2009; Brinsden 2003; McMahon 2011; Morrissey 2014). The surrogate in traditional surrogacy is, therefore, considered to be the biological mother of the baby born from the arrangement.

Gestational surrogacy involves an ART procedure using sperm from the intended father or a sperm donor and oocytes from the intended mother or an oocyte donor to create embryos that are then placed in the gestational surrogate's uterus (American Society for Reproductive Medicine (ARSM) 2013; Oultram 2015; Perkins et al. 2018). Therefore, a baby born from a gestational surrogacy arrangement could be genetically linked to one, both, or neither of the intended parents, and is not genetically related to the surrogate (Brinsden 2003; Frydman 2016).

Both traditional and gestational surrogacy are undertaken with either altruistic or commercial motives. Altruistic surrogates carry a baby for the intended parents without compensation beyond the reimbursement of medical and other reasonable expenses, while commercial surrogates carry a baby in exchange for a fee (Anderson, Snelling & Tomlins-Jahnke 2012; Armour 2012; Burrell & Edozien 2014; Stafford-Bell, Everingham & Hammarberg 2014; Van Zyl & Walker 2013).

The use of surrogacy, particularly gestational surrogacy arrangements, is steadily increasing. In the United States (US), there were 30,927 gestational surrogates over a 14 year period (1999–2013) (Centers for Disease Control and Prevention (CDC) 2016). In Canada, recent reports showed the use of 949 gestational surrogate cycles in 2018, an increase from 78 gestational surrogate cycles in 2001 (Canadian Fertility & Andrology Society (CFAS) 2019). In Australia and New Zealand, 275 gestational surrogate cycles were used in 2018, which was an increase from 39 gestational surrogate cycles in 2005 (Newman, Paul & Chambers 2020). The rising demand for gestational surrogacy has driven entrepreneurs seeking to exploit an opportunity within a medical grey area to establish commercial surrogacy businesses.

Commercial surrogacy is widely practised in the US, Russia, and Ukraine (and in India before it was banned in 2018), but is wholly banned or restricted in many countries, such as Australia, New Zealand, Canada, and the United Kingdom (UK) (Anderson, Snelling & Tomlins-Jahnke 2012; Armour 2012; Burrell & Edozien 2014; Van Zyl & Walker 2013). However, even though commercial surrogacy is banned in many countries, the practice continues. The supply of commercial surrogacy arrangements is more likely to come from women in low- to middle-income countries where the practice is legal or unrestricted, such as Thailand, India, and Laos (Whittaker 2011). Evidence shows that India was the most popular destination for commercial surrogacy arrangements until 2013 when a new law banned same-sex couples from using India's surrogacy services (Whittaker 2011, 2014). After the Indian ban in 2013, Thailand became the most popular jurisdiction. However, both Thailand and India completely banned commercial surrogacy arrangements in 2015 and 2018, respectively (The Surrogacy (Regulation) Bill, 2019 (India) 2019; Royal Thai Government Gazette 2015). Nevertheless, there are reports that the industry has been moved to operate in other countries, and that gestational surrogates have also crossed borders to participate in commercial surrogacy arrangements (Hibino 2020).

1.2 Thesis motivation

Surrogacy arrangements, and especially gestational surrogacy arrangements, have become a popular and effective fertility treatment in ART. Many aspects of the risks to gestational surrogates associated with gestational surrogacy arrangements, including commercial surrogacy, have been discussed worldwide. Therefore, this PhD thesis focused on gestational surrogacy arrangements and gestational surrogates rather than traditional surrogacy.

The surrogacy debate is of interest to me as I have a Thai background, and several high-profile cases have recently come to light in Thailand. For example, the case of 'Baby Gammy', a baby with Down's syndrome who was left behind with his commercial gestational surrogate in Thailand by his intended parents who took his twin sister, who did not have Down's syndrome, back home with them to Australia, was brought to the public's attention and led to the commercial surrogacy ban in Thailand in 2015 (Whittaker 2016). Other high-profile cases of commercial surrogacy in Thailand include that of 'Baby Carmen', who was born to a Thai commercial gestational surrogate who changed her mind about relinquishing the baby to her American-Spanish same-sex intended parents, and the 'baby factory' scandal, in which 13 children were born to Thai commercial gestational surrogates with the same Japanese biological father, 24-year-old Mitsutoki Shigeta, who wanted to have more than 1,000 babies and planned 10–20 surrogacies every year (Bangkok Post 2016; BBC News 2018). Generally speaking, most high-profile cases in Thailand involved commercial surrogacy arrangements, which were not known to the public before the 'Baby Gammy' scandal erupted in 2014. With limited evidence available, Thai surrogacy practices and the risk experiences of Thai gestational surrogates present an interesting issue to further investigate in order to improve surrogacy safety practices and advocate for women's overall health outcomes.

Although Thailand's commercial surrogacy arrangements are well known, current Thai gestational surrogacy practice and pregnancy and live birth outcomes cannot be traced, because Thailand does not prepare an annual ART report like some other countries, such as Australia. Thai fertility clinics offering gestational surrogacy services in the form of commercial surrogacy arrangements were shut

down after the surrogacy ban in 2015, and the data were subsequently concealed. Since then, only altruistic surrogacy arrangements have been allowed in Thailand. Although approximately 140 cases were approved from 2016 to 2018 for surrogacy treatment under the new surrogacy legislation (Hibino 2020), the data available for analysis are limited, and the pregnancy and live birth outcomes following gestational surrogacy in Thailand remain unclear. However, gestational surrogacy arrangements and the risk experiences of gestational surrogates in Thailand can still be clarified from (ex-)gestational surrogates. Their experiences could reflect the current trends in gestational surrogacy practice and indicate the risks to gestational surrogates in Thailand. I deemed that understanding the gestational surrogacy practice and risk experiences of gestational surrogates throughout the gestational surrogacy process in Thailand could provide useful information about the needed improvements to gestational surrogacy practices overall, and the related guidelines and regulations.

My conversations with friends working in fertility clinics that offer gestational surrogacy services made me acutely aware of and concerned about the risks to gestational surrogates. Thai surrogacy practices, particularly multiple embryo transfer (MET) and commercial surrogacy arrangements, came up in conversations, and it seemed that MET continues to be a routine practice among gestational surrogates, although single embryo transfer (SET) has been introduced into practice to prevent the adverse outcomes of MET (Practice Committee of the ARSM and the Practice Committee of the Society for Assisted Reproductive Technology (SART) 2017). While MET has been believed to improve pregnancy outcomes (Price 1989), the use of MET results in higher chances of producing multiple pregnancies compared to SET, posing greater risks for both mothers and babies (Büscher et al. 2000; Cassell, O'connell & Baskett 2004; Obiechina et al. 2011; Pingili, Bamigboye & Jegede 2007; Taebi 2014). Subsequent maternal risks associated with multiple pregnancies can include preeclampsia, hypertensive disorders of pregnancy, gestational diabetes, premature rupture of membranes, and antepartum and postpartum haemorrhage (Cassell, O'connell & Baskett 2004; Obiechina et al. 2011; Taebi 2014). Compared to single pregnancies, the risks of potential maternal life-threatening conditions, maternal near miss, severe maternal outcomes, and maternal death were

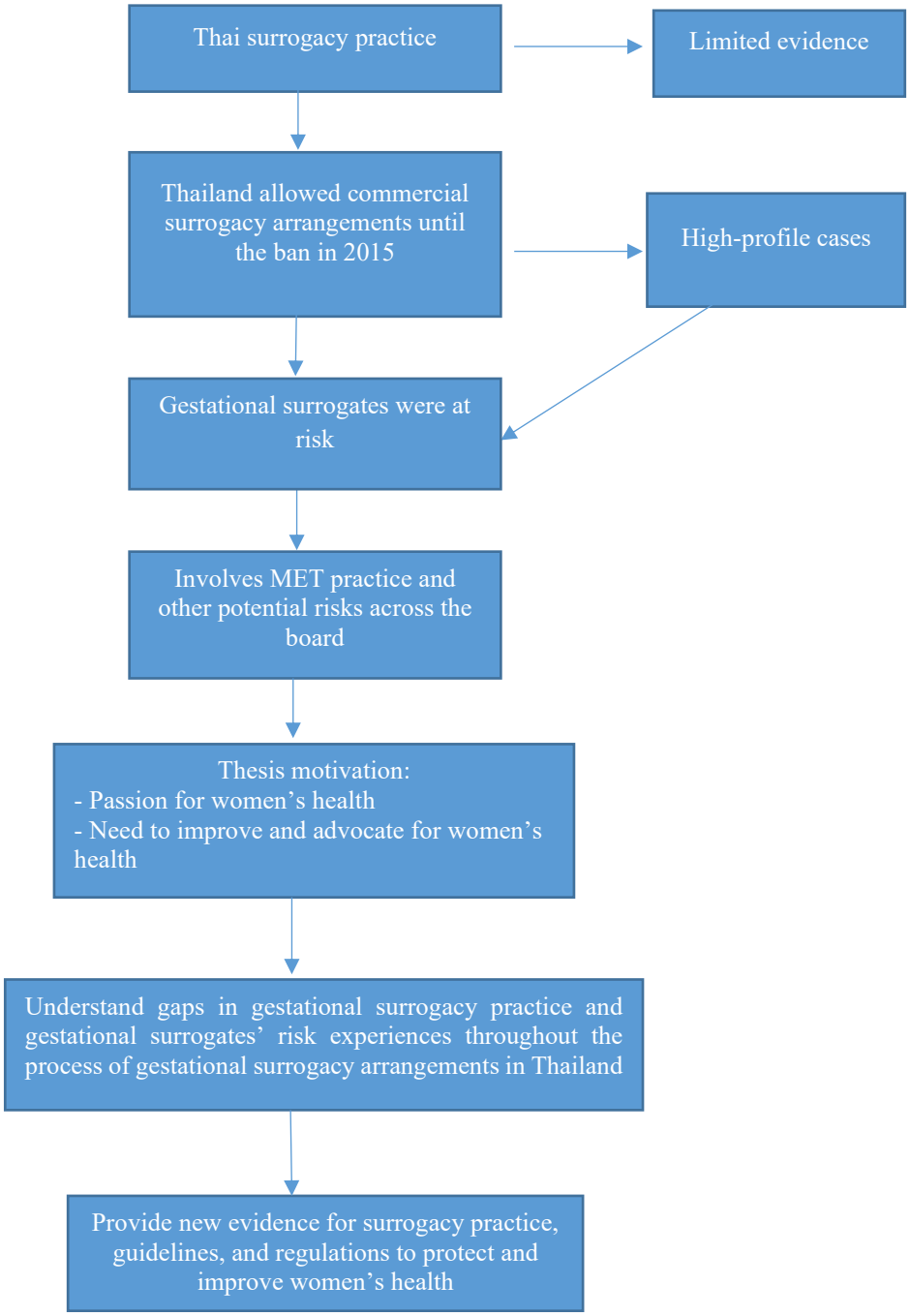
found to increase twofold, threefold, threefold and fourfold, respectively, in multiple pregnancies (Santana et al. 2016). Korb and colleagues (2020) also found that the risk of severe maternal morbidity including death, severe postpartum haemorrhage, hypertensive disorders, placenta abruption, eclampsia, HELLP syndrome (haemolysis, elevated liver enzymes, and low platelet count), and severe preeclampsia was higher among women with twin pregnancies using IVF oocyte donation (14%), compared to IVF using autologous oocytes (8.3%) or a natural twin pregnancy (5.3%). The results of this study are relevant and applicable to the context of gestational surrogacy, where women receive donated oocytes. Based on these results, multiple pregnancy is classified as higher risk for gestational surrogates.

Preterm delivery, which is a known risk factor for prenatal mortality and morbidity, is also a common adverse perinatal outcome resulting from multiple pregnancy (Büscher et al. 2000; Refuerzo, Momirova & Peaceman 2010; Su et al. 2015). Evidence suggests that babies born preterm are more likely to have short-term health problems, such as low birth weight, hypothermia, hypoglycaemia, respiratory distress syndrome, necrotising enterocolitis, intraventricular haemorrhage, and immune system problems (Pingili, Bamigboye & Jegede 2007). They are also more likely to have long-term health problems, including impaired learning, vision problems, hearing problems, behavioural and psychological problems, and chronic health issues (Büscher et al. 2000; Pingili, Bamigboye & Jegede 2007; World Health Organization (WHO) 2018). This issue raised questions for me regarding the necessity and benefits of MET for gestational surrogates. Thus, I deemed MET practices among gestational surrogates to be worthy of a systematic investigation, to provide evidence relevant to surrogacy safety practices and the health of surrogates.

Across the conversation and evidence reported, commercial surrogacy arrangements seem to be popular and to pose greater risks to gestational surrogates. From a different perspective, although commercial surrogacy arrangements are banned in many countries, altruistic surrogacy arrangements remain unpopular. Commercial surrogacy arrangements seem to be the preference of intended parents regardless of whether or not this option is available in their home country. Commercial surrogacy

agencies routinely advertise their clinical capacity and high rates of success in terms of pregnancy and birth outcomes; these advertisements are widely used on the Internet (ADONIS Fertility International 2019; ConceiveAbilities 2018) . For example, one such advertisement for commercial surrogacy claims to offer a live birth rate as high as 95% at fertility clinics in the US (ConceiveAbilities 2018). Other commercial surrogacy websites also claim to offer a live birth rate up to 75%, which is higher than the 50% average (Gezinski et al. 2017). These high success rates of live births and the less complicated process of accessing commercial surrogacy services tempt intended parents to use commercial surrogacy arrangements over altruistic ones. However, unacceptable practices and high risks to gestational surrogates, such as the use of MET, can explain commercial surrogacy's high rates of successful pregnancy and positive birth outcomes. This situation inspired me to evaluate the pregnancy and live birth outcomes of altruistic surrogacy arrangements using SET, in order to clarify the effectiveness of altruistic surrogacy arrangements and SET treatment, as the findings on their effectiveness will be important in the context of commercial surrogacy arrangements. Studies on advanced technologies in embryo transfer also report improvements in the success rate of pregnancy and live birth. The practice of transferring frozen-thawed embryo has increased dramatically over the past decade, as it is reportedly associated with a high live birth rate, and reduced incidence of low birth weight, small for gestational age, preterm birth, placenta previa, placenta abruption, and potential mortality, compared to fresh embryo transfer (Ernstad et al. 2019; Roque et al. 2019; Sha 2018; Singh et al. 2020; Wang 2017). The strategies of elective SET (eSET) and preimplantation genetic testing (PGT) are also shown to be associated with high chance of successful pregnancy and live birth, and prevention of pregnancy complications, such as multiple birth, miscarriage, and birth defects (Lee et al. 2016; Parikh et al. 2018; Tobias et al. 2016). In combination with advanced technologies on embryo transfer, I chose to investigate the outcomes of altruistic surrogacy in Australia, where only altruistic surrogacy arrangements are legally allowed and SET with frozen-thawed embryo is a well-established practice. My motivation to engage in this research is illustrated in Figure 1.

Figure 1: Thesis motivation



1.3 Aims

The overarching aim of this PhD thesis is to investigate the risks encountered by gestational surrogates through their gestational surrogacy experiences.

1.4 Research questions

This thesis offers different perspectives on the following three questions, which were set as guidelines to fulfil the overarching aim in order to fill gaps in the existing knowledge:

(1) What risks do gestational surrogates encounter through the process of gestational surrogacy and the related arrangements in Thailand?

Using interviews with Thai women who had experienced gestational surrogacy, Study 1 aimed to clarify the process of gestational surrogacy and the related arrangements in Thailand and the women's risk experiences throughout the process.

(2) What are the differences in surrogate pregnancy and live birth outcomes between SET and MET among gestational surrogates?

Study 2 systematically compared the synthesised evidence on pregnancy and birth outcomes between SET and MET in gestational surrogates to demonstrate pregnancy outcomes and risks resulting from embryo transfer in gestational surrogacy arrangements.

(3) What is the cumulative live birth rate (CLBR) among gestational surrogates in altruistic surrogacy arrangements?

Using Victorian Assisted Reproductive Treatment Authority (VARTA)'s Australia database, Study 3 evaluated the CLBR among gestational surrogates in altruistic form of gestational surrogacy arrangements in order to introduce new evidence and safe practices in surrogacy arrangements.

1.5 Significance of this PhD thesis

Gestational surrogacy is a controversial practice. The debate over the risks posed to gestational surrogates associated with gestational surrogacy arrangements is of global interest. Understanding gestational surrogates' risk experiences along with the trends in the practices and outcomes of gestational surrogacy arrangements may enable the development of surrogacy practices, policies, and regulations to protect gestational surrogates from additional health risks and optimise ART outcomes. The findings of this PhD thesis provide the parties involved in surrogacy with evidence to consider when making decisions on safe practices during the use of gestational surrogacy. The knowledge generated in this thesis also offers evidence-based research to allow researchers, public health officials, policymakers, and regulators to understand the gaps in existing surrogacy practice and draft guidelines and regulations to close these loopholes, improve surrogacy practices and outcomes, and protect gestational surrogates internationally.

1.6 Structure of this PhD thesis

This PhD thesis comprises seven chapters, including the present chapter—'Introduction' (Chapter 1). Chapter 2, 'Background and literature review', provides an outline of surrogacy arrangements, including traditional and gestational surrogacy and altruistic and commercial surrogacy arrangements, an overview of surrogacy arrangements in Southeast Asia, and surrogacy practices in Thailand and Australia; reviews the literature and summarises the gaps between surrogacy trends and pregnancy and birth outcomes; and outlines the surrogates' experiences.

Chapter 3, 'Research design, methodology, and methods', outlines the research design and theoretical approach to this thesis, which comprises three studies. The methods of data collection, analysis, and management, and the ethical approval of each of the three studies are detailed.

Chapter 4, ''Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand', explores the experiences of Thai women who have been gestational surrogates as they

reflect on their experiences regarding their risk exposure and gestational surrogacy practice in Thailand.

Chapter 5, 'Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis', compares surrogate pregnancy outcomes and surrogacy practice trends by the number of embryos transferred.

Chapter 6, 'Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements', investigates live birth rates among gestational surrogates in Australia, where only altruistic surrogacy arrangements are allowed, and SETs are restricted.

Chapter 7, 'Discussion, Recommendations and Conclusion', summarises the key findings of each study presented in Chapters 4 through 6, demonstrating the correlative findings in this PhD thesis for the purpose of advocacy and protection of women's health. Recommendations are provided based on the findings of each study to improve and promote women's health for prospective surrogates. This chapter also makes recommendations for further research.

1.7 Format

This PhD thesis is structured as a compilation thesis, which includes thesis chapters along with a series of publications. The structure of this thesis was approved by the Graduate Research School (GRS) of the University of Technology Sydney (UTS) in July 2017. The thesis includes three exhaustive studies (Chapters 4 through 6) with references provided at the end of each chapter. The supervisor-signed statement indicating that all co-authors have agreed to the submission of the nominated papers as part of the PhD thesis is presented at the beginning of the thesis.

1.8 Chapter summary

This chapter is an overview of the background to this PhD thesis, including the issues present in the wider international context and the motivation to engage in research on this topic. The research aim, questions, and significance as well as the structure of this PhD thesis have been outlined. The thesis format is a series of studies compiled as chapters. In the following chapter, the current available literature is reviewed and research gaps are identified.

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Chapter 2: Background and literature review

2.1 Chapter introduction

This chapter provides the background of surrogacy arrangements, including the history and types of surrogacy arrangements, the movement and trends in surrogacy practice, and the background of surrogacy regulations in Thailand and Australia. This PhD research used data based on surrogacy arrangements in Thailand and Australia. A literature review of surrogacy practices and risks to gestational surrogates is presented, identifying the gaps in the extant literature, and explaining the rationale of this thesis.

2.2 Background

Family, as a function of belonging, is a basic human need. Having our own children reflects a desire to fulfil the goal of forming a family. Infertile couples, gay couples, or individuals who are unable to reproduce struggle to achieve this goal. Advancements in fertility treatments allow such people the hope of having their own biological children. For example, a surrogacy arrangement is a fertility treatment that is becoming increasingly popular with infertile and childless couples, gay couples, individuals, and even celebrities who prefer to have children later in life (Berkowitz 2013; Brinsden et al. 2000; Goldfarb et al. 2000; Tigar 2019). In a surrogacy arrangement, a woman commits to carrying a foetus and gives birth to a child on behalf of another person or couple (Armour 2012; Wang et al. 2016). The woman who offers to carry a baby through pregnancy is known as a ‘carrier’, a ‘surrogate’, or a ‘surrogate mother’. The person or couple who intend to become the legal parents and raise the child resulting from a surrogate pregnancy are referred to as ‘intended parents’ or ‘commissioning parents’ (Armour 2012; Bhatia et al. 2009). Recent research by Hobzová (2018) indicates that the terms ‘surrogate’ and ‘intended parent’ are preferred to refer to surrogacy parties, while usage of terms such as ‘carrier’ and ‘commissioning parents’ is not considered appropriate; therefore, the preferred terminology will be used in this PhD thesis.

Surrogacy arrangements have assisted couples and individuals in having children, biologically their own or otherwise, for a wide range of medical and social reasons (Havins & Dalessio 2000; Larkey 2003). There are several serious medical conditions listed as criteria for surrogacy arrangements including uterine damage, absent uterus, and severe chronic conditions that contraindicate pregnancy, such as cancer, repeated failed in vitro fertilisation (IVF) attempts, and repeated miscarriage (Aittomaki, Eroila & Kajanoja 2001; Dar et al. 2015; Söderström-Anttila et al. 2016). A surrogacy arrangement takes one of two principal forms: traditional surrogacy or gestational surrogacy.

2.2.1 History of surrogacy: From traditional surrogacy to gestational surrogacy arrangements

2.2.1.1 Traditional surrogacy

Traditional surrogacy is defined as 'straight', 'partial', 'natural', or 'genetic' surrogacy in which the surrogate is inseminated with the sperm of the intended father or donor (Armour 2012). In the medieval period, traditional surrogacy was arranged through direct sexual intercourse between the intended father and the surrogate, known as sex surrogacy by profession (Kate 2009). In fact, traditional surrogacy was even cited in the Bible in the book of Genesis in the tale of Sarah, the barren wife of Abraham, who was unable to become pregnant and used her servant, Hagar, to carry a son, Ishmael, for her husband (Worldwide Surrogacy Specialists 2017). However, traditional surrogacy in contemporary times is more often achieved using the intended father's or donor's sperm to artificially inseminate the surrogate via her vagina or uterus (Armour 2012; Bhatia et al. 2009; Brinsden 2003; McMahon 2011; Morrissey 2014). In traditional surrogacy, the surrogate is considered the biological mother and has a parental right to the gestating baby (Hering 2010). When the baby is born, it is expected that the surrogate will relinquish her parental rights to the intended parents (Burrell & Edozien 2014; Hering 2010).

Traditional surrogacy does not require the intended mother to undergo medical procedures, which could be a benefit for the intended mother. However, regrettably, the intended mother has no option

but to be biologically related to the child. This could cause potential conflicts if the surrogate changes her mind and decides to keep the baby, as she has the parental right and power to do so for her biological child (Luke & Wilson 2012). Traditional surrogacy, thus, involves legal complications, and, in some cases, intended parents may be required to complete a stepparent adoption or a parenting order to be recognised as the child's legal parents (American Surrogacy 2021; Danna 2015; Luke & Wilson 2012).

In the 1980s, traditional surrogacy arrangements attracted global attention as a result of the 'Baby M' case, in which the surrogate decided to keep the baby (Morrissey 2014). Baby M, or Melissa, was born as the result of a traditional surrogacy arrangement between the surrogate, Mrs Whitehead, and the intended parents, the Sterns, who used a surrogacy agency. However, after the baby was born, the surrogate decided to keep her biological baby, which resulted in legal implications relating to the structures and risks of traditional surrogacy arrangements. The lessons learned from the Baby M case caused gestational surrogacy arrangements to evolve to eliminate legal and psychological complexities (Trowse 2011).

2.2.1.2 Gestational surrogacy

While traditional surrogacy has been practised for ages, gestational surrogacy evolved alongside the development of ART. ART includes medical procedures to treat infertility by collecting oocytes from the ovaries and fertilising them with partner or donor sperms, to make embryos that are then implanted in the woman's uterus (CDC 2019). IVF is presently the most commonly known and effective type of ART procedure. The birth of the first successful IVF baby, Louise Brown, was reported in July 1978 in Manchester, England (Steptoe & Edwards 1978), and in 1984 the world's first birth from donated oocytes was reported in Australia (Monash IVF 2019).

The combination of these two innovative ART treatments resulted in the emergence of gestational surrogacy, with the first successful gestational surrogacy reported in 1985 by Utian and colleagues (Utian et al. 1985). The intended parents were a couple that strongly wished to have children, but the

female partner had undergone a hysterectomy. The surrogate, a married 22-year-old mother with proven fertility, including two uncomplicated pregnancies, was a friend of the couple. A baby girl was born following the gestational surrogacy pregnancy, using the oocytes and sperm of the intended parents (Johnson 1987), allowing the couple to have their own genetic offspring (Utian et al. 1985).

Therefore, the practice of gestational surrogacy, also called 'IVF surrogacy', 'full surrogacy', or 'host surrogacy', involves an ART procedure (Blyth 1995; Oultram 2015; Perkins et al. 2018). Gestational surrogacy can use the sperm from the intended father or from a sperm donor, and oocytes from the intended mother or from an oocyte donor, to create embryos through IVF. The embryos are then transferred into the surrogate's uterus (ARSM 2013). The baby born from a gestational surrogacy arrangement is not genetically related to the surrogate, but could be either genetically related or not related to the intended parents (Brinsden 2003; Frydman 2016). In gestational surrogacy arrangements, in some practice, the surrogate must sign a written agreement to relinquish her parental rights; this condition is mandated prior to commencing an arrangement (Burrell & Edozien 2014; Hering 2010).

Since the first successful gestational surrogacy arrangement in 1985, the use of such arrangements has steadily increased. In the US, the ART annual report found that gestational surrogate cycles increased from 727 in 1999 to 3,432 in 2013, accounting for a 79% increase, which further increased to 88% in 2016 (CDC 2018; Perkins et al. 2016) . In Canada, the ART annual report stated that the use of gestational surrogate cycles increased by approximately 91% from 2001 to 2017 (CFAS 2016; Gundy, Daya & the Directors Group of the CFAS 2005). The use of gestational surrogacy cycles also increased by approximately 84% from 2005 to 2017 in Australia and New Zealand (Fitzgerald et al. 2018; Wang, Dean & Sullivan 2007). Such reports reveal that the use of gestational surrogacy has been increasing annually as it has become a popular surrogacy practice; traditional surrogacy cycles are not reported in the national ART registers.

The benefits of gestational surrogacy over traditional surrogacy are that the surrogate shares no genetic link with the baby and the legal process sets a precedent to protect both the surrogate and the intended

parents, which helps to address legal and psychological complexities (Wilson & Luke 2012). Additionally, gestational surrogacy provides the intended mother the option to be biologically related to the child, whereas traditional surrogacy does not allow for this possibility. Nevertheless, there is an ongoing debate that the risks of gestational surrogacy management increase the complexity of the routine IVF process from ovarian stimulation to embryo implantation (Simopoulou et al. 2018).

2.2.2 Altruistic versus commercial surrogacy arrangements

Surrogacy, traditional and gestational, can either be an altruistic or a commercial arrangement. Altruistic surrogacy is an arrangement in which the surrogate is willing to carry a baby for the intended parents without receiving any monetary compensation. In most cases, a surrogate in an altruistic surrogacy arrangement is someone close to the intended parents, such as their family member or friend (Söderström-Anttila et al. 2002), which could be beneficial, as familiarity is likely to increase the level of comfort and trust in the relationship between the surrogate and the intended parents. Although altruistic surrogacy arrangements are legal and acceptable in many countries (Table 1), due to the prolonged and complicated process of securing such agreements and accessibility, studies have found that such arrangements are rarely used by intended parents (Hammarberg, Stafford-Bell & Everingham 2015; Whittaker 2011). For example, Everingham, Stafford-Bell and Hammarberg (2014) found that 92% Australians considered and tended to use overseas surrogacy rather than domestic surrogacy. Consequently, most intended parents tend to seek commercial surrogacy arrangements abroad rather than making domestic altruistic surrogacy arrangements. However, in some countries, such as the UK, altruistic surrogacy remains the overwhelmingly favoured and used by intended parents (Mackle 2019; Norton et al. 2015).

Commercial surrogacy refers to an arrangement in which the surrogate agrees to carry a baby for the intended parents in exchange for monetary compensation for her service beyond the reimbursement of her medical expenses. Commercial surrogacy is legal in some countries, such as the US, Ukraine, and Russia, while many other countries have banned this practice (Table 1).

Table 1: International perspectives on the legality of surrogacy

Arrangement	Legal	Illegal
Altruistic surrogacy	Australia	Bulgaria
	Belgium	China
	Canada	France
	Greece	Germany
	India	Italy
	Iran	Japan
	Mexico	Portugal
	Netherlands	Spain
	New Zealand	The Nordic Countries
	Switzerland	
	Thailand	
	Ukraine	
	United Kingdom	
	United States	
Commercial surrogacy	Iran	Australia
	Israel (only for Israeli citizens, different-sex Israeli couples and single Israeli women)	Belgium
		Bulgaria
		Canada
	Russia	China
	South Africa	Cambodia
	Ukraine	Germany
	United States (varies according to state)	Greece
		India
		Italy
		Japan
		Nepal
		Netherlands
		New Zealand
		Portugal
		Spain
		Switzerland
		Thailand
		The Nordic Countries
		United Kingdom

(Anderson, Snelling & Tomlins-Jahnke 2012; Armour 2012; Burrell & Edozien 2014; Hibino 2020; Van Zyl & Walker 2013)

Note: Although surrogacy is illegal and not regulated in the Nordic countries, in some countries such as Denmark, Finland and Sweden, surrogacy is still practised (Nordic Information on Gender 2019).

Compensation to surrogates has raised the fundamental ethical issues regarding individual autonomy and human rights (of surrogates). Philosophical theories of autonomy advocate self-determination for individuals in the context of moral choices (Guyer 2003). Human rights are the basic rights and freedoms of every person, regardless of background, religion, belief, or any other factor (Bromfield & Rotabi 2014). Based on these principals, interestingly, supporters of commercial surrogacy argue that the surrogate has the right to determine what 'work' she does and how she 'uses' her own body (Wilkinson 2003). The surrogate sacrifices her body to carry the baby and bears the responsibility to perform her duties for nine months. In turn, she contents herself with a financial gain adequate for her sacrifices and responsibilities. Here, the ethical principal of fairness needs to be taken into consideration for altruistic surrogates, who agree to carry the baby without a fee exchange, whether or not they feel fairly treated or adequately compensated for their sacrifices and responsibilities. However, opponents of commercial surrogacy argue that the compensation for surrogates makes the conception a financial transaction in which illiterate and impoverished women may be taken advantage of and convinced to become surrogates in exchange for large sums of money (Kulkarni 2015). Some believe that the conception of financial transaction makes commercial surrogacy comparable to organ selling or even baby selling, and leads to the exploitation of surrogates (Haq 2015). Along with the issues of baby-selling and exploitation of surrogates, paternalistic intervention argues that commercial surrogacy has the potential to violate the principle of human value and dignity, and thus pose harm to children and surrogates, making commercial surrogacy a controversial issue and an unacceptable practice (Goold 2003; Haq 2015).

Since intended parents tend to seek surrogacy arrangements abroad, regardless of controversial issues, commercial surrogacy has turned into an international business, in spite of the prohibitions or restrictions implemented by many countries (Cohen 2015; Mohapatra 2012). The rapidly expanding business of commercial surrogacy overseas is a response to the current demand for surrogacy. According to Gezinski et al. (2017), South and Southeast Asia seem to be major marketplaces for commercial surrogacy services. Attractive online advertisements with affordable prices have increased the influx of

foreign couples seeking surrogacy in South and Southeast Asian countries such as India and Thailand. According to Smith (2014), the average prices of surrogacy services in India and Thailand are US$30,000 and US$40,000, respectively, whereas surrogacy services in the United States cost US$100,000–$200,000. Another factor that has made these destinations popular for commercial surrogacy is the legalisation of gay marriage. Local altruistic surrogacy can unfairly disadvantage male couples, as they can rarely access it (Tremellen & Everingham 2016). Therefore, seeking 'outsources' overseas, especially in South and Southeast Asia with affordable prices appears to be an attractive option for same-sex couples to build a family. This factor might also be responsible for the current demand of commercial surrogacy and, in the future, may possibly increase its demand. Responding to this increased demand has made South and Southeast Asia 'the surrogacy hub' of the world.

While commercial surrogacy arrangements are legal in few countries, as listed in Table 1, the practice continues to take place illegally in some countries in South and Southeast Asia, such as India and Thailand.

Usually, commercial surrogacy involves infertile or gay couples from high-income countries, such as Australia, Canada, and the UK, travelling to low- or middle-income countries in search of a surrogate (Cohen 2015; Everingham, Stafford-Bell & Hammarberg 2014; Mohapatra 2012; Whittaker 2011). Recent high-profile landmark surrogacy cases took place mostly in low- or middle-income countries that allow commercial surrogacy practices. Table 2 demonstrates the current regulations regarding surrogacy in South and Southeast Asia.

Table 2: Demonstration of surrogacy law in South Asia

Countries	Altruistic surrogacy arrangements	Commercial surrogacy arrangements
South Asia		
Afghanistan	Unregulated	Unregulated
Bangladesh	Unregulated	Unregulated
Bhutan	Unregulated	Unregulated
India	Currently legal	Regulated in 2002 and banned in 2018
Maldives	Unregulated	Unregulated
Nepal	Currently legal for infertile Nepali married (heterosexual) couple only	Banned in 2015
Pakistan	Prohibited/Illegal	Prohibited/Illegal
Sri Lanka	Unregulated	Unregulated
South East Asia		
Brunei	Unregulated	Unregulated
Cambodia	No legal regulation	Banned in 2016
Indonesia	Prohibited/Illegal	Prohibited/Illegal
Laos	Unregulated	Unregulated
Malaysia	Prohibited/Illegal	Prohibited/Illegal
Myanmar	Unregulated	Unregulated
Philippines	Unregulated	Unregulated
Singapore	Prohibited/Illegal	Prohibited/Illegal
Thailand	Legal	Banned in 2015
Timor Leste	Prohibited/Illegal	Prohibited/Illegal
Vietnam	Legal in 2015	Prohibited/Illegal

(Hibino 2019; Hibino 2020; Kooli 2019; Lee & Tedeschi 2015)

The international nature of the surrogacy business is controversial, particularly in South and Southeast Asia where the practice has gone underground. The following section maps the movement of the industry in South and Southeast Asia.

2.2.3 The movement of the commercial surrogacy business in Southeast Asia

2.2.3.1 India

The market of commercial surrogacy arrangements in South and Southeast Asia started with India's legalisation on commercial surrogacy in 2002 (Saxena, Mishra & Malik 2012) . India became the hub of surrogacy services that were notorious as 'rent-a-womb' arrangements (Ray 2018). A United Nations report in 2012 estimated that the commercial surrogacy business of over 3,000 fertility clinics in India was worth more than $400 million per year (Bhalla & Thapliyal 2013). The case of 'Baby

Manji' in 2008 illustrated the complexity of commercial surrogacy. The case reflected an arrangement that had been made between a Japanese couple and an Indian gestational surrogate. One month before the baby was born to the Indian gestational surrogate, the Japanese couple divorced. This case became complicated when the intended mother refused to take possession of Baby Manji and none of the mothers—the intended mother, the gestational surrogate, and the oocyte donor—were legally responsible for Baby Manji. Consequently, Baby Manji was refused a Japanese passport and was left in India for three months until the issue was resolved (Points 2009). This case led the Indian government to consider placing restrictions on commercial gestational surrogacy arrangements. India banned single parents and same-sex couples from engaging in commercial surrogacy in 2013, and banned the practice altogether in 2018 (Ray 2018; Smith 2014). However, the new surrogacy restrictions did not stop the commercial surrogacy business; instead, the business went underground.

2.2.3.2 Nepal

As a consequence of the Indian restrictions on commercial surrogacy in 2013, the Indian industry relocated to Nepal, initially making Nepal a commercial surrogacy hub for single parents and same-sex couples. A loophole in Nepal's surrogacy regulations allowed surrogacy to take place as long as the surrogate was not a Nepalese citizen. This loophole created an opportunity for India's fertility clinics to move their commercial surrogacy businesses across the border to Nepal and thereby avoid the ban in India (Rudrappa 2017). Indian surrogates were moved to Nepal for their entire gestation period, from impregnation to delivery, and the intended parents picked up the babies from Nepal, which did not breach Nepal's surrogacy regulations (Rudrappa 2017). This arrangement continued until a massive earthquake hit Nepal in 2015, leaving many Indian surrogates stranded; consequently, Nepal's government and the governments of the intended parents airlifted the babies belonging to their citizens (Bhowmick 2016; Duttagupta 2015). This issue led the country to suspend commercial surrogacy and completely ban it in late 2015 (Bhowmick 2016). However, commercial surrogacy continued to take place in neighbouring countries, such as Thailand, Cambodia, and Laos, where the practice was not regulated.

2.2.3.3 Thailand

Thailand's commercial surrogacy market expanded rapidly between 2006 and 2010. The emergence of a Thai surrogacy market was stuck in a legal limbo from the outset, as there were no laws governing surrogacy arrangements (Cohen 2015; Hibino & Shimazono 2013; Whittaker 2014). Surrogacy arrangements in Thailand were, therefore, neither legal nor illegal (Chaninat & Leeds 2015). A loophole in the Thai surrogacy law allowed entrepreneurs to establish commercial surrogacy businesses in Thailand. These businesses boomed after the Indian ban on surrogacy arrangements for same-sex couples in 2013 (Smith 2014). As the hub of commercial surrogacy arrangements, Thailand became notorious as the 'womb of Asia' (BBC News Asia 2015). The industry attracted little controversy until mid-2014, when a baby with Down's syndrome, named Gammy, was left behind with his commercial gestational surrogate in Thailand by his Australian intended parents who took his twin sister back to Australia (Whittaker 2016). Following the 'Baby Gammy' scandal, in early 2015, the Thai military government legislated against commercial surrogacy, banning foreign and same-sex couples from seeking the service (Royal Thai Government Gazette 2015; Sattaburuth 2015). Several surrogacy fertility clinics closed as a result, although others reportedly continue to operate in Bangkok, and some have moved their operations to neighbouring countries (Hibino 2020; Murdoch 2017).

2.2.3.4 Cambodia

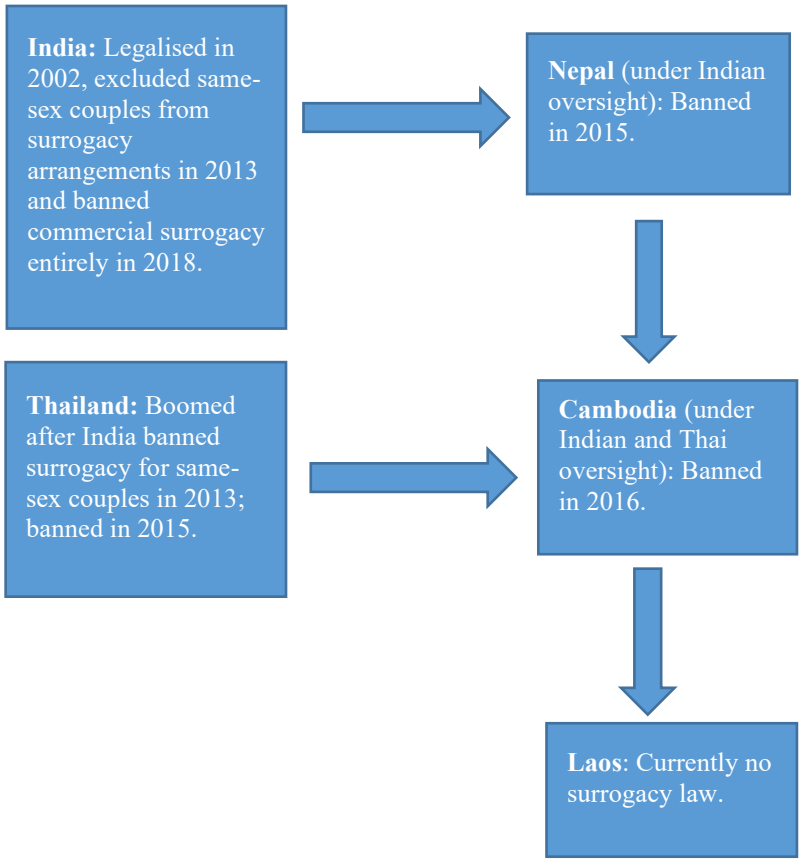
Following the effective closure of commercial surrogacy in India, Nepal (under Indian oversight), and Thailand, the marketplace briefly moved to Cambodia, where the surrogacy law was ambiguous. Some Indian and Thai fertility clinics were found to have been operating in Cambodia (Bhowmick 2016; Lefevre 2017). However, in 2016, Cambodia also imposed a commercial surrogacy ban (Lefevre 2017). From there, the industry moved to Laos, where it was not regulated.

2.2.3.5 Laos

From mid-2016, Laos flourished as a surrogacy hub following the bans in Thailand and Cambodia in 2015 and 2016, respectively. Indeed, some Thai surrogacy and fertility businesses that had been threatened with closure in 2015 reportedly continue their operations in Laos (Hibino 2020; Lefevre 2017; Murdoch 2017).

As Laos has no laws or regulations on surrogacy practice (Lefevre 2017), surrogacy arrangements in the country are neither legal nor illegal. This lack of regulation has made Laos a business destination for commercial surrogacy. The process of commercial surrogacy arrangements between Thailand and Laos is still unclear; however, the business trend may reflect a process similar to Indian and Nepalese commercial surrogacy arrangements by moving Thai surrogates across the border to Laos. There is a loophole in that Thai and foreign surrogates impregnated elsewhere but delivering babies in Thailand are not considered to be breaking Thai law (Lefevre 2017; Whittaker 2014). This loophole means that Thailand remains a key centre for surrogate births by allowing Thai surrogates and foreign surrogates who are impregnated in Laos to return to Thailand for the duration of their pregnancy and to stay for the delivery. Figure 2 demonstrates the evolution of the movement of commercial surrogacy arrangements in South and Southeast Asia.

Figure 2: Summary of the evolution of commercial surrogacy arrangements in South and Southeast Asia



The establishment of a commercial surrogacy business has navigated the complexity of the surrogacy process by moving surrogates from country to country to avoid breaking surrogacy laws of certain countries. The complexity of the process has put surrogates at risk, involving ethical, legal, social, and health impacts. Using commercial surrogacy arrangements not only puts surrogates at risk, but also makes the process of bringing the baby back to the intended parents' country risky, potentially adversely affecting the children. The legality of bringing a baby born to a surrogate overseas to the country of its intended parents varies from country to country. In some countries, such as Australia, while all states have banned commercial surrogacy, New South Wales (NSW), Queensland (QLD), and the Australian Capital Territory (ACT) also consider it an offence for a person residing in those

states to make a commercial surrogacy arrangement outside of Australia (Australian Government 2018). This means that engaging in commercial surrogacy may create a situation such that the intended parents fail to meet the requirements for the transfer of legal parentage under state law. For example, a report from the Family Law Council in 2011 noted that a Queensland couple, the Dudleys, who were the biological parents (by the intended father) of twin children born to a Thai gestational surrogate were not able to obtain a transfer of parentage order from the relevant state court because the commercial surrogacy arrangement used by the parties was not permitted under Queensland law (Family Law Express 2014). As a result, the intended parents were not given full parental rights, but were granted a legal relationship in the form of parental responsibility for the children while they were minors. This situation may impact the children's lives in areas such as applying for passports or school, seeking medical treatment, or registering with Medicare and health funds (Family Law Express 2014). The ban on commercial surrogacy in Australia not only prohibits the service arrangement, but also the import of gametes or donations by persons living in another country (NHMRC 2017). Thus, seeking independent legal advice is highly recommended for intended parents and surrogates before they engage in commercial surrogacy, to minimise legal risks for all parties including the children born through such arrangements.

2.2.4 Surrogacy regulations

As this thesis explores surrogacy practices based in Thailand and Australia, the following section provides details on Thai and Australian surrogacy regulations.

2.2.4.1 Thailand: Protection for Children Born through Assisted Reproductive Technologies Act 2015

Before the Baby Gammy scandal in 2014, Thailand did not have a formal position on surrogacy. The new Protection for Children Born through Assisted Reproductive Technologies Act was approved in May 2015 and took effect on 30 July 2015. Category 3 of the Act outlined acceptable surrogacy arrangements in Sections 21 through 28 (Hibino 2020; Royal Thai Government Gazette 2015).

According to Section 21 (Royal Thai Government Gazette 2015; Sattaburuth 2015), only infertile Thai couples—or those with at least one partner holding Thai citizenship—who have been legally married for three years or more are permitted to use surrogacy arrangements. The surrogate must be a blood relative of the couple, and if the couple has no relatives, the surrogacy committee will intervene. Additionally, the surrogate must not be nulliparous, and, if the gestational surrogate is married, her husband must consent to her being a surrogate.

As per Section 22, transferred embryos must be fertilised by using either the intended mother's oocytes or donated oocytes and the intended father's sperm or donor sperm. Surrogates' oocytes cannot be used in a surrogacy arrangement (Royal Thai Government Gazette 2015).

Sections 23 through 28 state that only fertility clinics with a licence to practise surrogacy can provide surrogacy treatment. Commercial surrogacy is completely banned from practice. Compensating surrogates is allowed only for medical expenses and reasonable reimbursements for costs associated with the pregnancy or birth. Furthermore, surrogacy agencies and surrogacy advertisements are prohibited in Thailand (Royal Thai Government Gazette 2015).

Clearly, only gestational surrogacy arrangements in altruistic forms are currently allowed in Thailand. The new surrogacy law bans foreign couples from seeking commercial surrogacy arrangements in Thailand. Thus, this surrogacy law has significantly impacted the Thai commercial surrogacy business, leading to the closure of several surrogacy fertility clinics in 2015 (Hibino 2020).

2.2.4.2 Australia: Regulations vary in each state

Australia comprises two territories—ACT and the Northern Territory (NT)—and six states: Victoria (VIC), NSW, QLD, Western Australia (WA), South Australia (SA), and Tasmania (TAS).

In the late 20th century, the practice of surrogacy gained popularity in Australia. The first successful surrogacy treatment in Australia was reported in VIC in 1986 (Leeton, King & Harman 1988). Following this case, the Victorian Government quickly legislated to prohibit all forms of surrogacy

arrangements. Around this period, other state governments also proclaimed that surrogacy practice was illegal. VIC and ACT passed the Infertility (Medical Procedures) Act 1984 and the Substitute Parent Agreements Act 1994, respectively, illegalising surrogacy arrangements. The acts distinguished between commercial and altruistic surrogacy arrangements by imposing severe penalties on commercial surrogacy arrangements while leaving altruistic surrogacy arrangements without penalties (*Infertility (Medical Procedure) Act 1984; Substitute Parent Agreements Bill 1994*). In essence, the proclamations of these acts allowed altruistic surrogacy arrangements to proceed despite the legal uncertainty. Meanwhile, other states in Australia, including SA, QLD, and TAS, announced that all surrogacy contracts were illegal and void (Stuhmcke 1996).

In the early years of the 21st century, surrogacy legislation began to change and be regulated by individual states. Surrogacy legislation was initially promulgated in ACT and VIC, where surrogacy arrangements are now an officially legal practice (Hammarberg, Johnson & Petrillo 2011). Later, other states passed their own surrogacy legislations, and surrogacy is now legal in most parts of Australia. Only NT has no surrogacy laws; therefore, all forms of surrogacy remain illegal in this part of the country. The current surrogacy legislations of each territory and state are detailed below.

2.2.4.2.1 Australian Capital Territory (ACT)

The Parentage Act of 2004 made ACT the first jurisdiction to regulate surrogacy. The relevant surrogacy legislation appears in Sections 23 through 31 (parental order) and Sections 40 through 45 (offences relating to substitute parent agreements). The act *(Parentage Act 2004)* renders altruistic surrogacy arrangements and gestational surrogacy lawful. Reasonable reimbursements associated with the costs of pregnancy, birth, or care for the resulting child in altruistic surrogacy arrangements are allowed. Only those intended parents who have failed to conceive through other ART methods, as verified in writing by gynaecologists, are eligible to enter altruistic surrogacy arrangements. Commercial surrogacy arrangements, domestically and transnationally, and all forms of advertisement of surrogacy are strictly prohibited in the Parentage Act 2004.

2.2.4.2.2 Northern Territory (NT)

No form of surrogacy is legal in NT.

2.2.4.2.3 Victoria (VIC)

In VIC, the Assisted Reproductive Treatment Act 2008 (Sections 39 through 45) allows a surrogacy treatment to proceed only if the surrogacy arrangement is approved by the Patient Review Panel. Singles and gay and straight couples unable to produce their own biological children are permitted to seek surrogacy arrangements. All parties are required to undergo a criminal record check and a child protection order check to become eligible to apply for a surrogacy arrangement (*Assisted Reproductive Treatment Act 2008*). Oocytes from surrogates are prohibited from use in the process. Women who are willing to be surrogates must be over 25 years old and must have given birth to at least one live child. Commercial surrogacy arrangements and all forms of advertisements for surrogacy are entirely banned in VIC. Only fees related to the medical expenses of pregnancy can be reimbursed to the surrogates (*Assisted Reproductive Treatment Act 2008*).

2.2.4.2.4 New South Wales (NSW)

The current surrogacy legislation in NSW is the Surrogacy Act 2010 No. 102. The act strictly prohibits commercial surrogacy arrangements and overseas commercial surrogacy arrangements (compensated transnational surrogacy). Only altruistic gestational surrogacy arrangements are allowed, and only if the intended parents are unable to conceive or give birth, or if they are at risk of passing on severe genetic defects to their offspring. Intended parents, regardless of their relationship status and sex, must be at least 18 years old and residents of NSW to apply for surrogacy arrangements; surrogates must be at least 25 years old. Compensation for the reimbursement of reasonable medical costs or any costs associated with the pregnancy or birth can be legally paid to surrogates. In NSW, surrogacy advertisements are not prohibited as long as no fees have been paid for them (*Surrogacy Act 2010 No 102*).

2.2.4.2.5 Queensland (QLD)

In QLD, unlike in some other states, the Surrogacy Act 2010 proclaims that different-sex or same-sex couples or singles are eligible to apply for surrogacy arrangements if they are unable to conceive on their own. Only altruistic gestational surrogacy arrangements are legal, with a hefty fine or imprisonment to be enforced in cases of commercial surrogacy arrangements or overseas surrogacy arrangements (*Surrogacy Act 2010*). However, compensating surrogates with reasonable reimbursements associated with pregnancy and birth is permitted (*Surrogacy Act 2010*).

2.2.4.2.6 Western Australia (WA)

Surrogacy arrangements in WA are governed by the Surrogacy Act 2008. The act bans commercial surrogacy and only allows altruistic surrogacy in the state. In WA, traditional surrogacy arrangements are not banned, and surrogacy advertisements are allowed as long as no fee exchanges hands (*Surrogacy Act 2008*). Reasonable and necessary compensation associated with surrogate pregnancies and births is legal. Intended parents who wish to enter surrogacy arrangements must be in a different-sex relationship, at least one of the partners must be aged 25 years or older, and the woman must be deemed unable to conceive a child due to medical reasons (*Surrogacy Act 2008*). The intended parents must be residents of WA. Surrogates must be at least 25 years old and must have previously successfully given birth to a live child.

2.2.4.2.7 South Australia (SA)

Lawful surrogacy arrangements in SA are recognised under the Family Relationship Act 1975. Again, the state authorises only altruistic surrogacy under the Act or the State Framework for Altruistic Surrogacy. Monetary compensation to cover the medical costs of the surrogate is allowed in an altruistic surrogacy arrangement. Further, surrogacy advertisements without payment are legal. All parties involved in surrogacy arrangements must meet the following strict requirements (*Family Relationship Act 1975*): Each of the parties must be at least 18 years old, the surrogacy procedure must be carried out in the state, both the intended parents must be SA residents and Australian citizens who

have been legally married or in a registered relationship for at least three years prior to applying for surrogacy, and the intended mother must prove that she has a medical condition preventing her from carrying to term or giving birth. Additionally, each of the parties must attend counselling services to obtain a lawyer's certificate in compliance with the requirements (*Family Relationship Act 1975*).

2.2.4.2.8 Tasmania (TAS)

In TAS, surrogacy arrangements are governed by the Surrogacy Act 2012. Same-sex couples, married couples, different-sex couples in de facto relationships, and singles are eligible to enter surrogacy arrangements as long as they meet the criteria set out in the act (*Surrogacy Act 2012*). The intended parents must be at least 21 years old with reasonable conditions requiring a surrogacy arrangement, and they must reside in the state at the time the agreement is made. Surrogates must be at least 25 years old, have previously given birth to a live child, and reside in TAS. Costs incurred by the surrogacy arrangement can be legally paid or reimbursed to surrogates (*Surrogacy Act 2012*).

In summary, Australia has different surrogacy legislation in each state and territory, but they all prohibit commercial surrogacy arrangements. Notably, Australian surrogacy legislation upholds the restriction on surrogates for its potential benefits, including protection against health risks or harm. Most states in Australia have a minimum age limit of 25 years for a woman to be a surrogate, which aims to prevent young and vulnerable women from entering gestational surrogacy arrangements and to ensure that surrogates are sufficiently mature to handle all the responsibilities of the surrogate pregnancy process (*Surrogacy Act 2010 No 102*). Additionally, the law only allows women who have previously given birth to a live child to be a surrogate. This restriction allows the surrogate to be in a better position to give informed consent, as she has prior experience and is able to understand the process and possible complications of pregnancy, as well as being an advantage for pregnancy risk assessment for surrogates and babies, and even helping the intended parents to understand the complications for the surrogate and the child (Bhatia et al. 2009). Furthermore, it prevents nulliparous women from entering surrogacy arrangements. This not only protects nulliparous women without experience of pregnancy and related complications, but also those who have had serious complications

in the past and have been unable to give a live birth, to prevent harm to both the surrogate and the child. Australian jurisdictions such as WA, SA, and TAS mandate legal advice and counselling for all parties concerned to ensure that they are sufficiently aware of the implications of their decision before proceeding with the surrogacy arrangement; this can help to assess the surrogate's fitness for the role and prevent potential risks of legal and psychological complexities for all parties (Bhatia et al. 2009; Dahstrom 2020; NHMRC 2017). All these restrictions in Australia are important aspects of surrogacy best practices and are focused on the potential benefits for surrogates by minimising the risk of coercion, as the decision to stop/go is out of the other parties' influence.

Since there is no governing body or federal legislation in Australia regulating surrogacy and ART services, all ART clinics are required to report ART treatments via the Australia and New Zealand Assisted Reproduction Database (ANZARD) to allow for monitoring and assessing the outcomes of ART treatments.

2.2.4.3 The process of bringing a child born abroad through surrogacy back to Australia

Generally speaking, the process of bringing a child born abroad through surrogacy back to Australia involves meeting the requirements of the jurisdictional country to exit and those of Australia to enter. In Thailand, a gestational surrogate is the legal parent of the child, which is in contrast to India, where the gestational surrogate does not have legal parental rights (ABC News 2020). Therefore, taking a child born to a Thai surrogate out of Thailand requires providing documents to the Thai authorities, including the child's birth certificate, a copy of the birth mother's (i.e. the gestational surrogate's) ID card, copies of the intended parents' passports, and the surrogacy contract and/or a court order issued by the Thai Family Juvenile Court to confirm that the gestational surrogate has given up her parental rights to the child (ABC News 2020). Next, for the child to enter Australia, Australian citizenship must be obtained for the child. The intended parents need to apply on their child's behalf for either Australian citizenship by descent or a permanent visa (Australian Government 2018). The application for Australian citizenship by descent is determined per the Australian Citizenship Act 2007, the Australian Citizenship Regulation 2016, and policy and operational guidelines. Other evidentiary

requirements may include DNA testing of the biological parents and the child, full information about the surrogacy arrangement, the gestational surrogate's identity documents and informed consent to the surrogacy arrangement, the surrogacy contract, and the responsible parents' consent and signatures. If the child becomes an Australian citizen by descent, the intended parents need to apply for the child's Australian passport. On the other hand, if the child is not eligible for Australian citizenship by descent, the intended parents need to apply for an Australian permanent visa for the child, depending on the circumstances and the visa subclass (Australian Government 2018). However, engaging in any form of commercial surrogacy arrangement is an offence for residents who live in ACT, NSW, or QLD (Australian Government 2018). Therefore, if a child is born as a result of an illegal commercial surrogacy arrangement, there are penalties applied for intended parents who live in these states. Additionally, there are risks associated with obtaining an Australian passport for a child, and if the intended parents fail to obtain a transfer of legal parentage under state law, the child's benefits will be affected (Australian Government 2018).

While the growth of the commercial surrogacy industry seems to be good for entrepreneurs, it also puts all the parties involved at risk. Moving gestational surrogates across borders may be a clever business strategy, but it poses a risk for gestational surrogates, both in terms of the law and their health, and is frowned upon internationally. Commercial surrogacy has been widely debated and discussed. The international movement of the commercial surrogacy industry has revealed gaps in individual countries' surrogacy practices and regulations. Reviewing the extensive literature on the subject helps in understanding the surrogates' experiences of the risks involved. Understanding the current trends in surrogacy practices and outcomes is necessary for improving the standardisation of surrogacy practices and protecting surrogates from harm. The following section presents a review of the literature on surrogacy arrangements.

2.3 Literature review

A literature review was conducted to develop a better understanding of the trends in gestational surrogacy practices and pregnancy and the live birth outcomes, along with gestational surrogates' experiences of the risks associated with gestational surrogacy arrangements. The literature review was initiated at the beginning of the PhD research process and updated periodically as the thesis was prepared.

2.3.1 Data sources

Cumulative Index of Nursing and Allied Health Literature (CINAHL (Ebsco)), Medline (Ovid), ProQuest, and Scopus databases were used to identify the literature exploring the current trends in gestational surrogacy practices, and pregnancy and birth outcomes. A population, intervention, comparison, and outcome (PICO) framework was utilised to focus on the search terms and to ensure the keywords were conceptually focused for narrowing the literature search. The search systematically covered the study's previously identified key terms: surrogacy, surrogates, surrogate mothers, gestational carriers, surrogacy arrangement, gestational surrogacy, commercial surrogacy, experiences, pregnancy outcomes, and live births. Key terms were also searched as subject terms using Medical Subject Headings (MeSH). Studies published between 1980 and 2019 were accessed without restrictions regarding study type. Database searches were limited to the English and Thai languages and human participants. Inclusion criteria were articles focusing on surrogacy arrangements, surrogates' experiences, and surrogate pregnancy and birth outcomes. Articles discussing the ethical, legal, and social aspects of surrogacy and opinion studies were excluded.

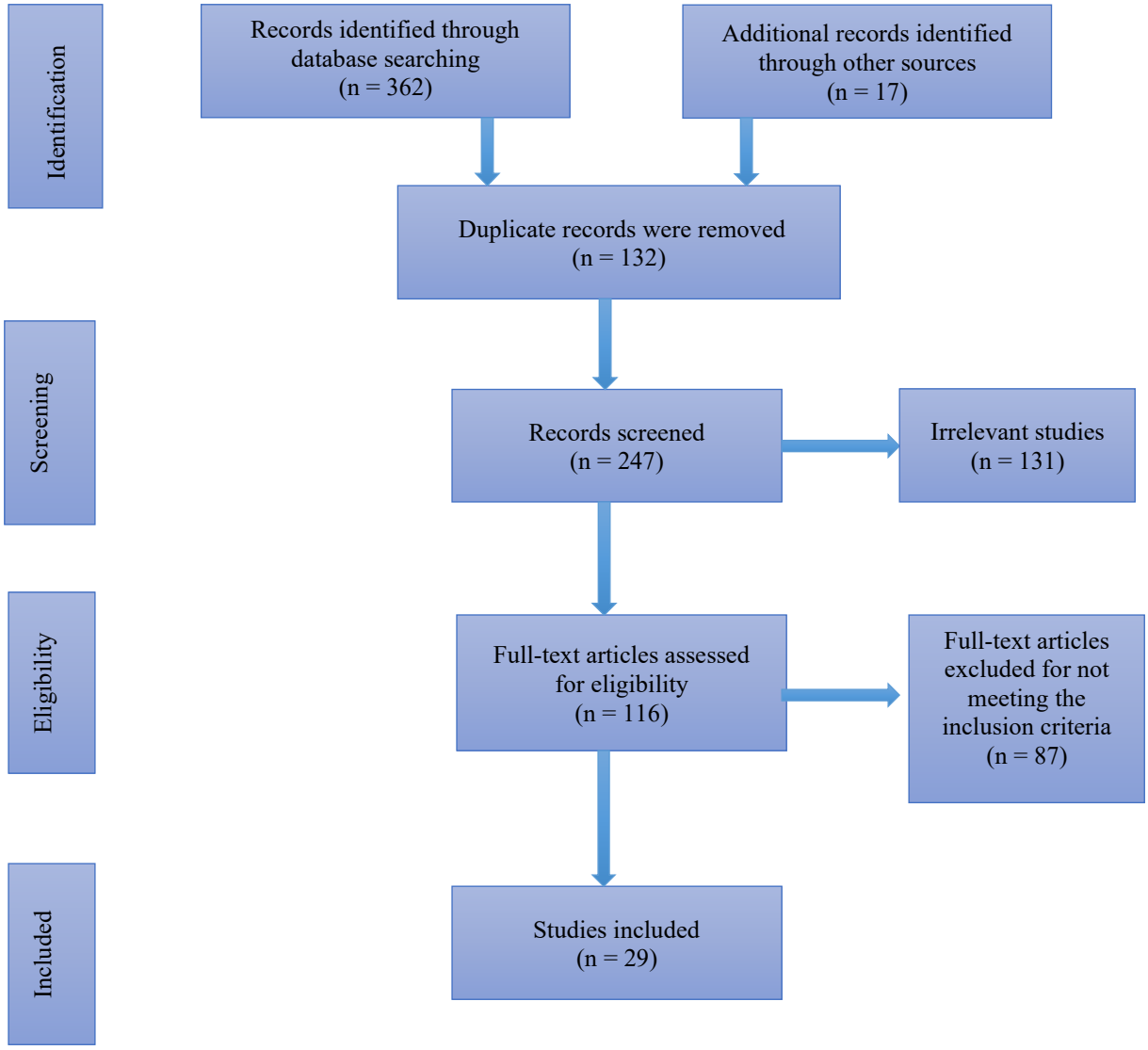
2.3.2 Data selection and analysis

The search results identified 362 articles from the CINAHL (Ebsco), Medline (Ovid), ProQuest, and Scopus databases. Seventeen cross-references of relevant papers were manually searched. Of these, a total of 29 articles met the inclusion criteria for this literature review (see Figure 3). The 29 included studies varied in terms of their method, research design, year of publication, and research setting. Twenty-five articles described research using mixed, multi, quantitative, or qualitative methods

(Appendix 1), while four articles presented secondary research, including a literature review, a systematic review, a meta-analysis, and a case study; one study was in the Thai language (Appendix 2).

National ART reports, including those from the ANZARD, the CDC, the European Society of Human Reproduction and Embryology (ESHRE), the Human Fertilisation and Embryology Authority (HFEA), and the Canadian Fertility & Andrology Society (CARTR), were also searched for additional references.

Figure 3: Results of the search strategy



Key themes and significant findings of the literature review related to trends in gestational surrogacy practice and its outcomes, and surrogates' experiences are detailed in the following section.

2.3.3 Current research

2.3.3.1 Trends in national ART reports on gestational surrogacy arrangements

Gestational surrogacy arrangement is the only type of surrogacy that has been reported in the ART registers. The ART reports show an increase in the demand for gestational surrogacy arrangements every year. ART annual reports from the US, Canada, Australia and New Zealand, the UK, and Europe have shown steady increases in the use of gestational surrogate cycles each year (CFAS 2018; CDC 2018; ESHRE 2018; HFEA 2018; NPESU 2018) . For example, in the US, the ART report showed that the number of gestational surrogate cycles increased by approximately 38% during the period 2010–2014 (Perkins et al. 2016; White 2018). Similarly, a recent report from CARTR showed an increase of almost 30% in the uptake of gestational surrogate cycles over one year from 2016 to 2017 (CFAS 2016, 2019). Australia and New Zealand had a six-fold increase in the use of gestational surrogate cycles over 12 years (2005–2017) (NPESU 2018; Newman et al. 2019). These reports reveal similar trends in terms of increased numbers of gestational surrogacy treatments, implying that gestational surrogacy arrangements have become the preferred fertility treatment option. Gestational surrogacy arrangements and gestational surrogates are, therefore, the focus of this study's literature review.

2.3.3.2 Trends in embryo transfer practices in gestational surrogacy arrangements

An extensive body of literature contends that gestational surrogates are at a higher risk of receiving MET when compared to non-surrogates (Parkinson et al. 1999; White 2016, 2017, 2018). Parkinson and colleagues' 1998 study showed that the average number of embryos transferred to gestational surrogates was 4.1±0.1 (Parkinson et al. 1999). Similarly, Perkins and colleagues observed that MET became more widespread in surrogacy practice from 1999 to 2013 among gestational surrogates as compared to non-surrogates (60.4% vs 54.6%) (Perkins et al. 2016). White (2017) reported that in the

US when intended mothers' oocytes were used in gestational surrogacy arrangements, there was no difference in the number of embryos transferred between gestational surrogates and non-surrogates. However, when embryos containing donor oocytes were transferred, gestational surrogates were at high risk (8% more likely) of receiving MET than non-surrogates (White 2017). Likewise, in Canada, gestational surrogates were nearly 24% more likely to receive MET than non-surrogates, regardless of where the oocytes originated (White 2018).

When considering the form of gestational surrogacy arrangement, the incidence of MET was found to be more common in commercial surrogacy arrangements than in altruistic surrogacy arrangements. Researchers found that in the US, where commercial surrogacy is an active industry, the practice of transferring two or more embryos was 7% riskier for gestational surrogates than for those in Canada, where only altruistic surrogacy arrangements are allowed (White 2018). Other studies also discovered that 50–80% of multiple embryos were transferred to paid or commercial surrogates, and this was seemingly the standard practice for commercial surrogacy (Birenbaum-Carmeli & Montebruno 2019; Perkins et al. 2016; Stafford-Bell, Everingham & Hammarberg 2014). By contrast, the average number of embryos transferred to altruistic surrogates per cycle was 1.8–1.9 (Cabra et al. 2018; Söderström-Anttila et al. 2002).

Although MET is an unacceptable practice and is not recommended in the clinical practice guidelines, it continues to occur and is particularly relevant to gestational surrogates (Duffy et al. 2005; Woo et al. 2017). It is evident that the MET trend in gestational surrogacy practice applies more strongly to gestational surrogates than non-surrogates, particularly when they are commercial surrogates rather than altruistic.

2.3.3.3 Trends in pregnancy and live birth outcomes in gestational surrogacy arrangements

Overall, gestational surrogate cycles result in higher rates of clinical pregnancy (45%–68%) and live birth (35%–59%) in comparison to non-surrogate cycles (43%–64% clinical pregnancy and 34%–55% live birth rates) (Murugappan et al. 2018; Serafini 2001). A study by Murugappan and colleagues

compared different sources of oocytes when fresh or frozen intended mothers' oocytes or donor oocytes were used in gestational surrogate and non-surrogate cycles, finding that clinical pregnancy and live birth rates remained higher in gestational surrogate cycles (Murugappan et al. 2018). Other studies showed that clinical pregnancy rates in gestational surrogate cycles ranged from 19% to 40%, with 30%–70% of the couples successfully becoming parents (Brinsden 2003; Peter et al. 2018; Söderström-Anttila et al. 2016; Wang et al. 2016). Live birth rates of 19%–60% were reported in gestational surrogate cycles, with 55%–85% of couples having at least one live birth (Brinsden 2003; Cabra et al. 2018; Peter et al. 2018; Stafford-Bell, Everingham & Hammarberg 2014; Wang et al. 2016). Evidence suggests that gestational surrogacy arrangements yield effective ART treatment results, with a high rate of success leading to couples becoming parents.

However, reports on the use of gestational surrogacy arrangements and the effectiveness of clinical pregnancy and live birth rates indicate that the multiple pregnancy rate, which is connected to MET, is higher when compared with standard IVF treatment. The ART report for the US for the years 2005–2014 found that gestational surrogate cycles led to a twofold increase in multiple births, compared to non-surrogate cycles (Perkins et al. 2016; White 2018). Similarly, during the same period, the national ART report for Canada showed a higher rate of multiple births among gestational surrogates (40%) than among non-surrogates (13%) (White 2018). Although the rate of multiple births among gestational surrogates has been gradually decreasing, it continues to be higher than it is among non-surrogates. The ART report for the US between 2010 and 2014 indicated that the rate of multiple births for gestational surrogates decreased from 34% to 25% and for non-surrogates from 26% to 21% (White 2018). There was also a similar trend in Canada, showing a decrease in the rate of multiple births among gestational surrogates from 32% to 15% from 2010 through 2014, and among non-surrogates from 23% to 13% (White 2018). The national ART reports undoubtedly show that gestational surrogates are more at risk of multiple birth delivery than non-surrogates.

Woo et al. (2017) investigated the comparison of pregnancy outcomes between gestational surrogacy and spontaneously conceived pregnancies in the same women (gestational surrogates) who had no

infertility conditions. The results showed that surrogate pregnancies were 33% more likely to be multiple compared to spontaneously conceived pregnancies (Woo et al. 2017). This result suggests that when gestational surrogacy arrangements are used, the pregnancy outcome is more likely to be a multiple pregnancy, confirming that gestational surrogates are at a higher risk of experiencing multiple births than non-surrogates.

2.3.3.4 Trends in the use of gestational surrogacy arrangements

The use of gestational surrogate cycles has grown every year, as shown in the national ART reports. Nevertheless, in some countries, intended parents tend to rely more on transnational surrogacy than domestic arrangements. For example, Australia reported that more than 350 children who were born through international surrogacy arrangements were brought back to Australia in 2011 (Wang et al. 2016), in contrast to the 73 babies born live through domestic altruistic surrogacy arrangements in Australia between 2004 and 2011 (Wang et al. 2016). Research by Everingham and colleagues (2014) investigating trends in Australians' use of surrogacy found that 92% of intended parents considered using compensated transnational surrogacy rather than domestic altruistic surrogacy arrangements (8%). The belief that the process would be long and complicated, concerns regarding relinquishment of the baby, and the inability to find an altruistic surrogate were the reasons reported as barriers discouraging the use of domestic altruistic surrogacy arrangements (Everingham, Stafford-Bell & Hammarberg 2014).

Simultaneously, compensated transnational surrogacy is marketed well and targeted to the needs of intended parents. Many websites advertise surrogacy services that offer a 'one-stop shop' that is easier and more convenient, ensuring parents' peace of mind (Gezinski et al. 2017). The websites feature attractive advertisements, affordable prices, and numerous options for intended parents, such as options for organising the legal documents or providing assistance according to each countries' requirements, choosing donor sperm or oocytes, and even matching gestational surrogates according to their preferences (Gezinski et al. 2017). Surrogacy service websites often promote the benefits of commercial surrogacy arrangements, claiming surrogacy success rates as high as 75% (Gezinski et al.

2017), while the live birth rate per intended parent in altruistic surrogacy arrangements is 33%–59% (Cabra et al. 2018; Peter et al. 2018; Söderström-Anttila et al. 2002). Framing commercial surrogacy services as the solution to a problem reassures intended parents; the high success rate guarantee encourages intended parents to choose compensated transnational surrogacy rather than domestic altruistic surrogacy arrangements.

However, behind the scenes, evidence has shown that the high rate of MET in commercial surrogates is a concern at the community level. The associated risks of MET and other risks involved in gestational surrogacy arrangements are discussed in the following section on gestational surrogates' experiences, including those of commercial surrogates.

2.3.3.5 Experiences of gestational surrogates

Since altruistic domestic surrogacy arrangements are not popularly used by intended parents, the commercial surrogacy business has boomed. Commercial surrogacy arrangements in low- to middle-income countries such as India and Thailand (before the ban) were popular destinations for such services (Everingham, Stafford-Bell & Hammarberg 2014). These services are also available in the US, where commercial surrogacy arrangements are legal, but they come at a higher price (AUD 100,000) than in low- to middle- income countries. Consequently, India (where the cost was AUD 30,000) and Thailand (where the cost was AUD 40,000) became the favoured surrogacy hubs (Everingham, Stafford-Bell & Hammarberg 2014; Gezinski et al. 2017; Hibino & Shimazono 2013; Singha 2016).

Research has revealed that commercial gestational surrogates in countries such India and Thailand usually came from rural provinces, had little education, and were as young as 21 years old (Hibino & Shimazono 2013; Saravanan 2013; Singha 2016; Tanderup et al. 2015). This is a stark contrast with the average age of 34–41 years for altruistic surrogates (Imrie & Jadva 2014; Jadva et al. 2003; Söderström-Anttila et al. 2002). While commercial surrogates' main justification for offering to be

gestational surrogates is financial need, altruistic surrogates are motivated to selflessly help childless couples (Hibino & Shimazono 2013; Jadva et al. 2003; Pashmi, Tabatabaie & Ahmadi 2010).

Gestational surrogates are exploited because their financial need makes them vulnerable. Studies have found that gestational surrogates, mainly commercial surrogates, often have less power or involvement in the process of surrogacy arrangements (Saravanan 2013; Tanderup et al. 2015). Research has found that in the commercial surrogacy process, gestational surrogates are often less involved in their treatment decisions (Saravanan 2013; Tanderup et al. 2015), which raises a public health concern as to whether gestational surrogates are fully aware of the risks and benefits associated with gestational surrogacy arrangements before they enter surrogacy treatment. Tanderup et al. (2015), investigating 14 Indian commercial surrogates, found that none of them knew how many embryos were transferred or were even able to explain the complications of multiple births. This finding could indicate that commercial surrogates' consent is uninformed, which is currently an issue debated worldwide.

Commercial surrogates were also found to experience physical, psychological, and emotional stress during surrogate pregnancy (Karandikar, Gezinski & Huber 2017; Tehran et al. 2014). Studies have found that commercial surrogates experience more stress if a pregnancy fails or is lost, worrying even more about the health or abnormalities of their babies during pregnancy, as this could affect their payment and most of them are the primary sources of financial support for their families (Berend 2010; Karandikar, Gezinski & Huber 2017). During the surrogate pregnancy, some commercial surrogates also reported their worries and concerns regarding the reactions of others and the social ramifications if they disclosed their pregnancy to their family, relatives, and friends (Tehran et al. 2014).

However, after surrogate pregnancy, commercial surrogates stated that they were happy with their decision to be surrogates and coped well with the decision to relinquish the babies to their intended parents because they were aware that the babies were not genetically linked to them (Hibino & Shimazono 2013). Likewise, altruistic surrogates reported that they were happy and had no doubts or

difficulties when it was time to hand over the babies (Jadva et al. 2003; Pashmi, Tabatabaie & Ahmadi 2010). This finding suggests that gestational surrogates have the mature capacity to cope with their feelings of motherhood and control their emotions.

Generally, the relationships between gestational surrogates and intended parents were reported to be good. However, in some commercial surrogacy arrangements, it was reported that the gestational surrogates' identities were unknown to the intended parents throughout the pregnancy (Hibino & Shimazono 2013; Pashmi, Tabatabaie & Ahmadi 2010). The relationship between gestational surrogates and intended parents, in most cases, was discontinued after delivery because this was the intended parents' preference (Pashmi, Tabatabaie & Ahmadi 2010). It could, therefore, be surmised that gestational surrogates and intended parents more likely only contact each other during pregnancy, or, in some cases in commercial surrogacy arrangements, they do not contact each other at all.

The literature shows that surrogacy arrangements and practices, especially commercial surrogacy arrangements, put gestational surrogates at risk. However, the legal issues surrounding commercial surrogacy arrangements vary in each jurisdiction, and their impact on surrogates needs to be considered further, and has not been covered in this literature review. The following section discusses the measures to protect surrogates from risk and improve surrogacy arrangement outcomes.

2.3.3.6 Trends in addressing the impact of risks to gestational surrogates

Public health authorities and policymakers have been alerted to the issues of the high rate of MET and multiple births among gestational surrogates. SET has been introduced to address the issue of multiple births and improve pregnancy and live birth outcomes. In fact, SET has been recommended by the Fertility Society of Australia (FSA), ESHRE, HFEA, ASRM, and the Joint Society of Obstetricians and Gynaecologists of Canada-Canadian Fertility and Andrology Society (JOINT SOGC-CFAS) for more than 10 years, but it has not been universally adopted in surrogacy practice. Research shows that SET guideline compliance was less than 50% in actual surrogacy practice (White 2018). However, in some countries, such as Australia and New Zealand, the SET guideline has been well established in

surrogacy practice, resulting in multiple birth rates as low as 7% (Wang et al. 2016). Although SET lowers the rate of multiple births, the SET guideline is not always implemented. Only Australia, New Zealand, Canada, and the UK have SET practice guidelines and policies in place for gestational surrogacy (Harbottle et al. 2015; Newswire 2017; Reproductive Technology Accreditation Committee 2017).

Other policies to protect gestational surrogates from risks include using quarantine to protect gestational surrogates from Human Immunodeficiency Virus (HIV). Under UK law, donor sperm must be frozen and quarantined for six months before it can be used to create fresh embryos for transfer to gestational surrogates (Brinsden 2003). In the US, legal advice and counselling are also provided for gestational surrogates to ensure that they give fully informed consent and that they fully understand the surrogacy process before entering the treatment (California Legislative Information 2013; White 2017).

Although implementing SET guidelines and policies, using HIV quarantine regulation, offering legal advice and counselling services, and providing the surrogates with complete information so they can give their informed consent have all been introduced to address issues surrounding the risks to gestational surrogates, these risks are still debated in the literature, albeit with gaps. The following section details the gaps identified through the literature review.

2.3.4 Gaps in the literature

2.3.4.1 Limited evidence of gestational surrogacy arrangements and risk experiences of gestational surrogates in Thailand

Currently, gestational surrogates are targeted in low- to middle-income countries such as India and Thailand. However, ART reports on gestational surrogacy arrangements are unavailable for these countries, making it difficult to track trends in current surrogacy practices, pregnancy outcomes, and adverse incidences, particularly in Thailand, which recently became a popular destination for commercial surrogacy. There are current media reports of the movement of gestational surrogacy

practice in Thailand and neighbouring countries in a commercial form, but there have been no studies investigating this practice in Thai surrogacy arrangements. Risk experiences of Thai gestational surrogates throughout the process of surrogacy treatment are also limited in evidence, although there have been several studies of risks to gestational surrogates. Investigating Thai women who have had experiences of surrogacy treatment is, therefore, needed to generate knowledge and gain insight into the gestational surrogacy practice and gestational surrogates' experiences in Thailand, and reflect the trend of current gestational surrogacy practice and risk experiences of gestational surrogates. In turn, this knowledge would facilitate the further development of international surrogacy policies, guidelines, and regulations.

2.3.4.2 Limited evidence of systematic outcomes of embryo transfer and pregnancy and live birth outcomes in surrogacy practice

MET is still a common practice in surrogacy treatment despite the promotion of SET guidelines and policies to reduce multiple births and improve perinatal outcomes. Consequently, rates of multiple births remain stubbornly high among gestational surrogates.

The belief in the higher chance of pregnancy following MET and intended parents' preferences for twins are driving the continued use of MET in the treatment of gestational surrogates (Price 1989; White 2018). In contrast, Wang et al.'s (2016) research in Australia claimed that there were no significant differences in clinical pregnancy and live birth rates between SET and MET in surrogacy practice. Inconsistent findings and limited systematic evidence of internationally comparable data on the pregnancy and live birth outcomes between SET and MET in gestational surrogates who have proven their fertility with their own previous pregnancies create gaps in the literature that need to be rectified to improve and evidence surrogacy practice.

2.3.4.3 Limitations in the measurement of the chance of live birth

Alongside the use of surrogacy treatment, commercial surrogacy arrangements are preferred over altruistic surrogacy arrangements. The higher than average chance of live birth (75% rather than 50%) is frequently advertised in commercial surrogacy arrangements to reassure intended parents (Gezinski et al. 2017). The live-birth rate is measured on a cycle basis, which may be of limited use for intended parents who want to know: (a) the chances of having a live birth after successive failed cycles, and (b) whether continued treatment is indicated (Adamson et al. 2006; Luke et al. 2012). CLBR is a population-based measure that provides a realistic indication of ART success and can thus inform intended parents' decision-making about whether to continue treatment (Abuzeid et al. 2014; Luke et al. 2012; McLernon et al. 2016). Therefore, commercial surrogacy providers' advertised live birth rates may not be informative, but there is also limited evidence of CLBR in altruistic surrogacy arrangements to inform intended parents' decisions and promote their use. An evaluation of CLBR among altruistic gestational surrogates is needed to provide significant data to guide practice and support effective treatment in altruistic surrogacy arrangements.

2.4 Rationale of this PhD thesis

Study 1—Research question: What are the risks encountered by gestational surrogates in the process of gestational surrogacy and the related arrangements in Thailand?

The ethics of the risks faced by gestational surrogates have been hotly debated. However, even as the risks involved in surrogacy arrangements have been identified, research in the context of gestational surrogacy practice in Thailand and risk experiences of Thai gestational surrogates is limited. This study (reported in Chapter 4) explore gestational surrogacy practice and gestational surrogates' risk experiences in Thailand. This chapter is based on interviews with Thai women who had experienced surrogacy. Gaining insight into the risks encountered by gestational surrogates in their surrogacy experiences throughout the process of gestational surrogacy arrangements in Thailand may benefit the

community, public health, and governments in planning for public health care and developing, reframing, or reconsidering international surrogacy regulations.

Study 2—Research question: What are the differences in surrogate pregnancy and live birth outcomes between SET and MET among gestational surrogates?

It has been assumed that the chances of pregnancy could be improved by increasing the number of embryos transferred using ART. However, the evidence regarding pregnancy and live birth outcomes is inconsistent in terms of whether or not MET improves results among gestational surrogates, given that they usually do not have infertility issues. MET has become a significant public health concern since the evidence shows that it is associated with a higher rate of multiple births. Although SET guidelines and policies have been encouraged in practice, including in surrogacy arrangements, in some countries, MET remains routinely used in gestational surrogacy. Research-based evidence identifying the differences in surrogate pregnancy and live birth outcomes between SET and MET in gestational surrogates must be synthesised to improve surrogacy-based practice and for further reference. Using existing research, the second study of this PhD thesis (reported in Chapter 5) systematically compares clinical pregnancy, live birth, and multiple birth rates between SET and MET gestational surrogate cycles. This study provides evidence that can be used to educate and counsel intended parents, surrogates, service providers, public health providers, and policymakers to promote women's health perspectives.

Study 3—Research question: What is the CLBR among gestational surrogates in altruistic surrogacy arrangements?

Commercial surrogacy arrangements have become a booming business used by intended parents. With their claims of higher than average success rates for live births, commercial surrogacy arrangements reassure intended parents and give them peace of mind. However, the reports of live birth rates per cycle are less informative than CLBR, which reflects the success of ART treatment most accurately.

Limited evidence of CLBR in altruistic surrogacy arrangements may limit intended parents' information and affect their consideration of using such arrangements. It is crucial to evaluate the likelihood of evidence-based CLBR in altruistic surrogacy arrangements to demonstrate the efficacy of treatment. The last study of this PhD thesis (reported in Chapter 6) will use VARTA data from Australia to estimate the likelihood that gestational surrogates will have a live birth following altruistic surrogacy arrangements that strictly adhere to SET practice. This study will provide evidence for benchmarks, patient counselling, service providers, and the community to support the use of altruistic surrogacy arrangements and SET practice with gestational surrogates. Using gestational surrogate population-based evidence, this study will also suggest the maximum number of gestational surrogate cycles that gestational surrogates should undergo, which will offer new evidence and benefit all parties involved in surrogacy prior to initiating the surrogacy treatment.

2.5 Chapter summary

This chapter gave an overview of surrogacy arrangements including the history, types of surrogacy, trends and movement of surrogacy arrangements, and surrogacy regulations in Thailand and Australia. It also presented a summary of the literature review and identified the gaps in the literature that have informed the conceptualisation and rationale of this PhD thesis and the three studies that have been conducted to fill the said gaps. Research design, methodology and method of the three studies conducted are described in the following chapters.

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Chapter 3: Research design, methodology and methods

3.1 Chapter introduction

This chapter outlines the research design and methods used in this PhD thesis to explore the trends in gestational surrogacy practice and outcomes, and the risk experiences of gestational surrogates. The chapter explains the research design, multimethodology, and methods of the three studies that comprise this PhD thesis. The methods section of each study includes the details of the study design and approach, data collection, data analysis, and ethical considerations. The research design and methods were used to meet the overarching aim of this PhD thesis and answer the research questions.

3.2 Research design

'Research design' refers to the overall strategy according to which the researcher structures and plans the research process to address particular research questions (Creswell 2014). In this PhD thesis, the three questions of interest require a multimethod approach. The applied methods include both quantitative and qualitative research methods, including descriptive qualitative research, systematic review and meta-analysis, and a retrospective cohort study. Evidence supporting the decision to use a multimethod approach is outlined in the following section.

3.3 Multimethodology

Multimethodology—or multimethod research—is the use of more than one method of data collection or research in a study. While specific research methods enable researchers to understand and explain phenomena of interest, a combination of research methods within a research study provides different perspectives and a more complete picture of human behaviour and experiences, allowing researchers to achieve their research goals quickly (Brewer & Hunter 1989; Jirojwong, Johnson & Welch 2014). In the related literature, the terms 'mixed method', which is commonly found, 'multimethod', and 'multiple method' are often used interchangeably. However, it is imperative to understand the difference between 'mixed method' and 'multimethod' research.

A mixed-method research design explicitly mixes quantitative and qualitative methods within a single research study (Creswell 2014). A multimethod research design, on the other hand, can use any combination of methods, qualitative or quantitative, within one research study, wherein each method is rigorously and thoroughly conducted and is relatively complete in itself (Hunter & Brewer 2015; Morse 2003).

Morse (2003) identified the basic theoretical drive of a study—inductive or deductive—as the principal factor determining the methods used in a multimethod research design. All research studies must be theoretically driven either inductively (qualitative) or deductively (quantitative); they can neither be neutral nor be informed equally by inductive and deductive theoretical drives (Morse 1991). Morse (2003) paired each second theoretical qualitative and quantitative method within dominance of the theoretical drive of the research study, developing four possible combinations with an inductive theoretical drive and four with a deductive theoretical drive. Each of the four combinations with the theoretical drives is subdivided into a simultaneous or sequential timing of the deployment of the methods. The types of multimethod designs are summarised in Table 3.

Table 3: Types of multimethod designs

Inductive theoretical drive	**Deductive theoretical drive**
Simultaneous design:	Simultaneous design:
1. QUAL + qual: two qualitative methods are used simultaneously, one of which is dominant or forms the base of the research study as a whole, while the second method used to provide additional insights. This design is used when more than one perspective on a research topic needs to be obtained.	1. QUAN + quan: two quantitative methods are used simultaneously, one of which is dominant. This is the most common type of design used for triangulation in which a research question demands the measurement of different dimensions or the administration of several instruments for validity check.
2. QUAL + quan: qualitative and quantitative methods are used simultaneously with an inductive theoretical thrust, which may require the measurement of the phenomenon at some point.	2. QUAN + qual: quantitative and qualitative methods are used simultaneously with a deductive theoretical drive. Qualitative research provides contextual data for further interpretation of the quantitative data.
Sequential design:	Sequential design:
3. QUAL → qual: two qualitative methods are used sequentially, one of which is dominant—usually the one used in the first study. The second study supplements the findings from the first stage of research.	3. QUAN → quan: two quantitative methods are used sequentially, one of which is dominant—usually the one used in the first study. The second quantitative study is conducted to examine particular dimensions of the first study.
4. QUAL → quan: qualitative and quantitative methods are conducted sequentially with an inductive theoretical thrust. This design is often used to develop a model or theory. Often, the quantitative method is then used to test the theory.	4. QUAN → qual: quantitative and qualitative methods are conducted sequentially with a deductive theoretical drive. The qualitative study is conducted to ascertain the reasons for the results when the results of the quantitative study are unexpected.

(Morse 2003)

In this PhD thesis, a multimethod design with an inductive theoretical drive is used to answer the research questions, addressing the overarching research aim. Qualitative research is conducted simultaneously with quantitative research. Overall, this PhD thesis is driven by an inductive theoretical framework of working on the *discovery mode*. Minor deductive research studies were

simultaneously conducted to provide new evidence and enrich the qualitative description. Each research design is methodologically independent, exquisite, and adheres to its own methodological assumptions. The research method of each study is detailed in the following section.

3.4 Research methods

Study 1 is a qualitative descriptive study—interviews with Thai women. Study 2 is a systematic review and meta-analysis, and Study 3 is a retrospective cohort study.

3.5 Study 1

Study 1: 'Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand

Research question: What are the risks encountered by gestational surrogates in the process of gestational surrogacy and the related arrangements in Thailand?

3.5.1 Study design

The study was a qualitative descriptive study. Qualitative description is qualitative research that is descriptive in nature; this research design is common in healthcare and nursing-related research (Kim, Sefcik & Bradway 2017). Qualitative description is suitable for qualitative inquiry when there is (1) limited evidence in a particular research area, (2) confusion or contradiction in the existing evidence, or (3) the research topic is highly complex in terms of discovering the who, what, and where of experiences and gaining insights into phenomena (Elliott & Timulak 2015; Kim, Sefcik & Bradway 2017). The literature identifies six characteristics of a qualitative descriptive study (Kim, Sefcik & Bradway 2017). First, qualitative description is designed to examine a phenomenon from a naturalistic perspective. Second, it is less theory-driven than other qualitative research designs, which facilitates flexibility in theory or framework when designing and conducting a study. Third, the collected data are mainly derived from individual or focus groups with minimally structured or semi-structured interviews. Fourth, purposeful sampling techniques are commonly used to obtain rich information. Fifth, descriptive statistics and thematic analysis are usually applied to describe the study sample and

results. Finally, the findings presented are straightforward, such as providing interpretation with a low level of inference, thus allowing the reader to become familiar with and readily recognise the topic and experience.

In this Study 1, a qualitative description was used, as it was deemed to be the most appropriate study design for examining the limited evidence regarding gestational surrogacy practice and the risk experiences of gestational surrogates in Thailand. The approach of qualitative description design is also flexible, allowing me to obtain naturalistic information of phenomena of interest in a straightforward manner.

3.5.2 Setting and samples

This qualitative study was conducted in the context of surrogacy practice in Thailand with women who had been gestational surrogates. Thailand is a Southeast Asian country with a total area of approximately 513,000 km^2 and a population of 68,863,514 people (Wikipedia 2018). The country is divided into six regions, which consist of 77 provinces and the capital, Bangkok (Wikipedia 2018).

3.5.3 Sampling considerations and recruitment

Thai women aged 20–40 years who had been gestational surrogates within the past seven years (beginning from 2013, when Thailand became a booming surrogacy business, to the current year, that is 2020) and were not currently pregnant were eligible for this study. The potential participants were invited to participate in the study through a single private surrogacy agency in Bangkok, Thailand, which was no longer in operation; I was known to the agency prior to the study. I contacted the private surrogacy agent in Bangkok, Thailand and sought assistance from the former manager, requesting her to advertise the research study among gestational surrogates with whom she had been in contact. The Thai language version of the invitation letter was sent to advertise the research study for sample recruitment. The letter instructed interested potential participants to contact either me directly or my

representative in Thailand. Two potential participants contacted me directly via the LINE chatting application; one of them was not eligible as she was pregnant during the study period.

At the beginning, only one woman was eligible for this study, so a snowballing technique for recruiting participants was also used to fulfil the required number of participants. Snowballing, also known as chain sampling or nominated sampling, is a sampling method that initially identifies one or two participants who meet the inclusion criteria and then relies on them to identify or refer other potential participants to the researcher (Welch 2011). This form of sampling is reportedly commonly used in qualitative research to seek appropriate participants (Welch 2011). In this study, the snowballing technique was found to be an effective process of sampling recruitment since it facilitated the identification of suitable participants and increased the number of study participants in a relatively short time.

3.5.4 Sampling procedure and sample size

A total of 15 Thai women who had been gestational surrogates at least once were interviewed in this study. Creswell (1998) suggests approximately 5–25 participants are required for a qualitative research study to reach a phenomenon called ‘saturation’. However, others have proposed that among a relatively homogeneous group, saturation often occurs at around 12 participants (Boddy 2016; Guest, Bunce & Johnson 2006). In total, 15 participants were recruited for this study, thus reaching the data saturation and theme identification requirements.

The participation of all 15 participants (one who enrolled directly and 14 recruited via snowballing) was voluntary. As potential participants were interviewed to determine their eligibility, they were asked to either suggest potential participants or to advise potential participants to contact me directly using the LINE chatting application, or my representative in Thailand via the mobile phone number provided. Contact details were provided to all participants, and my representative and I were available 24 hours per day, seven days per week.

The study involved a strict system of confidentiality to protect the privacy and identities of the participants and the researcher. Potential participants and participants who referred others were informed that all identities—including the researcher's and the participants'—were to be strictly confidential, even among themselves. They were asked to strictly adhere to the privacy agreement, agreeing to not reveal their identities to each other or to the researcher. In the case that potential participants were introduced to me, their permission to be contacted for the study was obtained through the participant introducers before they were contacted. In the case that potential participants preferred to contact me directly, it was ensured that the participant introducers and the potential participants understood the rule of confidentiality and followed it strictly. Most potential participants contacted me directly rather than calling my representative in Thailand or having me to contact them.

Using the LINE chatting application, all participants were provided with an invitation letter and information sheet in Thai language, detailing the research study, purpose, method, and any potential harm or benefits through their participation in the study for their consideration before agreeing to participate (Appendix 3). The participants also provided their written and verbal consent prior to data collection through the LINE chatting application. The interview method was used for data collection. Interview arrangements were made at the participant's preference of time and date.

3.5.5 Data collection

The interview method was used to collect data. The use of interview methods can range from highly structured to a wholly unstructured format. There are three reported types of interview approaches: structured, semi-structured, and unstructured. In this study, the semi-structured interview approach was employed for data collection. Semi-structured interviewing, also called the 'focused' or 'general interview guided' approach, is a continuum between unstructured and structured interviews (Welch & Jirojwong 2011). Semi-structured interviews involve a flexible set of open-ended questions. This set of questions is a framework of the topic being explored, which guides the researcher and enhances consistency in the data collection process. In the semi-structured interview approach, new questions—which are akin to probes—can be brought up in

accordance with the participant's responses, which flexibly allows the participant to discuss a particular point or aspect of their experience (Welch & Jirojwong 2011). Using the semi-structured interview assisted the researcher to maintain a focus on the research topic and avoid deviating from areas not covered by the framework of the question guide.

3.5.5.1 Interview process

The semi-structured interviews were conducted via audio-recorded one-on-one telephone calls between March and May 2020. Interviews were recorded for transcription and translation for data analysis. Permission to record the conversation was obtained from the participants in advance. Each telephone interview was conducted in Thai and lasted approximately 30 minutes.

3.5.5.2 Development of tools

The interview questions were developed from sets of questions from previous studies and surrogacy websites (CoParents.com 2018; Imrie & Jadva 2014; Jadva, Imrie & Golombok 2015; Jadva et al. 2003; Monique 2016). The set of questions also incorporated the principles of the Protection for Children Born Through Assisted Reproductive Technologies Act 2015 and the surrogacy process of the Thai Medical Council. The interview questions, aimed to find answers to the research question of the study, included six open-ended questions from the ten original questions. Information about the intended parents or involvement of other parties (apart from the gestational surrogate) and one sensitive question, which was deemed as potentially harmful to the participants were excluded from the interview question guideline in compliance with the ethics committee's recommendation. The six open-ended questions covered the background of gestational surrogates and their families; reasons for becoming gestational surrogates; their experience before, during, and after being gestational surrogates; the information they received during their gestational surrogacy arrangements; and their awareness of potential risks and complications during surrogate pregnancy (Appendix 3).

3.5.6 Data analysis

The data were analysed using thematic analysis. Thematic analysis is a widely used method for identifying patterns or themes within qualitative data (Whitehead 2014). Themes can be developed from two approaches: theory-driven and content-driven (Guest, Macqueen & Namey 2012; Whitehead 2014). Theory-driven or hypothesis-driven approach is also known as a confirmatory approach where the data analysis is guided by a theory or specific ideas to explore or compare themes generated through previous research (Guest, Macqueen & Namey 2012; Whitehead 2014). In contrast, in a content-driven approach, also known as an exploratory approach, the researcher inductively explores raw data with multiple readings to obtain keywords, trends, themes, or ideas without any consciously expressed predetermined interest (Guest, Macqueen & Namey 2012; Whitehead 2014). Table 4 presents the differences between theory- and content-driven thematic analysis approaches.

Table 4: The differences between thematic analysis approaches

Theory-driven (Confirmatory)	**Content-driven (Exploratory)**
Explore the application of theory to the data collection. Design to confirm hypotheses.	No theory application. Reads and rereads raw data to generate hypotheses for further study.
Predetermined analysis of specific codes and themes	Not predetermined analysis of specific codes and themes
Typically uses existing data	Generates raw data
Random sampling use	Often uses purposive sampling
Less common approach	Common approach
For example: use X exploring Z to confirm Y.	For example: use X to explore Y

(Guest, Macqueen & Namey 2012)

In this study, a content-driven approach guided by Gibbs's (2007) framework was used for thematic analysis. The approach includes 1) transcription and familiarisation, 2) code building, 3) dis/confirmatory theme development, and 4) data consolidation and interpretation. Following this

framework, the interview was prepared for analysis by a verbatim transcription. A professional service was engaged to transcribe the audio record of each interview in Thai. The transcript was then translated into English by the professional service for data analysis. Next, I performed data analysis in English using the NVivo program to facilitate code and theme development. I systematically analysed and searched for patterns and trends via an iterative process discovering the common themes among gestational surrogates' risk experiences and gestational surrogacy practice in Thailand. The data were analysed 'line-by-line' with codes to identify patterns within the data to develop themes. The iterative analytical process enabled patterns to coalesce into major themes (Wolcott 2008). The data were (re)-analysed until 'thematic saturation' was reached, confirming that no new themes emerged (de Laine 2000). The advisor (Dr Jane Walker) reviewed the analysed data and advised further if there were any ambiguities in the data interpretation. Together with the advisor, any disagreements regarding data analysis were revolved by discussion and consensus.

3.5.7 Ethical considerations

The ethical approval of this study required multiple-site ethical considerations from Thailand and Australia. First, ethical considerations in Thailand were completed and submitted for the local grant and the central ethical committee approval. For the local grant, permission was sought from the private surrogacy agent in Bangkok, Thailand before asking the agent to advertise the research study among gestational surrogates. I contacted the national ethics committee at the Ministry of Public Health (MOPH) in Thailand to confirm the ethical process in Thailand before conducting the research. The information specified that permission is given *'For participating sites with no ethic committee, notification that the study is being conducted at the site is required. Notification is made by the site Principal Investigator (PI) to institutional director and/or their supervisor; depending on the local requirement, a letter usually suffices. The institutional director and/or the supervisor will provide acknowledgement of receipt of this notification.'* According to the information, permission and notification from the private surrogacy agent were needed at the participant's site. Therefore, I sent an email to the private surrogacy agent in Bangkok, Thailand where I previously knew the agent,

explaining the research study, the purpose of the study, the process of the study including privacy and confidentiality, the benefit of the research findings, and the potential risks of involvement in the study. The private surrogacy agent responded by issuing a notification letter of their willingness to support the research study, as this is a part of a doctoral degree. To maintain privacy and confidentiality, the name of the surrogacy agency and the agent's name have not been not disclosed in this PhD thesis. The notification letter from the private surrogacy agency was obtained through email.

In Thailand, as the ethical committee was not available at the investigating site, the application had to go to the central ethical committee. Second, the application for permission from the Central Research Ethics Committee (CREC), Thailand, was completed and submitted to ensure the protection of the rights and welfare of the participants. This project was deemed of low and negligible risk and was approved by CREC in Thailand (CREC001/63SCs).

Lastly, in Australia, the application of Human Research Ethics Committees (HREC) to UTS was also submitted. The HREC approvals were ratified by UTS (ETH17-1945).

3.5.7.1 Informed consent process

Informed consent was obtained from the participants according to the guidelines provided in the National Statement of Ethical Conduct in Human Research (National Health and Medical Research Council (NHMRC) 2018). It was required that the participants are provided with an adequate understanding of the research and any potential risks that might occur from the process or results (NHMRC 2018). The Thai women who participated in this research study were provided information with full disclosure of the research aim and methods, the benefit of the research findings, and the possible impact of the research study. Participants were also informed of the likelihood of the findings being published in academic journals while ensuring the participants' privacy and confidentiality (NHMRC 2018). Signed consent forms were obtained from all participants through the LINE chatting application prior to the interview. Verbal consent to audio recording was also obtained before partaking in the interview process. Participants were notified that they might withdraw from the study at any time without incurring any disadvantage.

3.5.7.2 Participant risks versus benefits

Acknowledging the possibility that some of the interview questions might emotionally affect the participants, causing them to relive or remember distressing events, the distress and safety protocol was placed and strictly followed during the interview process (Appendix 3). As per this protocol, if the participants show signs of distress or feeling upset when answering the questions, the researcher would discontinue the interview process and immediately assess the participant's feelings and safety. The participants would be encouraged to call Mental Health Hotline 1323 immediately, which is a free service. Information about psychological counselling would be provided based on the participant's residency (according to the Department of Mental Health website https://www.dmh.go.th). My representative and I would take immediate action to contact and arrange the service and would be responsible for the fee incurred if the participant required further therapy. The participants would also be contacted the following day to ensure their wellbeing and safety. Thai culture is accepting of seeking psychological help; therefore, it is appropriate to advise the participants to use the counselling service if needed, as they would be able to speak freely about their experiences and feelings in a safe environment.

I was aware that Thailand had no position on surrogacy law until 2015. Furthermore, I was aware of the Protection for Children Born Through Assisted Reproductive Technologies Act 2015 and the surrogacy process of the Thai Medical Council. I complied with and did not act outside of the regulations. This issue of whether the study project was within legal bounds became a concern for participants involved in this research. The new law, the Protection for Children Born through Assisted Reproductive Technology Act 2015, was mandated in April 2015. The new surrogacy law clearly states that gestational surrogacy arrangements are legal in Thailand. Therefore, this study, which investigated gestational surrogacy in Thailand, could be conducted legally. I believe that conducting this research project, by interviewing women who had been gestational surrogates, was not a breach of the current regulations in Thailand. Notably, the aim of this research project was to explore the

experiences of women who were gestational surrogates to clarify about the risks they encounter during an arrangement of gestational surrogacy.

3.5.7.3 Anonymity and confidentiality

To preserve participants' privacy and confidentiality, no identifying information of any participant, including their full name, date of birth, or residential address, were collected. Interview data were anonymised for each participant, using a code and pseudonym for identification. For example, code Participant 1, Participant 2, and so forth were assigned to participants for the recorded interviews, transcriptions, translations, and data analysis; additionally, pseudonyms were used when presenting the findings. Furthermore, no participant was identified in any way in the dissertation or the publication of findings.

3.5.8 Data storage and management

The audio record and transcripts in Thai and English were stored and managed in the research data management plan in Stash, which has restricted access and is password protected. The original audio records were deleted once the transcriptions were complete. The consent form files obtained from Thai women via the LINE chatting application were automatically destroyed by the system within 21 days. Only digital-based data were stored in Stash, and no paper-based material was stored for this study. All data collected will be kept secure in accordance with the local HREC and UTS expected standards for five years, and files will be deleted after this period (NHMRC 2018).

3.6 Study 2

Study 2: Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis

Research question: What are the differences in surrogate pregnancy and live birth outcomes between SET and MET among gestational surrogates?

3.6.1 Study design

The study used a systematic review and meta-analysis research design. Systematic review is a research method used to review existing literature by identifying, appraising, and synthesising all evidence relevant to the research question (Higgins & Green 2011; Uman 2011). Systematic reviews rely on rigour, transparency, and replicability of the approach, providing precise, reliable, and comprehensive results, as the methods of systematic reviews are broader and deeper than those of other traditional reviews (Mallett et al. 2012). However, the quality and biases of the individual studies included in a review must be recognised and assessed. Often, systematic reviews include a meta-analysis component—a statistical method used to synthesise the data from multiple studies into a single quantitative estimate (Higgins & Green 2011; Uman 2011). By combining studies, a meta-analysis increases the sample size and thus the power over individual studies to resolve uncertainty when reports disagree (Fernandez, Johnson & Griffiths 2014). The systematic review and meta-analysis research method is, therefore, a powerful approach to address the third research question of this PhD thesis for drawing the conclusions and then confirming evidence of the phenomena of interest.

3.6.2 Protocol and registration

The protocol of this systematic review is registered (PROSPERO ID number: CRD42017084126) in the PROSPERO registry (https://www.crd.york.ac.uk/PROSPERO/), an international database for the prospective registration of systematic reviews in health and social care, welfare, public health, education, crime, justice, and international developments where there is a health-related outcome.

3.6.3 Data collection

The existing literature was searched through electronic databases once the inclusion and exclusion criteria and primary and sub outcome measures were established for the review. CINAHL (Ebsco), Medline (Ovid), Embase (Ovid), Scopus, and ProQuest, which cover worldwide journals and research studies, and published and unpublished articles, were searched. Cross-references pertaining to this study review were also searched manually. Search terms included ‘surrogacy’, ‘surrogates’, ‘gestational carriers’, ‘gestational surrogacy’, ‘surrogate mothers’, ‘embryo transfer’, ‘double embryo

transfer', 'DET', 'multiple embryo transfer', 'single embryo transfer', 'SET', 'pregnancy outcome', 'live births', 'live delivery', and 'multiple births'. Key terms were also searched for subject terms using MeSH. Studies published from 1980, regardless of language or study type, were accessed. National ART reports including ANZARD, CDC, ESHRE, HFEA, and CARTR were also searched. Covidence online software was used for primary screening and data extraction (www.covidence.org 2018). A PRISMA flow chart was used to document the selection process of this study review.

3.6.4 Study selection

Outcome measures: The primary outcomes included clinical pregnancy rate, live delivery rate, and multiple deliveries. Adverse events following SET and MET were also recorded and discussed.

Inclusion criteria: Articles that reported SET and MET among gestational surrogate cycles, the comparison between SET and MET gestational surrogate cycles, and primary outcome measures of clinical pregnancy, live delivery, or multiple delivery between SET and MET were included. Only the most recent study was included in the case of duplicate publications.

Exclusion criteria: Articles that did not state the number of SET and MET gestational surrogate cycles, and those with no events of primary outcomes in SET and MET gestational surrogate cycles were excluded. The reasons for exclusion were recorded.

3.6.5 Extraction and quality assessment

Covidence online software was used for study selection and data extraction (www.covidence.org 2018). The titles and abstracts of the articles were screened for potential eligibility by me (JA) and the supervisor Associate Professor Alex Wang (AYW). Disagreements regarding study eligibility were solved through discussion and consensus. The full text of the selected articles was evaluated for the level of evidence once all inclusion/exclusion criteria had been verified. Independently, JA and AYW extracted the data. The authors of the relevant articles were contacted for additional data. Söderström-Anttila et al. (2002) provided raw data for this review. The Newcastle-Ottawa Scale (NOS) was used for quality and risk of bias assessment. NOS, which is an on-going collaboration between the

Universities of Newcastle, Australia and Ottawa, Canada (Lo, Mertz & Loeb 2014), is a tool used for assessing the quality of non-randomised studies in systematic reviews and/or meta-analyses. Three broad perspectives were assessed: the selection of the study group, the comparability of groups, and the ascertainment of the exposure or outcomes of interest (Lo, Mertz & Loeb 2014). Any disagreements regarding study appraisal were solved through discussion and consensus.

3.6.6 Data analysis

Review Manager 5 (RevMan 5) program, which is endorsed by the Cochrane Collaboration, was used to perform the meta-analysis. The outcome measures were calculated with Mantel-Haenszel risk ratios (RRs) with 95% confidence intervals (CIs) using a fixed-effects model. It was considered whether the clinical and methodological characteristics of the included studies were sufficiently similar for meta-analysis to provide a clinically meaningful summary. Statistical heterogeneity was assessed using the I^2 statistic, taking a value greater than 50% as indicative of substantial heterogeneity (Higgins & Green 2011). Sensitivity analysis was also performed to examine the stability and robustness of the results of this review.

3.6.7 Ethical approval

Systematic and meta-analyses are considered secondary studies; therefore, they do not require research approval.

3.7 Study 3

Study 3: Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements

Research question: What is the CLBR among gestational surrogates in altruistic surrogacy arrangements?

3.7.1 Study design

Study 3 used a retrospective cohort study design. A retrospective cohort study, also known as a historical cohort study, is a type of observational research that allows the researcher to look backwards and examine exposures to suspected risks or protection factors concerning an outcome at the time the

study is conducted (El-Masri 2014). Retrospective cohort study also provides the researcher with the advantage of examining multiple outcomes for a given exposure during the historical observation period with fewer costs and faster completion than longitudinal and other research studies (Song & Chung 2010). However, due to limited control of over data collection, the researcher must be aware of information bias (Song & Chung 2010). The retrospective cohort study design is an appropriate approach to answer the last research question of this PhD thesis evaluating the exposure of interest in the population that has never been examined in the past.

3.7.2 Data collection

The ART data of all gestational surrogate cycles from 1 July 2009 and 30 June 2016 were collected using VARTA. Participants were given a follow-up regarding the clinical outcomes from their first gestational surrogate transfer cycle until June 2016 or until a live birth was achieved. Data on pregnancy and birth outcomes up to the end of June 2017 were included and used the analyses of pregnancy and birth outcomes.

VARTA is a statutory authority funded by the Victorian Department of Health and Human Services to administer aspects of the *Assisted Reproductive Treatment Act 2008* (Vic). VARTA's dataset is a census of all initiated ART treatment cycles undertaken in Victoria, Australia where only altruistic surrogacy arrangements are permitted. All fertility clinics in Victoria are required to report data to VARTA on a financial year basis. The VARTA dataset includes 94 items on demographics of women/couples, type of ART treatments and procedures, number of embryos transferred, and pregnancy and births outcomes (VARTA 2019).

3.7.3 Outcome measures

The primary outcome was the CLBR, which is defined as deliveries with at least one live birth per gestational surrogate resulting from the first embryo transfer cycle and the subsequent embryo transfer cycles (Zegers-Hochschild et al. 2017).

3.7.4 Data analysis

Descriptive statistics were obtained (using SPSS Statistics 25 Armonk, NY, US: IBM Corp.) to describe demographic, clinical, and treatment characteristics for the categorical and continuous variables. The CLBRs were calculated using a life-table, which represents, for each gestational surrogate cycle, the probability that the gestational surrogate of that cycle will have a chance of live birth before the next cycle. The 95% CIs for CLBR were calculated using the Wilson score method, which is an interval estimation of a binomial proportion for small numbers wherein the actual coverage probability is closer to the nominal value (Brown, Cai & DasGupta 2001).

3.7.5 Ethical approval

Ethical approval for Study 3 was granted by the HREC of UTS (ETH16-0800). Permission to access the VARTA data was granted by VARTA.

3.8 Chapter summary

The research design, methodology, and methods were outlined, providing a clear picture of how the overarching aim of this PhD thesis was met. A multimethod was designed to answer the different research questions. The three studies were conducted simultaneously using both quantitative and qualitative approaches. Each study was completed and adhered to its method, analysis, and findings. The findings of each study enhance the overall evidence of this PhD thesis, which was driven by the inductive theory to explore the risk experiences of gestational surrogates and the trend of gestational surrogacy practice. The following chapters present the manuscripts in preparation/submission and the published studies of this PhD thesis.

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Chapter 4: 'Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand

The material of this chapter has been prepared for the manuscript. The manuscript has been re-submitted on 11th November 2020 and under reviewed by *Human Fertility* Journal.

This manuscript has been accepted and published in the *Human Fertility* journal, 2021.

List of presentations and publications from this study:

- The material of this chapter were presented at the 3MT, Research Student Forum at UTS in 2018
- The material of this chapter was submitted to Visualise Your Thesis competition, 2018 at UTS.
- Attawet, J. 2020, 'Understanding self-perceptions and risk experiences of gestational surrogate mothers in gestational surrogacy arrangement, Thailand'. [Poster presentation], *ASRM 2020 Scientific Congress & Expo Goes Virtue (17–21 October 2020)*, Portland, OR. (Appendix 4).
- Attawet, J. 2020, 'Understanding self-perceptions and risk experiences of gestational surrogate mothers in gestational surrogacy arrangement, Thailand' [ASRM Abstracts], *Fertility & Sterility*, vol. 114, no. 3, pp e275-6. (Appendix 5)
- Attawet, J., Wang, A. Y. & Sullivan, E. 2021, ''Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand', *Human Fertility*, < https://doi.org/10.1080/14647273.2021.1937716>. (Appendix 6)

4.1 Chapter introduction

Chapter 4 addresses the first research question:

- What are the risks encountered by gestational surrogates in the process of gestational surrogacy and the related arrangements in Thailand?

This study is a descriptive qualitative study, the result of which is the essence of this PhD thesis. Data were collected from interviews with Thai women who had experience being a gestational surrogate. Using interviews of Thai women from their experiences could help the researcher to reflect on their risk encounter and gestational surrogacy practice in Thailand. Informal conversations with a friend of the researcher who worked in the industry, published news and articles, and online surrogacy advertising were also used to bring together the results. The submitted manuscript is outlined in the following section.

4.2 Abstract

Introduction: Risks to gestational surrogates became as concern for public health. In commercial gestational surrogacy arrangements, gestational surrogates are commonly recruited from low- to middle-income countries. Thailand is well known as a surrogacy hub in this regard. However, little is known concerning Thai surrogacy practice and Thai gestational surrogates' risk experiences.

Methods: Interviews with fifteen Thai women who had been gestational surrogates were conducted to investigate these gestational surrogates' risk experiences and surrogacy practice in Thailand. The semi-structured interviews were conducted individually over the telephone in Thai between March and May 2020 and lasted approximately 30 minutes. Thematic analysis was applied to analyse the translated interviews.

Results: The findings indicated that womb for work was perceived as a surrogacy career among Thai women. 'Womb for work' was defined as a superordinate theme which consisted of three subthemes: (1) gestational surrogacy arrangements in Thailand; (2) the business model of gestational surrogacy

arrangements in Thailand; and (3) risk experiences of gestational surrogates. All the interviewees were working as commercial surrogates despite the 2015 surrogacy ban. Risk encounters for Thai women were observed emerging from the surrogacy business model. Risk experiences of Thai women involved in gestational surrogacy arrangements included those associated with embryo transfer, transnational gestational surrogacy, and unsupported pregnancies.

Conclusions: Clear deficiencies in surrogacy practice and regulations were identified, which put gestational surrogates at risk. This study shows the urgent need to introduce regulations to protect women's health transnationally in this domain more effectively.

Keywords: Commercial surrogacy, reproductive tourism, gestational surrogacy, surrogates, Thailand

4.3 Introduction

Risks to gestational surrogates, especially women who are commercial surrogacy arrangements, have been of concern internationally evident with successive banning of such arrangements in Southeast Asia (Hibino 2020; Whittaker 2011). The rapidly expanding industry of commercial surrogacy in low- and middle-income countries is a response to the growing demand of reproductive tourism (Deonandan 2015; Whittaker 2011). According to Gezinski et al. (2017), India and Thailand have emerged as major marketplaces for commercial surrogacy services. Commercial surrogacy arrangements had been legal in India, giving it a reputation as a 'rent a womb' country, before this practice was halted in 2018 (Ray 2018). Despite surrogacy being banned by the Thai government in 2015, Thailand had been branded 'the womb of Asia' (Kaufman 2015), and commercial surrogacy continues in various forms.

Thailand previously had no surrogacy laws and became a key market, between 2006 and 2015, for intended parents from high-income countries including Australia (Cohen 2015; Whittaker 2011). Demand increased further in 2013, following India's ban on commercial surrogacy arrangements for same-sex couples. The operation of commercial surrogacy arrangements in Thailand did not attract public interest until controversy erupted concerning a baby with Down's syndrome, named Gammy, in

mid-2014. Gammy was left with his commercial gestational surrogate in Thailand by the Australian intended parents (and biological father), whilst his twin sister was taken back to Australia (BBC News Asia 2015). Public interest in the case was heightened further as it emerged that the intended father was a convicted sex offender (Whittaker 2016). Australian authorities investigated the welfare of Baby Gammy's sister while a public campaign raised money to support baby Gammy, who became an Australian citizen on January 2015 and remains in the care of his commercial gestational surrogate (Whittaker 2016).

Following the 'baby Gammy' scandal, in early 2015, the Thai military government legislated against commercial surrogacy, banning foreign and same-sex couples from seeking the service and allowed only altruistic surrogacy arrangements in Thailand for infertile Thai or Thai who had married foreigners (Royal Thai Government Gazette 2015; Sattaburuth 2015). As a result of this surrogacy ban in Thailand, several surrogacy fertility clinics closed, but others reportedly continued to operate underground, shifting gestational surrogates across the border to countries where commercial surrogacy was not regulated (Murdoch 2017), such as Cambodia. However, in 2016, Cambodia also imposed a commercial surrogacy ban, so the industry moved to Laos, where it remains unregulated (Hibino 2020; Lefevre 2017). Indeed, some Thai surrogacy and fertility businesses threatened with closure in 2015 reportedly continue their operations in Laos (Hibino 2020). Table 5 shows the changing trend in destinations for 'reproductive tourism' in Southeast Asia.

Table 5: Changing destinations for reproductive tourism in Southeast Asia

Commercial surrogacy 'boom years'	Destination	Regulation	Landmark case
2002-2015	India	Commercial surrogacy legalized in 2002. Same-sex couples excluded in 2013; banned altogether in 2018.	- Baby Manji in 2002. - Indian surrogacy businesses moved their operations to Nepal after surrogacy for same-sex couples was banned in 2013.
2013-2015	Nepal	Surrogacy legal, then banned in 2015	- After a massive earthquake hit Nepal in 2015, many Indian surrogates were stranded while Nepal's government airlifted babies belonging to their citizens. - Indian surrogacy businesses move their operations to Cambodia in 2015.
2006-2015	Thailand	No surrogacy law until banned in 2015.	- Baby Gammy in 2014. - Thai surrogacy businesses move their operations to Cambodia in 2015.
2015-2016	Cambodia	No surrogacy law until banned in 2016.	- Tammy Davis-Charles, the Australian nurse and the founder of a surrogacy agency in Thailand before relocating to Cambodia, was arrested in 2016 with two Cambodians for their roles in a surrogacy business. - 33 surrogates were charged for human trafficking. - Thai surrogacy businesses move their operations to Laos in 2016.
2016-Present	Laos	No surrogacy law.	Nil

(BBC News Asia 2015; Lefevre 2017; Murdoch 2017; Ray 2018)

The publicity surrounding landmark cases that emerged following the changing trend in destinations for reproductive tourism in Southeast Asia indicated clearly the risks to and effects on gestational surrogates, which have been considered unacceptable within the various affected communities. Since Thailand became a surrogacy jurisdiction and the scandal broke, Thai gestational surrogates' risk experiences are of interest to the authors. However, only a few studies have described gestational surrogacy practice in Thailand and the risk experiences undergone by Thai gestational surrogates themselves.

4.4 Aim

This study aims to investigate Thai gestational surrogacy arrangements and the risk experiences of Thai gestational surrogates. Investigation through interviews with Thai women who have been gestational surrogates could aid in understanding Thai gestational surrogacy arrangements better and in clarifying the risks encountered by Thai gestational surrogates throughout the process.

4.5 Materials and methods

A qualitative study was conducted with semi-structured interviews undertaken between March and May 2020. The interview participants were fifteen Thai women, aged 20–40 years, who had surrogacy experiences and who were not currently pregnant. Potential participants were invited to participate in this study through a single private surrogacy agency in Bangkok, Thailand, which is no longer in operation but was known to the researcher (JA). JA contacted the private surrogacy agency and sought assistance to publicize this intended study through the agency's connections with Thai gestational surrogates. An invitation letter in Thai was used to determine whether there were any interested participants, with potential participants asked to contact JA directly or JA's research assistant. Two potential participants did so, one of whom was not eligible as she was currently pregnant; a snowballing technique was used to recruit the fourteen other participants. Written consent was sought using the LINE™ chatting application and verbal consent was also sought prior to the interview. The interviews were conducted by JA over the telephone in Thai, which were undertaken at a time convenient to the participants.

Information of the intended parents or involvement of other parties (apart from the gestational surrogate) was deemed as potentially harmful to the participants. The interview question guideline excluded questions on these groups in compliance with the ethics committee's recommendation. The semi-structured interview guide included six open-ended questions that covered the background of gestational surrogates and their families; reasons for becoming gestational surrogates; their experience before, during and after being gestational surrogates; the information received during their surrogacy arrangement; and their awareness of potential complications during surrogate pregnancy. The interviews were conducted in Thai and lasted approximately 30 minutes per participant, with audio record for the purpose of transcribing and translating. The distress and safety protocol was in place, providing suggested counselling services located near where the participants resided, if required.

4.5.1 Data analysis

The overall results of this study were derived using thematic analysis (de Laine 2000; Wolcott 2008). JA did the initial data transcription in Thai. A translation service was used to translate the data transcription from Thai to English. JA performed data analysis including coding, generating themes, reviewing themes and defining themes. Other authors reviewed the themes and offered advice if there were any ambiguities in thematic analysis. All the authors resolved any disagreements regarding data analysis through discussion and consensus.

4.5.2 Ethical consideration

Ethical approval was granted by the HREC of UTS, Australia (ETH17-1945) and the CREC, Thailand (CREC001/63SCs).

4.6 Results

Seventeen women, who had gestational surrogacy experience, expressed an interest in taking part in the study. Two were excluded as they were pregnant at the time of interviews. Fifteen women met the study inclusion criteria. Their ages at the time of our interviews ranged from 23 to 35 years, while their ages at the time of being gestational surrogates ranged from 21 to 34 years (Table 6). The women

recalled their gestational surrogacy experiences from two months to seven years prior to the interview (between 2013 and 2020). All fifteen women had been compensated for carrying a pregnancy, demonstrating that the women had been gestational surrogates involved in some form of commercial arrangement up to 2020.

Table 6: Gestational surrogate's demographics

Participants	Age group during surrogacy (Mean 27.8)	Age group at interview (Mean 30.5)	Number of own children	Relationship status before being a surrogate	Relationship status after being a surrogate
1	25-29*	30-34	2	Divorced	N/A
2	20-24	20-24	1	Divorced	N/A
3	30-34*	30-34	1	Married	Divorced
4	30-34	35-39	3	Married	Divorced
5	30-34	35-39	1	Divorced	N/A
6	30-34	30-34	2	Married	Married
7	25-29	30-34	1	Cohabitation	Cohabitation
8	30-34*	35-39	2	Divorced	N/A
9	25-29	25-29	1	Married	Married
10	20-24*	25-29	0	Single	Single
11	20-24	20-24	2	Cohabitation	Cohabitation
12	20-24	25-29	2	Married	Married
13	25-29	30-34	2	Cohabitation	Cohabitation
14	30-34	35-39	2	Divorced	N/A
15	20-24	25-29	2	Cohabitation	Married

*2 surrogacy

'Womb for work' was identified as a superordinate theme. This superordinate theme addresses Thai women's risk experiences who had been a gestational surrogate in the context of Thai gestational surrogacy practice. These women perceived surrogacy as involving 'womb for work', which was better than other forms of work available to them, as Mai stated: "*I left my last job to become a gestational surrogate, which makes more money. Surrogacy is my career now and I had done it twice*". In terms of these women's experiences of 'womb for work', three subthemes were identified.

4.6.1 Gestational surrogacy arrangements in Thailand

Thai gestational surrogacy practice tends to take a commercial form. All the interviewed Thai women were identified as engaging in commercial gestational surrogacy as they became gestational surrogates in exchange for a fee. Women made the decision to engage commercial surrogacy arrangements due to

several factors, including dependent children and family, responsibility, debt, and culture—the woman's or daughter's social role in Thai culture is more active and she is responsible for her other family members (Hibino & Shimazono 2013; Teerawichitchainan, Pothisiri & Long 2015). Of the fifteen women, fourteen were the main income earners in their household and were responsible for their families, including dependent children. Hence, the main justification for becoming a commercial gestational surrogate was the compensation, which allowed them to earn a sum of money and was one of the better careers available to them. For example, one of them, Fon, stated that: *"I can have a sum of money to pay off my debt while my current job cannot help"*.

Thai women are generally recruited by surrogacy agencies. In some case, Thai women reported that they contacted a broker privately after seeing an advertisement on the internet, while others became involved through friends who were already gestational surrogates. Interaction with a surrogacy agency or private broker was the first step in the service career of the women in this study. Thai women believed that the agency or broker was their employer, which they would call the 'big boss' ('บอสใหญ่' or 'Boss Yai' in Thai). The women said they listened to and complied with all the instructions given by the surrogacy agency, which they considered to be their benefactor, as Hong stated: *"The agency gave me all the details about the surrogacy arrangement and told me what I needed to do and where I needed to go. I basically listened to the agent because she gave me a job".*

Interaction between the women and their *big boss* was formalized through signing a contract, which the women perceived as a commitment to work for their boss throughout the process of the commercial surrogacy arrangement. The surrogacy agency or broker introduced the women to fertility clinics to receive their initial treatment in Thailand. The arrangement included domestic and transnational treatments following the initial treatment. Six women, who were involved prior to 2015, had undergone embryo transfer at fertility clinics in Thailand, while others had undergone embryo transfer outside Thailand (in Laos or Cambodia) after 2015. In the latter cases, the women were flown accompanied by the surrogacy agency's nurses to those countries and then back to Thailand following embryo transfer, to continue with their pregnancy in Thailand. Mai stated *"I flew to Cambodia with*

the agency nurse for the embryo implantation. After the procedure, I stayed there for three days, and then flew back to Thailand and continued my pregnancy here".

At or around 38-40 weeks' gestation, all the women in the study underwent a caesarean section, as per their surrogacy protocol requirements. Six women who were gestational surrogates prior to 2015 delivered their babies in Thailand, while others had to fly to the intended parent's countries, such as China, at 28 weeks gestation and stayed in the intended parents' place or the provided accommodation by the intended parents until delivery. In contrast, Cambodia and Laos were restricted to the embryo transfer component of reproductive services as both countries have limited capacity and specialist facilities including neonatal intensive care units required for complicated births (BBC News Asia 2017; Murdoch 2017). Therefore, Thailand remains a key centre for surrogate births because it has access to specialist maternity and neonatal care providers and neonatal intensive care facilities. Table 7 shows the process of commercial gestational surrogacy arrangements in Thailand.

Table 7: The process of commercial surrogacy arrangements in Thailand

Step	Action
1	Agreement made and contract signed between intended parents and surrogacy agency.
2	Surrogacy agency approaches fertility clinic for treatment or vice versa. Agreement made between surrogacy agency, fertility clinic and intended parents.
3	Recruitment of gestational surrogates according to age, health conditions, history of previous pregnancy, and based on intended parents' specific request. Agreement made and contract signed between surrogacy agency (Big boss) and gestational surrogates.
4	Health screening and initial treatment for endometrial preparation in gestational surrogates before embryo transfer. Provided in the initial fertility clinic.
5	Embryo placement in gestational surrogates' uterus. Domestic embryo transfer in the initial fertility clinic in Thailand or transnational embryo transfer in fertility clinics in Cambodia or Laos.
6	Gestational surrogates carry pregnancy in Thailand (both domestic and transnational embryo transfer).
7	Delivery by Caesarean Section only. Country of delivery is upon intended parents' request and may be outside Thailand.
8	Relinquishing of babies through surrogacy agencies or directly to intended parent(s). Some intended parents may remain unidentified to Thai gestational surrogates throughout the surrogacy process. Some met intended parents and remain in contact after relinquishing babies.

4.6.2 The business model of gestational surrogacy arrangements in Thailand

Through examining these Thai women's experiences and gestational surrogacy practice, it was possible to gain insight into the business model used for 'womb for work'.

Table 8: The business model for commercial surrogacy in Thailand

<table>
<tr><td rowspan="2">Partners

Fertility clinics

Surrogacy agencies</td><td>Activities

Match intended parents with a woman who has agreed to carry a foetus through pregnancy

Facilitate antenatal care/ birth in other jurisdictions

Multiple Embryo Transfer (MET)

Birth by Caesarean Section

Shifting gestational surrogates across the border</td><td rowspan="2">Value proposition

Fulfilment of a family

Screened gestational surrogates- age, health check, history of previous pregnancy.

Confidentiality

Affordability</td><td>Customer relationships

Intended parents</td><td rowspan="2">Target customer

Infertile couples, gay couples, individuals

High-income countries

Locations where gestational surrogacy is illegal</td></tr>
<tr><td>Resources
Gestational surrogates ≤ 35 years, in low to middle income countries

Assisted Reproductive Technology</td><td>Channels
Surrogacy agencies in various locations and countries

Advertisement via Internet

Online consultation</td></tr>
<tr><td colspan="2">Cost structure
Attractive prices for intended individuals/couples are achieved by paying gestational surrogates less (about AUD 13,000 per complete pregnancy. Currently minimum wage in Thailand is AUD 415 per month). Double payment for carrying twins or more, or for embryos fertilised by infected sperm or oocytes.</td><td colspan="3">Revenue streams
Attractive online advertising and affordable prices maintained by recruiting gestational surrogates from low- to middle-income countries</td></tr>
</table>

(This business model framework was developed from published news and articles, surrogacy online advertising, informal conversations with people who work in the surrogacy arrangement service, and surrogate interview.)
Table 8 provides a summary of the business model for 'womb for work'. The Thai women interviewed came from diverse backgrounds, ranging from middle- to very low-income status. The incentive component of multiple and potentially infected embryo transfer formed part of the surrogacy business model attracting gestational surrogates. According to Pink, Ream and Sam, a double pay was possible when carrying "*twins or potentially infected embryos fertilized by infected sperm or oocytes".*

While the surrogacy agencies or private brokers sought customers and resources, the fertility clinics provided the fertility service through assisting gestational surrogates to become pregnant based on the intended parent(s)'s request. Surrogacy agencies or private brokers advertise online, normally targeting a customer base in high-income countries. These agencies approach fertility clinics to arrange a gestational surrogacy for the intended parent. At the same time, surrogacy agencies or private brokers advertise online for gestational surrogates. Some women in our study reported that they had responded to such advertisements, while others were recruited by friends who were already gestational surrogates. For example, Sam stated: *"I had friends who were gestational surrogates and they suggested me to the surrogacy agency",* and Pairin observed: *"I was looking for how to get a loan on the Internet and I saw the surrogacy advertisement with good compensation. I then responded to the advertisement".*

Attractive online advertisements involving affordable prices in Thailand has encouraged increasing numbers of productive tourists or foreign couples to seek surrogacy treatment. The influx of foreign couples using gestational surrogacy arrangements in Thailand has allowed Thailand to become a commercial surrogacy hub and led to the creation of 'womb for work' for Thai women. However, the information of intended parents was out of the scope of our study, so we could not identify their nationality or status.

4.6.3 Risk experiences of gestational surrogates emerging from the surrogacy business model

The business model details in Table 7 is all about the transnational production of a healthy baby. The experiences and potential risks to Thai women engaged in gestational surrogacy practice in Thailand are poorly described. Thai women's risk encounters were observed as having the following themes:

4.6.3.1 Risk experiences associated with embryo transfers

Risks arising from MET and potentially infected embryo transfers were identified in the business model. The majority of Thai women (n=11/15) interviewed received MET. Of those, three women delivered twins and one woman suffered a miscarriage. In one instance, a miscarriage was noted following a triple-embryo transfer. The interviewed woman, Khawn, stated: *"I had three cycle attempts for embryo implantation. In each cycle, I received a triple-embryo transfer. I became pregnant in the third embryo transfer cycle. At week 8 of my gestation, I had a regular check-up and the doctor could not detect the baby's heartbeat. I was informed that I had to undergo a D&C [dilation and curettage] procedure. The procedure was really painful, and I took a while to recover. I received less payment because I could not get through the pregnancy and delivery process. I received only 30,000 baht (or approximately AUD 13,000). This was not worthwhile, and I swore to myself that I wouldn't be a gestational surrogate again"*. MET not only results in multiple pregnancies, but also results in the adverse consequences associated with multiple pregnancies. Reflecting from Khawn's surrogacy experience, although there were clear opportunities for Thai women to earn money engaging in 'womb for work' as part of a career goal, there was some uncertainty found concerning the extent to which gestational surrogates would be likely to encounter financial and health risks during the surrogacy process. Apart from this case, none of the participants reported suffering pregnancy complications, such as hypertensive disorder, gestational diabetes, preeclampsia, preterm birth, or stillbirth. The only pregnancy complication noted by the participants was morning sickness.

Transfer of embryos from HIV positive person(s) were another concern among Thai women. The interviewed women mentioned that they had the choice to receive incentives if they became involved in an embryo transfer from a HIV positive person. One woman decided to have an embryo transfer from a HIV positive person. Pink noted: "*I received fresh embryos that were fertilized from an intending father who had HIV [human immunodeficiency virus]. Personally, I always do research before I see the doctor and ask the doctor to explain things again. I did research about the chances of HIV infection affecting the pregnancy and found that there has a less chance to affect me. I also asked the doctor again. The doctor explained to me in detail that such infection was very rare, less than 1%, with his embryo transfer technique*".

Pink knew that the embryos transferred to her were fertilised with sperm from a HIV positive person. After her research and perception that there was a low risk of infection, she agreed to undergo the transfer and signed the contract, encouraged also by an increased level of financial incentive. She also sought an opportunity to clarify the risk of infection further with the doctor after signing the contract. Pink delivered a singleton healthy baby following a triple embryo transfer and she did not become infected with HIV. From her surrogacy experience, Pink received an agreed sum of money from the surrogacy agency, as well as further money from the intended parents, which helped her to become free from debt and has provided her with ongoing improved living conditions. Pink also stated that "*I did surrogacy only once and that was also my last. I earned enough money and now I have full-time work. I won't put myself at risk anymore even though I knew there was really little risk*".

The risk associated with the process of embryo transfer was triggered by the inadequate information provided. Most of the women (n=14/15) had limited knowledge and understanding of the procedure that they had undergone and the potential risks involved in MET; in terms of possible infection—only one had researched and clarified the procedure with the fertility professional. This situation subsequently limited their ability to raise concerns and questions about their treatment with the fertility professionals. Some of the women said that they did not receive information about potential risks. Neither the surrogacy agency nor the fertility clinic provided written information regarding the

potential risks and complications associated with MET and potentially infected embryo transfer. These women's limited knowledge, and the limited information offered by the fertility clinic, could readily create an impression that surrogacy arrangements always proceeded with ease, with the women unintentionally accepting the risks involved due to their unawareness of them.

4.6.3.2 Risk experiences associated with transnational gestational surrogacy

Transnational movement of gestational surrogates from Thailand to other countries for fertility treatment and/or birth is one business model employed to circumvent the regulation in the country and sustain commercial viability. In order to avoid the 2015 surrogacy ban in Thailand, gestational surrogacy arrangements involved embryo implantations taking place in neighbouring countries such as Cambodia (no surrogacy law until banned in 2016) and Laos (currently no surrogacy law). This process placed gestational surrogates at legal risk, not only in respect of the surrogacy laws in Thailand, but also for facing charges in these neighbouring countries. All interviewed Thai women expressed that they were unsure about local (Thai) surrogacy law or what occurred in other countries. *"I was not actually sure about the surrogacy laws in Thailand or other countries. I was not sure what punishment I could face. I was only thinking that I helped an infertile couple pursue having a family, and, in turn, I received a reward for my work",* Ream said. However, none of the interviewed Thai women experienced prosecution or imprisonment.

A further risk was the shifting of gestational surrogates to the intended parents' country for delivery at 38-40 weeks. *"At my 38 weeks I flew to China to give birth there. I stayed there for about two weeks. The intended parents looked after me very well and I gave birth to a healthy baby"*, Pui said. Although none of the interviewed Thai women who travelled by air in the third trimester reported adverse outcomes, international air travel at gestations from 32 weeks is not advised (The Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG) n.d) and the rights and financial and legal liabilities of the women (surrogates) and their families are unclear in case they experience an adverse birth or baby outcome or in case of a maternal death.

4.6.3.3 Risk experiences associated with unsupported pregnancies throughout the process of gestational surrogacy arrangements

The Thai women talked about a range feelings while participating in commercial surrogacy arrangements. Fear was a common feeling experienced by the women, specifically in relation to possible legal issues. They felt unsure about what they were doing because they did not know whether surrogacy arrangements were acceptable or not in Thailand at the time of their pregnancy. Therefore, they chose to keep their surrogate pregnancies secret from everyone in response to this fear. As Nui claimed: *"I felt scared and I did not want anyone to know what I was doing. I wasn't sure that surrogacy arrangements were legal in Thailand".*

Being unclear as to whether surrogacy was legal at the time of their pregnancies negatively affected the women's willingness to clarify whether any support systems were available in Thailand other than their *big boss* and the fertility clinic in case of adverse health or medical events or when the baby is abandoned by the intended parents. All the interviewed Thai women believed that there were no support systems or organizations that could help them if something went wrong. They all believed they had to rely on their *big boss* and, perhaps, the fertility clinic to help them; otherwise, they understood that they would be solely responsible for themselves. Mai stated: *"I think there was no support organisations for surrogacy if something went wrong. For me, for example, if the intended parents did not take the baby home and if my big boss could not help me to return the baby to the intended parents, I have to responsible for this and I did not think I can ask or find any organisations to help or support me. I would rather keep my surrogacy secretly and responsible for my own as I was not sure the legal status of surrogacy and I would face at that time".*

An unclear understanding of the legal issues was not the only reason for keeping pregnancy a secret. Thai women were also covering their feelings of stigmatization influenced by Thai culture. The majority of the interviewed Thai women chose to keep their pregnancy secret and isolated themselves from society and even their family. *"I did not tell my family about my decision. At that time, I decided to live alone and communicated with my family via Face Time—they did not know at all that I was*

pregnant. I did not see my family until I had delivered—finished my 'womb for work'. But I still sent my family money. If I explained about my pregnancy, I knew my family would not understand about surrogacy", Sam said. *"I did not tell anyone other than my mom. I rather stayed home throughout my pregnancy. I did not go outside at all—my neighbour did not know about my pregnancy. They will gossip about me and my pregnancy out of wedlock and will not understand about 'surrogacy' if they find out about it",* Ream said. Excluding oneself from society and support during pregnancy therefore became the sensible choice among Thai women influenced by their perceptions of cultural norms.

4.7 Discussion

This study illustrates the complexity of gestational surrogates' experience of risk arising through their participation in the gestational surrogacy process in Thailand. Our study included interviews of Thai women with surrogacy experience before and after the commercial surrogacy ban in 2015. The ban clearly states penalties for all violations. In case of noncompliance to the Protection for Children Born through Assisted Reproductive Technologies Act 2015, there are sentences upon conviction to imprisonment for up to ten years or to pay a fine of up to 200,000 baht (about AUD 9,000) for anyone involved in surrogacy for profit (Stasi 2017). A healthcare provider who is unqualified to perform the surrogacy service in a commercial form can be imprisoned for one year and/or fined up to 20,000 baht (about AUD 890), and anyone who acts as an intermediary by requesting or accepting money, property, or other benefits in return for managing or giving advice about surrogacy will be sentenced upon conviction to imprisonment for up to five years and/or to pay a fine of up to 100,000 baht (about AUD 4,500) (Stasi 2017).

Despite the ban of commercial surrogacy in Thailand, the Covid-19 pandemic has revealed that transnational commercial surrogacy arrangements persist, leaving numerous newborn babies of commercial gestational surrogates stranded in Thailand because of international travel bans enforced during the pandemic (Bangkok Post 2021; Wipatayotin 2021). These reports support our findings of unacceptable risk and loss of agency for women engaged in 'womb for work' and for the babies born in illegal transnational commercial surrogacy arrangements in Thailand. Thai women were continuing to

work as commercial gestational surrogates in an environment where they were unsure of the legality of the arrangement. The surrogacy agency was found to be powerfully influential in encouraging Thai women to enter into surrogacy. The Thai women in this study were found to be willing to comply with the surrogacy agency as they believed that the agency was the ultimate authority in relation to their 'womb for work' career. Fertility professionals were found to be only responsible for medical procedures, in contrast to India where, concerning commercial surrogacy arrangements, fertility professionals have been reported to play the major role in mediating and organizing throughout the surrogacy process (Saravanan 2013). Although the Protection for Children Born through Assisted Reproductive Technologies Act 2015 (Royal Thai Government Gazette 2015) in Thailand prohibited surrogacy agencies and surrogacy advertisements, online advertising of Thai surrogacy still occurs. This advertising reflects an ongoing demand for commercial gestational surrogates and surrogacy, and demonstrates that commercial gestational surrogates are still operating in Thailand, as this study discovered from the interviews. Within this context, gestational surrogates are likely to be negatively affected in terms of their health and in their legal, emotional, social, and financial status. Such negative effects have also become part of a global debate concerning gestational surrogacy (Hibino & Shimazono 2013; Karandikar, Gezinski & Huber 2017; Saravanan 2013; Tanderup et al. 2015; Tehran et al. 2014; Tremellen & Everingham 2016). The recently study of Söderström-Anttila et al. (2016) systematically reviewed the outcomes for gestational surrogates including physical and psychological risks. Although this systematic reviews demonstrated risks to gestational surrogates with no different outcomes of complications in surrogate pregnancy compared to non-surrogates and less seriousness of psychological outcomes, this study findings add differently important value to gestational surrogates' risks, especially in a commercial form. The findings conceptualised the surrogacy business model adding evidence risks to gestational surrogates emerging from the commercial surrogacy business.

This study's findings further highlight the risks faced by individual gestational surrogates within the surrogacy business model, while the industry continues to thrive. When entering into gestational surrogacy arrangements, the gestational surrogates had to face the risk of potentially inadequate support

from family, relatives, close friends, community, and healthcare organizations. Uncertainty concerning practice and regulations led these Thai women to be unsure whether what they were doing was legal and appropriate within their community. The effect of Thai cultural norms and of censure (pregnancy outside of wedlock is not approved within Thai society generally) also had conflicting effects on their behaviour and perceptions. A study from UNICEF Thailand (2015) noted that, within Thai society, a pregnant woman is commonly stigmatized if the child is conceived out of wedlock. Consequently, these Thai women decided to isolate themselves throughout their pregnancies and kept their surrogacies secret from their communities. Goffman and Link have theorized that the effect of stigmatization leads to the individuals concerned devaluing themselves in their society, as they feel that they are failing to comply with social norms and have become unacceptable, with negative effects in terms of mental illness (Goffman 1963; Link 1987). Isolation from the community at this stage (during pregnancy), therefore, could be even more damaging, and might place gestational surrogates at greater potential risk of psychological harm. This potential psychological risk factor is likely to be considerably addressed if gestational surrogates were supported or knew to whom or to what organizations and support services they could turn to for help.

In the surrogacy business model, MET and financial incentives were highlighted in this study's findings. MET seems to be a routine practice in the surrogacy business model which is in contrast to accepted practice at the community level (Attawet et al. 2020; White 2016, 2017). MET are known to more frequently involve adverse events with multiple pregnancy which could negatively impact on mother's and baby's health (Duffy et al. 2005; Tanderup et al. 2015; Wang et al. 2016).

This study also showed that gestational surrogates were incentivized to accept fresh embryo transfer from HIV positive couples. Although transferring infected fresh embryos involves only a low chance of infection and there has been no clinical report of HIV transmission to pregnancy women through embryo transfer thus far, there theoretically remains a possibility of such occurrence (Barnes et al. 2014; Marques, Guerreiro & Soares 2015). In Australia, it is recommended that only cryopreserved embryos should be transferred to gestational surrogates, to avoid the potential risk of infectious

disease transmission (Wang et al. 2016). Additionally, the policy of quarantine to protect gestational surrogates from HIV is also in place in the UK (Brinsden 2003). Under UK law, the donor sperm must be frozen and quarantined for six months before it can be used to create fresh embryos for transfer to gestational surrogates (Brinsden 2003). Supporting the protection of women at risk, and in relation to this study's findings, it is essential that women contemplating surrogacy are fully informed of potential health risks and that there are standard guidelines regarding practice, including single embryo transfer.

During the surrogacy process, this study additionally found a degree of risk experience for those gestational surrogates who had to travel abroad for embryo transfer and baby delivery. The Thai women involved had to sign a contract to deliver the baby in the intended parent's country and had to travel abroad from 28 gestational weeks as per the commercial surrogacy protocol. Although most international flights restrict travel from 32 gestational weeks, travelling in the third trimester of pregnancy (from week 28) has been reported to increase the risk of miscarriage and preterm delivery (Hezelgrave et al. 2011; RANZCOG n.d.). Flying while pregnant is also reported to involve significantly greater risk of deep vein thrombosis (DVT), and the risk can remain higher up to two weeks after travel (RANZCOG n.d.). Although this study did not identify any adverse events in relation to gestational surrogates travelling in the third trimester, this issue requires urgent attention, including the formation of international regulations and policies to protect the health of the mother and baby during the surrogacy process.

This study also highlighted the risk factor of financial insecurity among gestational surrogates when there was a failure to deliver. Through the commercial surrogacy process, compensation was paid in instalments until successful delivery. Thus, there was no guarantee that the gestational surrogates would receive the full amount while being unable to perform other paid work to support themselves. This study found that the interviewed Thai women received 15% of the total amount for the process of embryo transfer and a positive pregnancy result. The remainder was then paid via instalments through each trimester of pregnancy until delivery. One of the interviewees experienced pregnancy loss after

eight weeks. She did not receive full compensation for a successful pregnancy and was put at a further financial disadvantage due to the time taken for her recovery after a Dilation and Curettage (D&C) procedure. This outcome not only highlights the financial risk taken during the process of gestational surrogacy, but also the health impact of pregnancy loss.

Although this study highlights gestational surrogates' risk encounters and their unintentional acceptance of risk through their *womb for work* in the surrogacy business model, Jacobson (2016) demonstrated the positive perspectives of gestational surrogates in a commercial from their *'labour of love'.* Even though gestational surrogates could face risks, they valued their work as they enjoyed gestating a baby as it became part of their routine over the pregnancy period (Jacobson 2016), which contrasts with our results that gestating a baby is perceived as a career and an incentive is their motivation.

This qualitative study focused on the health risk profiles of gestational surrogates during the process of gestational surrogacy rather than seeking the live experiences of a phenomenon throughout the gestational surrogacy arrangement. Therefore, the time afforded by in-depth semi-structured interviews was appropriate to gain insight into gestational surrogates' health risk experiences during the process of gestational surrogacy. The results have implications for building a consensus on the practice, guidelines, and possible advances in regulations in commercial surrogacy arrangements. However, this study has a small sample size that requires interpretation with caution. The cohort of 15 Thai gestational surrogates who provided gestational surrogacy services was taken from a single surrogacy agency. Therefore, the findings can only be generalised to the particular surrogacy agency and not to the Thai gestational surrogacy industry in general. The commercial surrogacy practice in this study is also based in Thailand and the period of surrogacy bridges the period before and after the introduction of the 2015 surrogacy regulation; therefore, the insights from this study may not be generalizable to other settings where commercial surrogacy is either legal or to contexts where gestational surrogacy is practiced differently.

4.8 Conclusion

This study found that commercial gestational surrogacy arrangements in Thailand persisted after commercial surrogacy arrangements became illegal in 2015. Transnational surrogacy has emerged in response to the ongoing demand from reproductive tourists, making it imperative to address any excess risks associated with being a commercial surrogate. Women experienced both agency in their 'womb for work' and fear at community "sanction and stigma" of surrogacy. They experienced both financial gain and financial risk on entering surrogacy arrangements, and common practices such as MET placed women at greater risk for adverse health outcomes. It is likely that risk factors will differ and vary in extent in countries where commercial surrogacy is legal. Although the risks affecting gestational surrogates have been identified internationally, those risks have yet to be addressed effectively. There is a need for a (re)consideration of commercial surrogacy arrangements within country and transnationally to ensure a uniform approach to women's health overall. Further research on the drivers and outcomes of reproductive tourism is needed that focuses on intended parents and brokers to ensure transparency and community acceptability; and the agency, safety and autonomy of gestational surrogates.

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4.10 Disclosure Statement

The authors confirm that they have no conflicts of interest in relation to this work.

4.11 References

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Chapter 5: Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis

The material of this chapter has been presented at the International Federation of Fertility Societies (IFFS) 2019 World Congress in Shanghai and published in the *Human Fertility* journal, 2020.

List of presentations and publications from this study:

- Attawet, J., Wang, A. Y., Farquhar, C. M., Jordan, V., Li, Z. & Sullivan, E. A. 2020, 'Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangement: a systematic review' [Oral presentation], *The 2019 IFFS World Congress (11–14 April 2019)*, Shanghai, China.
- Attawet, J., Wang, A. Y., Farquhar, C. M., Jordan, V., Li, Z. & Sullivan, E. A. 2020, 'Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangement: a systematic review' [IFFS Abstracts], *Global Reproductive Health World Congress Abstracts*, vol 4, no. 1, p. 55. (Appendix 7).
- Attawet, J., Wang, A. Y., Farquhar, C. M., Jordan, V., Li, Z. & Sullivan, E. A. 2020, 'Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis', *Human Fertility,* vol. 23, no. 2, pp. 1-12, < https://doi.org/10.1080/14647273.2020.1794062>. (Appendix 8)

5.1 Chapter introduction

Chapter 5 addresses the third research question:

- What are the differences in surrogate pregnancy and live birth outcomes between SET and MET among gestational surrogates?

This study is a systematic review and meta-analysis of embryo transfer (SET versus MET) among gestational surrogates. The number of embryo transfer was found being an issue of the surrogacy business model (Chapter 4). Updating evidence of the number of embryo transfer among gestational surrogates is therefore noteworthy for surrogacy practice and guidelines. This chapter serves to provide updated reference of embryo transfer practice among gestational surrogates. The published article commences from the next section.

5.2 Abstract

Introduction: MET is associated with both an increased risk of multiple pregnancy and of live birth. In recent years, MET has become standard practice for most surrogacy arrangements. There has limited review of the use of MET versus SET in surrogacy practice. The present review systematically evaluated the pregnancy outcomes of gestational surrogacy arrangements between MET versus SET among gestational surrogates.

Methods: A systematic search of five computerized databases without restriction to the English language or study type was conducted to evaluate the primary outcomes; clinical pregnancy, live delivery and multiple delivery rates.

Results: The search returned 97 articles, five of which met the inclusion criteria. The results showed that clinical pregnancy (RR = 1.21, 95% CI: 1.06–1.39, n = 5, I^2 = 41%), live delivery (RR = 1.29, 95% CI: 1.10–1.51, n = 4, I^2 = 35%) and multiple delivery rates (RR = 1.42, 95% CI: 6.58–69.73, n = 4, I^2 = 54%) were statistically significantly different in MET compared to SET. Adverse events including miscarriage, preterm birth and low birthweight were found following MET.

Conclusion: Our findings support the existing evidence that MET results in multiple pregnancy and subsequently more adverse outcomes compared to SET. From a public health perspective, SET should be advocated as the preferred treatment for gestational surrogates.

Keywords: assisted reproductive technology; embryo transfer; gestational surrogacy; multiple pregnancy; pregnancy outcomes; surrogacy

5.3 Introduction

Overtime surrogacy arrangements have assisted individuals and couples to have a baby, for a wide range of medical and social reasons (Havins & Dalessio 2000; Larkey 2003). A number of serious medical conditions are listed as criteria for surrogacy arrangements including uterine damage, absent uterus, severe chronic conditions that contraindicate pregnancy such as cancer, repeated failed in vitro fertilization (IVF) attempts and repeated miscarriage (Aittomaki, Eroila & Kajanoja 2001; Dar et al. 2015; Hammarberg, Stafford-Bell & Everingham 2015; Lindenman, Shepard & Pescovitz 1997; Rudrappa & Collins 2015; Söderström-Anttila et al. 2016). Gay couples or single individuals also have the opportunity for a biological child through surrogacy arrangements (Berkowitz 2013; Brinsden et al. 2000; Goldfarb et al. 2000). A surrogacy arrangement is an agreement where a woman offers to carry a fetus and give birth to a child on behalf of another person or couple (Armour 2012; Burrell & Edozien 2014; FIGO committee report 2008; Jadva et al. 2003; Wang et al. 2016). The woman who offers to carry a baby through pregnancy is known as a 'carrier' or 'surrogate' (Armour 2012; Shayestefar & Abedi 2017). The person or couple who intend to become the legal parents and raise the child resulting from surrogacy pregnancy is referred to as 'intended parents' or 'commissioning parents' (Armour 2012; Bhatia et al. 2009; Shenfield et al. 2005). In this review, the term 'surrogate' is used for the woman who is carrying a baby and the term 'intended parents' is used for the intended legal parents.

Gestational surrogacy is where practice involves an ART procedure using the sperm from the intended father or a sperm donor and the egg from the intended mother or an egg donor to create embryos in a

laboratory; these are transferred into the surrogate's uterus (ARSM 2013; Oultram 2015; Perkins et al. 2018). Therefore, the baby born from a gestational surrogacy arrangement could be genetically linked to one, both or neither the intended parents and not genetically related to the surrogate (Brinsden 2003; Frydman 2016). There has been a steady increase of gestational surrogacy practice. Between 1999 and 2013, there were 30,927 gestational surrogate cycles reported in the US (CDC 2016). The most recent reports showed 895 gestational surrogate cycles in Canada in 2017 (CFAS 2016), and 220 gestational surrogate cycles in Australia and New Zealand in 2016 (Fitzgerald et al. 2018).

However, there is very limited information available globally on gestational surrogacy arrangements and associated pregnancy outcomes, in part because surrogacy is prohibited in many countries such as France, Germany, Italy, Spain, Portugal, Bulgaria and Iceland. In contrast, in a number of countries such as Australia, New Zealand, Canada and the UK, altruistic surrogacy arrangements are accepted. (Anderson, Snelling & Tomlins-Jahnke 2012; Armour 2012; Burrell & Edozien 2014; Van Zyl & Walker 2013). Only a few countries such as Australia and New Zealand (NPESU 2018), Canada (CFAS 2018) , Europe (ESHRE 2018), the UK (HFEA 2018) and the US (CDC2018) provide an annual report of gestational surrogacy arrangements.

Tracking from the annual reports of gestational surrogacy arrangements, the high rate of MET among gestational surrogate has been concerned. The annual ART report from the US between 2009 and 2013 indicated that almost 80% of gestational surrogate cycles involved a MET resulting in about 30% multiple births (Perkins et al. 2016). Similarly, White (2016) reported an incidence of about 60% of MET among gestational surrogate cycles between 2001 and 2009 and a resultant 25% multiple births in Canada.

Historically, MET has been believed to yield a higher pregnancy rate than SET (Price 1989). However, the evidence that MET increases the risk of multiple pregnancy and subsequent pregnancy complications as well as adverse perinatal outcomes compared to SET is incontrovertible (Büscher et al. 2000; Cassell, O'connell & Baskett 2004; Duffy et al. 2005; Expert Panel on Infertility and

Adoption 2009; Obiechina et al. 2011; Pingili, Bamigboye & Jegede 2007; Taebi 2014). The recent evidence for autologous cycles shows that two SETs can result in the same chance of a live birth as one MET and, simultaneously, reduce the risk of multiple births (Luisa López Regalado et al. 2014; McLernon et al. 2010; Min, Hughes & Young 2010; Tannus et al. 2016). As a result, SET is now recommended in most high-income countries (CDC 2017; Reproductive Technology Accreditation Committee 2017; Siristatidis & Hamilton 2007). However, the SET recommendation has not been widely accepted or implemented in gestational surrogacy arrangements (Perkins et al. 2016; White 2016, 2017). This is partially explained by the fact that many intended parents would prefer twins rather than a singleton (Ezugwu & Van der Burg 2015; Mendoza et al. 2018).

As SET is not the preferred practice in many countries with surrogacy arrangements, a significantly higher and unacceptable increase in multiple pregnancy rates in surrogate pregnancies is consistently reported from the available national reporting of gestational surrogacy arrangements (Parkinson et al. 1999; Perkins et al. 2016; Serafini 2001; White 2016, 2017; Woo et al. 2017). A systematic review by Söderström-Anttila et al. (2016) showed the rate of multiple pregnancy in surrogacy treatments was as high as 75% regardless of the number of embryos were transferred. The review also showed adverse outcomes including hypertensive disorders, preterm birth and low birthweight consistent with the higher rate of multiple pregnancies than for non- surrogate pregnancies (Söderström-Anttila et al. 2016). Nevertheless, there is a lack of internationally comparable information on the pregnancy and live birth outcomes of SET and MET among gestational surrogates. There is also a lack of evidence to show that MET increases the rate of clinical pregnancy in surrogacy practice since surrogates have proven fertility with their own pregnancy (Rodgers et al. 2014; Wang et al. 2016). This has implications for evaluating current practice and clinical guidelines for gestational surrogacy arrangements.

5.4 Aim

This systematic review aims to provide synthesized evidence on pregnancy and birth outcomes between SET and MET among gestational surrogates.

5.5 Materials and methods

5.5.1 Protocol and registration

The protocol of this systematic review has been registered (PROSPERO ID number: CRD42017084126) in the PROSPERO registry (https://www.crd.york.ac.uk/PROSPERO/).

5.5.2 Search strategy

Searches of electronic databases were conducted May 2019. Databases searches included CINAHL (Ebsco), Medline (Ovid), Embase (Ovid), Scopus and ProQuest. Search terms included surrogacy, surrogates, gestational carriers, gestational surrogacy, surrogate mothers, embryo transfer, double embryo transfer, DET, multiple embryo transfer, single embryo transfer, SET, pregnancy outcome, live births, live delivery, and multiple births. Key terms were also searched for subject terms using MeSH. Studies published from 1980 regardless of language or study type, were accessed. Reference lists of identified studies were manually searched for additional references. National ART reports including ANZARD, CDC, ESHRE, HFEA, CARTR, and Japan Society of Obstetrics and Gynecology (JSOG) were also searched.

5.5.3 Study selection

Inclusion

Studies of any design were included as long as they reported SET and MET among gestational surrogate cycles, the comparison between SET and MET gestational surrogate cycles and the primary outcome measures of clinical pregnancy, live delivery, or multiple delivery between SET and MET. In the case of duplication, the more recently published article was included.

Exclusion

Studies that did not report the number of SET and MET gestational surrogate cycles and no events of primary outcomes in SET and MET gestational surrogate cycles were excluded.

5.5.4 Extraction and quality assessment

COVIDENCE software was used for study selection and data extraction (www.covidence.org 2018). The titles and abstracts of the articles were screened for potential eligibility by JA and AYW. Disagreements regarding study eligibility were solved by discussion and consensus. The full text of the selected articles was evaluated for the level of evidence once all inclusion/exclusion criteria had been verified. Independently, two review authors (JA and AYW) extracted the data. The articles' authors were contacted for additional data. Söderström-Anttila et al. (2002) provided raw data for this review. The NOS was used for quality and risk of bias assessment. Any disagreements of study appraisal were solved by discussion and consensus. The selection process of this review was documented with a PRISMA flow chart.

5.5.5 Outcome measures

The primary outcomes included clinical pregnancy rate, live delivery rate and multiple delivery. Clinical pregnancy was defined as evidence of a gestational sac with or without fetal heart motion, confirmed by ultrasound, at six to eight weeks of gestation. Live delivery was defined as delivery of a live foetus. Multiple delivery was defined as the delivery of two or more babies. Adverse events including miscarriage, preterm birth and low birthweight were also monitored as secondary outcomes. According to the International Committee for Monitoring Assisted Reproductive Technologies (ICMART), miscarriage is defined as the spontaneous loss of a clinical intra-uterine pregnancy prior to 22 completed weeks of gestational age. Preterm birth is defined as a birth that takes place after 22 weeks and before 37 completed weeks of gestational age. Low birthweight is defined as a birth weight less than 2,500 grams (Zegers-Hochschild et al. 2017).

5.5.6 Measures of treatment effect

All outcomes were dichotomous. We calculated Mantel-Haenszel RRs with 95% CIs, using the numbers of event outcomes in SET and MET gestational surrogate cycle groups of each study.

5.5.7 Unit of analysis issues

The primary analysis was by the SET and MET gestational surrogate cycles and the events of primary outcome measures. One SET was compared with one MET regardless of fresh or frozen, cleavage or blastocyst embryo transfer. Data that did not allow for valid analysis (by cycle data) was briefly summarised. Multiple delivery (twins or triplets) were counted as one delivery event. Any adverse events of SET and MET were also briefly described to provide an overall description of the outcomes.

5.5.8 Assessment of heterogeneity

Statistical heterogeneity using the I^2 statistic was assessed by taking a value greater than 50% as indicative of substantial heterogeneity (Higgins & Green 2011).

5.5.9 Data synthesis

Meta-analysis was conducted using RevMan 5 which is endorsed by the Cochrane Collaboration. The data from identified studies comparing outcomes were combined with the number of embryo transfers using a fixed-effects model.

5.5.10 Sensitivity analysis

Sensitivity analysis was performed to examine the stability and robustness of the results to determine the different values of the independent variables' effects on the dependent variables.

5.6 Results

5.6.1 Search result

The PRISMA flow diagram details our search results (Figure 4). The systematic search identified 97 records from databases and manual searches, including 16 duplicate articles. By screening titles and abstracts (n = 81), 70 articles were excluded, as they were out of the scope of the study. A total of 11 full-text articles were assessed for eligibility: six articles were excluded because primary outcome measures and number of embryo transfers in gestational surrogate cycles were not reported. A final number of five cohort studies were included in the systematic review (Coates et al. 2017; Corson et al. 1998; Rodgers et al. 2014; Söderström-Anttila et al. 2002; Wang et al. 2016). Additional data on the number of embryos transferred and pregnancy outcomes were further clarified by contacting the articles' authors. The author, Söderström-Anttila, et al. (2002) provided the additional data for this review. The characteristics of the included studies are given in Table 9. A total of 918 gestational surrogate cycles (898 gestational surrogates) were included. The age of gestational surrogates ranged from 21 through 52 years. Of the 895 cycles with embryo transferred, 432 (48%) were SET and 463 (52%) MET.

Figure 4: PRISMA Flow chart of the literature search and selection process

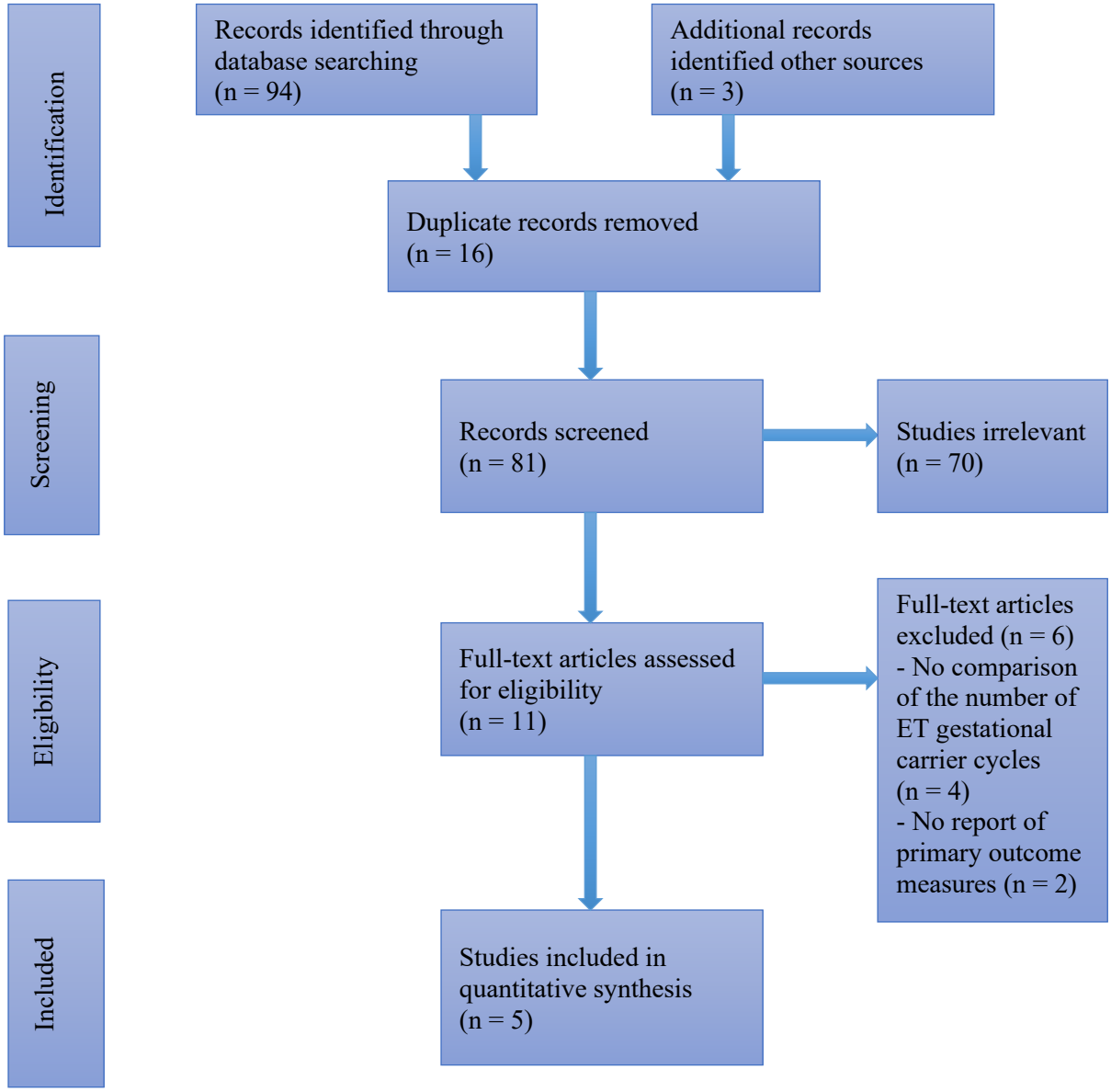


Table 9: Characteristics of included studies

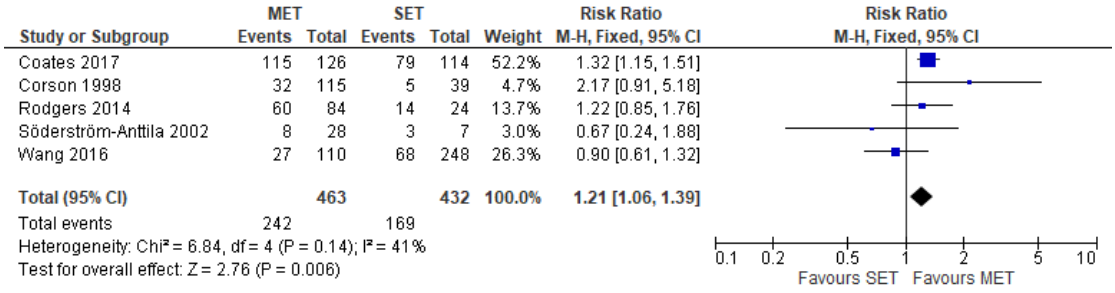
Author	Setting	Method	Gestational surrogate cycles	SET vs MET	Outcome measures	Note
Coates et al. 2017	One center in The United States	Retrospective cohort study	240 surrogate cycles	114 SET 126 DET	Clinical pregnancy Live delivery Multiple delivery	Donor egg frozen ET
Corson et al. 1998	Private IVF program	Retrospective cohort study	144 surrogate cycles	39 SET 115 MET	Clinical pregnancy	Fresh and frozen ET
Rodgers et al. 2014	The United States	Retrospective cohort study	108 surrogate cycles	24 SET 84 DET	Clinical pregnancy Live delivery Multiple delivery	Donor fresh, blastocyst ET Using elective SET
Söderström-Anttila et al. 2002	Family Federation of Finland	Retrospective cohort study	28 surrogate cycles	7 SET 28 MET	Clinical pregnancy Live delivery Multiple delivery	Fresh and frozen ET
Wang et al. 2016	Australia and New Zealand (ANZARD)	Retrospective cohort study	388 surrogate cycles	248 SET 110 DET	Clinical pregnancy Live delivery Multiple delivery	Fresh and frozen ET

5.6.2 Clinical pregnancy rates

Five retrospective cohort studies reported on clinical pregnancy for gestational surrogacy arrangements (Coates et al. 2017; Corson et al. 1998; Rodgers et al. 2014; Söderström-Anttila et al. 2002; Wang et al. 2016). The studies included a total of 432 (48%) SET gestational surrogate cycles and 463 (52%) MET gestational surrogate cycles. Of the 432 SET gestational surrogate cycles, 39% (169) resulted in a clinical pregnancy. Of the 463 MET gestational surrogate cycles, 52% (242)

resulted in a clinical pregnancy. The rate of clinical pregnancy following MET was significantly different from SET (RR = 1.21, 95% CI: 1.06–1.39, n = 5, I^2 = 41%) (Figure 5). A sensitivity analysis was performed by removing the data from one couple in Söderström-Anttila et al. (2002) study. In this study, the data of gestational surrogate cycles, which were from one couple per gestational surrogate, were used for data analysis. The data from one couple who had used two gestational surrogates with a total of eleven cycles were removed for sensitivity analysis as it could influence the dependent variable. The sensitivity analysis resulted consistent with the primary analysis (RR = 1.22, 95% CI: 1.06–1.40, n = 5, I^2 = 33%).

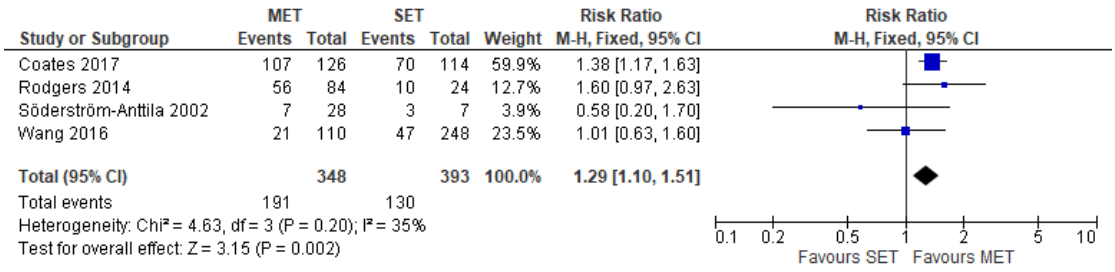
Figure 5: The comparison of clinical pregnancy per gestational surrogate cycle between one SET and MET



5.6.3 Live delivery rates

Four studies reported the outcome of live delivery per cycle per embryo transfer between SET and MET gestational surrogate cycles (Coates et al. 2017; Rodgers et al. 2014; Söderström-Anttila et al. 2002; Wang et al. 2016). One study (Corson et al. 1998) was excluded for meta-analysis for live delivery, as there were no results reporting the number of live delivery events in comparison between the two groups. Of the four studies, SET accounted for 53% (393) of the gestational surrogate cycles, and MET accounted for 47% (348) of the gestational surrogate cycles. The live delivery rate was 33% (130/393) for SET and 55% (191/348) for MET. The live delivery rate was statistically significant difference in MET compared to SET (RR = 1.29, 95% CI: 1.10–1.51, n = 4, I^2 = 35%) (Figure 6). The sensitivity analysis was consistent with primary analysis (RR = 1.30, 95% CI: 1.11–1.53, n = 4, I^2 = 2%).

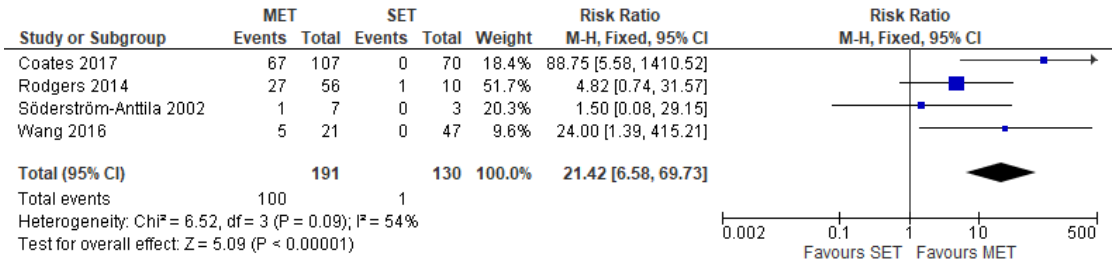
Figure 6: The comparison of live delivery per gestational surrogate cycle between one SET and MET



5.6.4 Multiple delivery

Multiple deliveries were recorded in five retrospective cohort studies (Coates et al. 2017; Corson et al. 1998; Rodgers et al. 2014; Söderström-Anttila et al. 2002; Wang et al. 2016). But only four studies (Coates et al. 2017; Rodgers et al. 2014; Söderström-Anttila et al. 2002; Wang et al. 2016) were included in the Meta-analysis for multiple delivery per live delivery. One excluded study (Corson et al. 1998) did not provide data of live delivery in comparison between the two groups. There were 130 live deliveries following 393 SET and 191 live deliveries following 348 MET. Of the 130 live deliveries in SET, one set of twins was delivered (0.8%). There were 100 (52%) multiple deliveries following the 191 live deliveries in MET. Of the 100 multiple deliveries, there were 99 sets of twins and one set of triplets. There was a statistically significant increased risk of multiple delivery in MET compared to SET (RR = 21.42, 95% CI: 6.58–69.73, n = 4, I^2 = 54%) (Figure 7). The sensitivity analysis was consistent with primary analysis (RR = 21.64, 95% CI: 6.61–70.83, n = 4, I^2 = 52%).

Figure 7: The comparison of multiple delivery per live delivery between one SET and one MET



Additionally, one excluded study (Corson et al. 1998) reported the results of multiple delivery. They found six sets of twins were delivered following 115 MET gestational surrogate cycles, but there were no multiple deliveries following 39 SET gestational surrogate cycles. One of these multiple pregnancies was a selective reduction of triplets to twins.

5.6.5 Adverse outcomes: miscarriage, preterm birth and low birthweight

One study (Söderström-Anttila et al. 2002) reported one miscarriage (1/ 28MET) as a result of placenta insufficiency and disturbance of glucose metabolism in one gestational surrogate following a triple-embryo transfer; there were no reports of adverse events for SET. Corson et al. (1998) also reported one spontaneous abortion and one therapeutic abortion due to abnormal chromosomal complement with no record of the number of embryos that were transferred. Wang et al. (2016) reported preterm births and low birthweights were significantly higher in MET than SET gestational surrogate cycles. They found that 31% of babies (8/26 liveborn babies) were preterm births; 19% of babies (5/26 liveborn babies) had low birthweights following MET gestational surrogate cycles in contrast to SET, which resulted in 13% of babies (6/47 liveborn babies) being preterm births and 11% of babies (5/47 liveborn babies) having low birthweights.

5.7 Discussion

This systematic review reports on the pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements. At the time of this review, there are no reviews which include analyses of SET versus MET in gestational surrogacy arrangements. This review is the first to systematically compare the pregnancy and live birth outcomes of SET and MET among gestational surrogates which is important for evaluating current surrogacy practice and developing surrogacy guidelines and regulations.

The review found that MET is routine practice for gestational surrogates despite being associated with higher rates of adverse outcomes, as previously described in the systematic review by Söderström-

Anttila et al. (2016). As expected, there was a significantly higher multiple delivery rate following MET than following SET, with less than 1% of twins from SET gestational surrogates but 52% of twins coming from MET gestational surrogates. Following this analysis, this review found adverse outcomes including miscarriage (13%), preterm birth (31%) and low birthweight (19%) in MET. This is compared with the perinatal outcomes of preterm birth and low birthweight in SET, which were extremely low at less than 13%. Other risks and complications associated with multiple pregnancy, which were not included in this review, include preeclampsia, premature rupture of membranes, postpartum haemorrhage, and operative delivery (Cassell, O'connell & Baskett 2004; Obiechina et al. 2011; Taebi 2014).

Single embryo transfer has been recommended by FSA, ESHRE, HFEA, ASRM and JOINT SOGC-CFAS for more than ten years. Our review included studies that predated and post-dated the SET guidelines. But many countries including China, the United States, the United Kingdom and some countries in Europe still have slow adoption of SET practice (Farquhar et al. 2019). In some countries such as Australia, New Zealand, the Netherlands, Belgium and Sweden, the SET guideline has been well established with sequel of the lowest multiple pregnancy rates (≤5%) (Farquhar et al. 2019). In the surrogacy context, adhering to the SET guidelines was found lower than 50% in actual practice (White 2018). Research found gestational surrogates still continue to experience a higher level of multiple births than non- surrogates, although the annual ART reports showed the multiple birth level has gradually decreased over the last 10 years (White 2018). In the US, White (2018) found that the level of multiple births among gestational surrogates between 2003 and 2014 decreased from 34% to 26% and among non- surrogates decreased from 25% to 21%. Similarly, the trend of multiple births among gestational surrogates in Canada between 2003 and 2014 decreased from 32% to 15% and from 23% to 13% among non- surrogates (White 2018). It is evident that gestational surrogates are at a higher risk of receiving MET than non-surrogates. There are reports showing gestational surrogates also had 6% and 13% higher relative risks of receiving MET when embryos contained third-party donor ova in the US and Canada, respectively, compared to non-surrogates (White 2018). Hence, there

is no reason that the SET guidelines cannot be regulated in surrogacy arrangements in order to promote equivalence in treatment with gestational surrogates and optimise women's health and perinatal outcomes. However, SET practice guidelines and policies for gestational surrogacy have not been universally adopted and are only in place in Australia, New Zealand, Canada and the UK (Harbottle et al. 2015; Newswire 2017; Reproductive Technology Accreditation Committee 2017).

Two studies (Corson et al. 1998; Söderström-Anttila et al. 2002) predated the SET guidelines and this is reflected in their higher percentages of MET (75% and 80% respectively). Since SET guidelines has been introduced, only one study from Wang et al. (2016) in this review reported a higher proportion of SET (n = 248) than MET (n = 110) among gestational surrogates. However, in this review, studies published after the SET guidelines were introduced report higher proportion of SET (55%) than MET (45%) (Coates et al. 2017; Rodgers et al. 2014; Wang et al. 2016).

MET among gestational surrogates are more likely found in, particularly, commercial surrogacy practice where surrogates agree to carry a pregnancy in exchange for a fee and are incentivized through compensation to carry twins (Hibino & Shimazono 2013; Singha 2016). There is evidence that MET practices reflect the different settings between commercial and altruistic surrogacy arrangements. In the US, where commercial surrogacy arrangements are an active industry, gestational surrogates are 16% more likely to have MET than gestational surrogates in Canada, where only altruistic surrogacy arrangements are allowed (White 2018). The study by Stafford-Bell, Everingham & Hammarberg (2014) reported 70% of MET among gestational surrogates in commercial surrogacy arrangements while another study by Tanderup et al. (2015) also found that MET were seemingly standard practice for paid or commercial gestational surrogates. Commercial surrogacy arrangements in two different settings between the US and Israel were investigated demonstrating that approximately 50% of surrogate babies were born in multiple births, making it significantly evident that MET is a more common practice in commercial surrogacy arrangements (Birenbaum-Carmeli & Montebruno 2019). Contrastingly, the average number of embryo transferred per cycle in altruistic surrogacy arrangements was between 1.8 and 1.9 (Cabra et al. 2018; Söderström-Anttila et al. 2002).

The preferences of having twins by intended parents because of the perceived benefits and efficiencies, and the higher payment to gestational surrogates for carrying twins, are perhaps the main driver of MET in commercial surrogacy arrangements. This implies that economic and financial factors are the motivations for commercial surrogates regardless of the risks involved in multiple pregnancy (Saravanan 2013). Altruistic surrogates, in contrast, feel for the intended parents and are willing to help them create a family (Jadva et al. 2003). Without considering the types of surrogacy arrangements, research found that surrogates use 'love metaphors' to frame their main justification to become gestational surrogates, establishing a long-term relationship with intended parents, rather than establishing a market relationships (Berend 2012). Success for intended parents is taking home a neonate, which is a powerful influencer in treatment and may overshadow the gestational surrogate's voice and love conceptualization.

This may have the unintended consequence of driving fertility treatment practice that finds a spectrum treatment options acceptable. There remains a lack of evidence of what consideration of potential risks is undertaken with the gestational surrogates. Our review is consistent with other studies that found MET resulted in a significant risk of multiple deliveries compared to SET. This risk maybe acceptable to intended parents but iatrogenic multiple pregnancy as a practice at a community level is an unacceptable risk for gestational surrogates. The approach and practice of MET in surrogacy arrangements should be re-considered with a focus on risk minimization fully informing intended parent(s) and gestational surrogates. SET should be standard practice for women using ART. Therefore, SET should be also encouraged in gestational surrogacy practice.

This review had consistency between the results of primary analysis and sensitivity analysis strengthening this review and credibility of the findings. However, not surprisingly the systematic review did not find any randomized controlled trial studies in the search. Only retrospective cohort studies were included in this review. Known and unknown confounders of the five included cohort studies may affect the findings of this study. The small sample sizes of gestational surrogate cycles were used in a meta-analysis to calculate pregnancy and live birth outcomes which could not be

generalized in the large number of cycles. The review compared one SET versus one MET regardless of the quality of embryos. Studies have shown that taking embryo quality of single-embryo fresh and subsequent frozen transfer can result the same chance of live birth rate, when compared to a MET (Luisa López Regalado et al. 2014; Tannus et al. 2016). Therefore, the results of this review should be interpreted with caution and the limitation that we did not have the equivalence of SET cycles that included both a fresh and frozen SET to a MET. The quality and limited number of embryo transfer impacting on the pregnancy and birth outcomes among gestational surrogates are needed for further exploration. Additionally, this review reported live birth rate on a per-cycle basis which may result the inaccuracy of pregnancy outcomes. Further study of gestational surrogate-based measure is therefore recommended to investigate a more accurate estimate of the live birth chance to provide with ongoing treatment to all parties involved in surrogacy arrangements.

5.8 Conclusions

Surrogacy is an integral component of fertility management. SET should be the standard practice for women using ART including for gestational surrogacy practice. This review shows this is not the case with MET in 52% of surrogacy cases. It is not surprising our findings show that METs resulted in higher rates of clinical pregnancy and live delivery compared to SET, as this finding is expected. However, what is of concern is that there persists a lack of equivalence in treatment with surrogates at a population level exposed to MET and an unacceptable level of risk for iatrogenic multiple pregnancy and its potential adverse outcomes for the gestational surrogates. This study urges international regulations of SET in surrogacy practice to minimize the risk to potential gestational surrogates who undergo fertility treatment. Further evaluation of compliance with the SET guidelines in surrogacy practice is needed, including seeking insight into why SET is not internationally regulated for gestational surrogates.

5.9 Acknowledgements

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5.10 Disclosure statement

The authors confirm that they have no conflict of interest in relation to this work.

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Chapter 6: Cumulative live birth rates among Gestational surrogates in altruistic surrogacy arrangements

The material of this chapter has been presented at ESHRE virtual 36th annual meeting and published in the *Human Fertility* journal, 2020.

List of presentations and publications from this study:

- Attawet, J., Wang A. Y., Li, Z., Johnson, L., Hammarberg, K. & Sullivan E. A. 2020, 'Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements' [ESHRE Abstracts], *Human Reproduction*, vol. 35, supp 1, pp. i470-1. (Appendix 9).
- Attawet, J., Wang A. Y., Li, Z., Johnson, L., Hammarberg, K. & Sullivan E. A. 2020, 'Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements' [Poster presentation]. *ESHRE virtual 36th annual meeting (5–8 July 2020)*, Copenhagen, Denmark. (Appendix 10).
- Attawet, J., Wang A. Y., Li, Z., Johnson, L., Hammarberg, K. & Sullivan E. A. 2020, 'Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements', *Human Fertility*, vol. 23, no. 2, pp. 1-9, <https://doi.org/10.1080/14647273.2020.1794062>. (Appendix 11).

6.1 Chapter introduction

Chapter 6 addresses the fourth research question:

- What is the CLBR among gestational surrogates in altruistic surrogacy arrangements?

Chapter 4 and 5 evidently present risks to gestational surrogates, particularly in a commercial form. An alternative arrangement, altruistic surrogacy, is thus needed further study. The fourth study investigated the altruistic surrogacy arrangement using a retrospective cohort study design. Using data collection from VARTA, this study serves to provide new evidence of CLBR among gestational surrogates in an altruistic form demonstrating the effectiveness of the use of altruistic surrogacy arrangements. The publication commences from the next section.

6.2 Abstract

Introduction: Understanding the likelihood of a live birth is important for fertility treatment planning, particularly when one cycle fails and further treatment may be contemplated. This study aims to estimate the chance of live birth among gestational surrogates undergoing altruistic surrogacy arrangements between 2009 and 2016 in Victoria, Australia.

Methods: VARTA data were used. A total of 81 gestational surrogates with 170 embryo transfer cycles were included.

Results: Of the 170 embryo transfer cycles, the majority were SETs (97.1%), using frozen/thawed embryos (97.6%) which had been fertilized by intracytoplasmic sperm injection (ICSI) (77.6%). The CLBR was 23.5% (95% CI, 15.6-33.8%) after the first cycle and increased to 50.6% (95% CI, 40.0-61.2%) after the sixth cycle. Of the 41 deliveries, 40 were singletons and one was a twin delivery. Two of the 42 deliveries were preterm, two were low birthweight and one was small for gestational age.

Conclusion: The findings imply that surrogacy treatment can be offered up to six consecutive embryo transfer cycles to gestational surrogates. SET is encouraged in surrogacy practice to improve perinatal outcomes. These estimates can be used in counselling and decision-making for intended parents and

gestational surrogates to continue a surrogacy treatment, and informing public policy on assisted reproductive technology treatment.

Keywords: Altruistic; Assisted reproductive technology, Cumulative live birth rate; Gestational carrier

6.3 Introduction

ART is the technology used to achieve pregnancy in procedures including gestational surrogacy treatment. Traditionally, the measurement of ART success was reported as pregnancy, delivery and live birth per cycle or per embryo transfer (Adamson et al. 2006; Luke et al. 2012). This cycle-based measure, however, has limited usefulness for patients who want to know both the chance of a live birth after successive failed cycles and whether to continue treatment. The CLBR has been later suggested as the most appropriate way to measure the success of ART (De Neubourg et al. 2016; Maheshwari, McLernon & Bhattacharya 2015; Malizia, Hacker & Penzias 2009; McLernon et al. 2016; Tigges et al. 2016). It is a measure of the chance of a live birth per woman following successive fresh and or frozen embryo transfer cycles. Since the CLBR gives an estimate of the chance of a live birth over time, it provides a realistic indication of ART success and can, therefore, inform patient decision-making about whether to continue treatment (Abuzeid et al. 2014; Luke et al. 2012; McLernon et al. 2016)

Most of the published literature on CLBR is of women undergoing autologous treatment cycles in which women used their own oocytes or embryos in treatment (Abuzeid et al. 2014; Chambers et al. 2017; McLernon et al. 2016; Pouly et al. 2012; Raz et al. 2018; Tigges et al. 2016). Several studies have also reported the CLBR among donor oocyte recipients but to date, no published study has measured the CLBR for gestational surrogacy arrangements (Clua et al. 2012; Doyle et al. 2017; Hogan et al. 2019; Paulson 2014; Paulson et al. 1997; Wang, Farquhar & Sullivan 2011).

Gestational surrogacy is where a woman, known as a gestational surrogate, who has agreed to carry a pregnancy for an intended parent(s) has an embryo transfer with an embryo that is genetically

unrelated to her (ASRM 2013). Intended parents may use their own or donor gametes to create the embryos to be used in gestational surrogacy arrangements. In gestational surrogacy treatment cycles, intended mothers or oocytes donors normally undergo ovarian stimulation while the uterine lining of the gestational surrogate is prepared with exogenous hormones for potential implantation of an embryo. Uterine environment at the time of embryo implantation is therefore an important difference between autologous and gestational surrogacy treatment cycles which could affect pregnancy outcomes (Yeh et al. 2014).

Gestational surrogacy can be altruistic or commercial. In altruistic surrogacy, the gestational surrogate agrees to carry a pregnancy for the intended parent(s) without compensation, beyond reimbursement of medical and other reasonable expenses (Burrell & Edozien 2014). In contrast, in commercial surrogacy arrangements, the gestational surrogate agrees to carry a pregnancy in exchange for a fee (Anderson, Snelling & Tomlins-Jahnke 2012; Armour 2012; Van Zyl & Walker 2013). From the perspectives of intended parents, the gestational surrogates and healthcare providers, understanding the likelihood of a live birth in surrogacy arrangements is crucial, particularly when one cycle fails and further treatment may be contemplated.

6.4 Aim

The aim of this study is to provide evidence-based estimates of the likelihood that a gestational surrogate in altruistic surrogacy arrangement will have a live birth.

6.5 Materials and methods

6.5.1 Data source

A retrospective population-based study was conducted using data, collected by VARTA, of all gestational surrogate cycles in the state of Victoria, Australia, where only altruistic surrogacy arrangements are legal. Data were collected from January 2009 to June 2016. VARTA is a statutory authority funded by the Victoria Department of Health and Human Services to administer aspects of the Assisted Reproductive Treatment Act 2008 (Vic). VARTA provides independent information and

support for individuals, couples and health professionals on fertility and matters related to ART. VARTA's dataset is a census of all initiated ART treatment cycles undertaken in Victoria which is mandatory reporting. The VARTA dataset includes 94 items comprising demographic information on women and their partners, type of ART treatments and procedures (including surrogacy, method of fertilization, and stage of embryo at transfer), number of embryos transferred, pregnancy outcomes (multiple pregnancy) and birth outcomes (live/stillborn, gestational age, birthweight and small for gestational age) (VARTA 2015).

6.5.2 Study population and follow-up

The study population was all gestational surrogates who had at least one embryo transfer cycle for intended parents between January 2009 and June 2016. Data on the clinical outcomes from the first gestational surrogate transfer cycle, until June 2016 or until a live birth was achieved, and data on pregnancy and birth outcomes, up to the end of June 2017, were included in the analyses.

6.5.3 Outcome measures

The primary outcome was the CLBR which was calculated for up to eight cycles. The CLBR was defined as deliveries with at least one live birth per gestational surrogate resulting from the first embryo transfer cycle and subsequent embryo transfer cycles (Zegers-Hochschild et al. 2017). A live birth was defined as a baby born at ≥ 20 weeks gestation and or birthweight ≥ 400 g showing signs of life (Fitzgerald et al. 2018). Multiple births were counted as one live birth.

6.5.4 Statistical analysis

Descriptive statistics were generated (SPSS Statistics 25 Armonk, NY, US: IBM Corp.) to describe demographic, clinical and treatment characteristics for categorical and continuous variable. A life-table was used to calculate the CLBR by dividing accumulative number of live births after successive cycles of treatment, by the total number of gestational surrogates starting treatment. The 95% CIs for CLBR were calculated using the Wilson score methods. Wilson score is an interval estimation of a binomial proportion for small number in that the actual coverage probability is closer to the nominal

value (Brown, Cai & DasGupta 2001). Therefore, it was suggested to use Wilson score interval for this study as it contained the small sample size.

6.5.5 Ethical approval

Ethical approval for this study was granted by the HREC of UTS, Australia (ETH16-0800). Access to the VARTA data was granted by VARTA.

6.6 Results

6.6.1 Demographic and treatment characteristics of the study population

During the study period, 81 gestational surrogates had 170 embryo transfer cycles on behalf of 66 intended parents. The demographics of participants and causes of infertility prompting the use of surrogacy arrangements are shown in Table 10. The median age of intended mothers was 34.5 years. 10.6% of intended mothers were aged ≥ 40 years. Among gestational surrogates, the average age was 37.9 years. 29.6% of gestational surrogates were aged ≥ 40 years. Of the embryo transfers, the majority were single (97.1%), frozen/thawed embryo transfer cycles (97.6%) that had been fertilized using intracytoplasmic sperm injection (ICSI) (77.6%) (Table 11).

Table 10: Demographic characteristic of participants in altruistic surrogacy arrangements in Victoria, Australia between 2009 and 2016 (at the initiate cycle for intended parents and the first ET cycles of gestational surrogates)

Age	Intended parents (N = 66), N	(%)	Gestational surrogate (N = 81), N	(%)
Female age (year)				
Mean (SD)	34.5 (4.7)		37.9 (6.0)	
<25	2	3%	0	0%
25-30	9	13.6%	5	6.2%
30-34	15	22.7%	18	22.2%
35-39	33	50.0%	34	42.0%
40-44	6	9.1%	11	13.6%
≥45	1	1.5%	13	16%
Male partner age (year)				
25-30	8	12.1%	-	
30-34	19	28.8%	-	
35-39	25	37.9%	-	
40-44	8	12.1%	-	
≥45	2	3.0%	-	
Cause of infertility				
Male only	4	6.1%	-	
Female only: tubal disease	1	1.5%	-	
Female only: endometriosis	1	1.5%	-	
Other female factor	7	10.6%	-	
Combine male-female factors	6	9.1%	-	
Unexplained	47	66.7%	-	
Not stated	3	4.5%	-	
Previous pregnancy of ≥ 20 wk				
Yes	10	15.2%		
No	56	84.8%		

Table 11: Number of embryo transfer cycles by treatment type and procedure and stage of embryo development for gestational surrogates

Treatment	Embryo transfer cycles N (%)
Method of fertilisation	
IVF procedure	38 (22.4%)
ICSI procedure	132 (77.6%)
Type of embryos transfer	
Fresh	4 (2.4%)
Thawed	166 (97.6%)
Cryopreservation	
Slow freezing	93 (56.0%)
Vitrification	69 (41.6%)
Unknown	4 (2.4%)
Stage of embryo development	
Cleavage	99 (58.2%)
Blastocyst	71 (41.8%)
Number of embryos transferred	
1	165 (97.1%)
≥2	5 (2.9%)

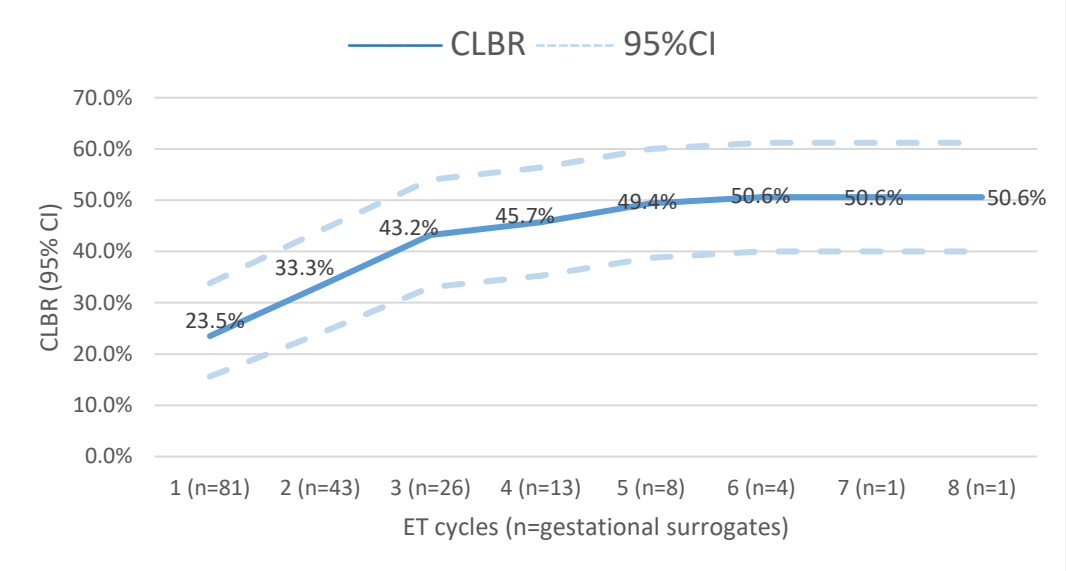
6.2.2 Live Birth Rates

Table 12 shows the number of pregnancies and live births. The 170 embryo transfers over eight cycles among gestational surrogates resulted in 41 deliveries. Of these, 40 were singleton deliveries (97.5%) and one was a twin delivery (2.5%). The only twin delivery followed a multiple embryo transfer. The CLBR among gestational surrogates is shown in Figure 8. The CLBR increased with continuing treatment. After the sixth embryo transfer cycles, the observed CLBR reached 50.6% (95% CI, 40.0-61.2%) with no additional increase in pregnancies or deliveries thereafter.

Table 12: Pregnancy outcomes per cycle and CLBR per gestational surrogate

Treatment cycle	Gestational surrogates N	ET cycles N	Clinical pregnancies N (%)	Live births N (%)	Cumulative live birth rate (95%CI)
1	81	76 (93.8%)	25 (30.9%)	19 (23.5%)	23.5% (15.6-33.8%)
2	43	42 (97.7%)	10 (23.3%)	8 (18.6%)	33.3% (24.0-44.1%)
3	26	25 (96.2%)	11 (42.3%)	8 (30.8%)	43.2% (33.0-54.0%)
4	13	13 (100%)	2 (15.4%)	2 (15.4%)	45.7% (35.3-56.4%)
5	8	8 (100%)	3 (37.5%)	3(37.5%)	49.4% (38.8-60.0%)
6	4	4 (100%)	1 (25%)	1 (25%)	50.6% (40.0-61.2%)
7	1	1 (100%)	0	0	50.6% (40.0-61.2%)
8	1	1 (100%)	0	0	50.6% (40.0-61.2%)

Figure 8: CLBR among gestational surrogates



6.6.3 Perinatal Outcomes following Altruistic Surrogacy Arrangements

Table 13 shows the perinatal outcomes following altruistic surrogacy arrangements. Eighty-one gestational surrogates gave birth to 42 babies with most women (56%) having vaginal births. Of the 42 neonates, seven (16.7%) babies were preterm with 35 (83.3%) term babies. Two (5.0%) babies were of low birthweight (< 2,500 g) and one (2.4%) was small for gestational age (birth weight below the 10th centile for gestational age) (Zegers-Hochschild et al. 2017).

Table 13: Perinatal outcomes following altruistic surrogacy arrangements

Perinatal outcomes	N (%)
Deliveries*	41 (100%)
Caesarean birth	16 (39.0%)
Vaginal birth	23 (56.1%)
Unknown	2 (4.9%)
Number of babies	42 (100%)
Live birth	41 (97.6%)
Stillbirth	1 (2.4%)
Plurality	
Singleton	40 (97.6%)
Twins	1 (2.4%)
Gestational age at the end of pregnancy (weeks)	
34	2 (4.9%)
35	1 (2.4%)
36	3 (7.3%)
37	3 (7.3%)
38	16 (39.0%)
39	7 (17.1%)
40	8 (19.5%)
41	1 (2.4%)
Mean birthweight grams for singletons (SD)	3464.0 (529.2)
Low birthweight for singletons	
Yes	2 (5.0%)
No	34 (85%)
Unknown	4 (10.0%)
Small for gestational age	
Yes	1 (2.4%)
No	40 (97.6%)

* One set of twins refer to one delivery.

6.7 Discussion

This study provides the first population-based estimates of cumulative live births among gestational surrogates following altruistic surrogacy. It shows the CLBR increased to over 50% during the first six cycles of single and frozen-thawed embryo transfers (or FET) among gestational surrogates. In contrast, our findings show that the CLBR following the first cycle (23.5%) was similar to the CLBR using autologous oocytes (22.5% by IVF and 21.7% by ICSI) with both studies using the same VARTA data (Li et al. 2018). Our CLBRs in the first six cycles were also similar to those for autologous oocytes (22.9% for the first cycle and 47.0% for the sixth cycle) as detailed in the annual national Australian and New Zealand report on ART (Newman et al. 2019). It shows that CLBRs are sustained or higher in gestational surrogate cycles compared to autologous cycles. These novel findings can assist intended parents, gestational surrogates and healthcare providers to make informed decisions about initiating and continuing gestational surrogacy treatment.

Cycle-based studies, which report the outcomes per cycle or per embryo transfer, have shown the success rates of pregnancy and live birth outcomes following gestational surrogate cycles (Perkins et al. 2016; Söderström-Anttila et al. 2016; Wang et al. 2016). The live birth rate has ranged from 19% to over 80% following MET and from 19% to 60% following SET cycles among gestational surrogates (Coates et al. 2017; Rodgers et al. 2014; Wang et al. 2016). To date, there is no evaluation of the CLBR following gestational surrogate cycles.

The findings from our study add, significantly, to the body of evidence evaluating the CLBR of gestational surrogates, particularly for altruistic surrogacy in the setting of Victoria, Australia. Surrogacy practice and policy vary between countries. In Australia, only altruistic surrogacy is permitted (Hammarberg, Johnson & Petrillo 2011). Gestational surrogates are not covered by health care insurance and not allowed to receive any payment or reward other than medical bills and reasonable expenses which are covered by the intended parents (*Parentage Act 2004* ; *Surrogacy Act 2010 No 102* ; VARTA 2019). Practice guidelines for the SET of frozen-thawed embryos and policies

for gestational surrogacy are also in place in Australia (Reproductive Technology Accreditation Committee 2017). Overall, SET practice has been adopted as the preferred ART practice, increasing from 73.2% in 2012 to 89.4% in 2017 (Newman et al. 2019). This has led to a decrease in ART-related multiple births, from 6.5% in 2012 to 3.6% in 2017 (Fitzgerald et al. 2018; Newman et al. 2019). In our study, all, but only 2.9% embryo transfer, were of a single embryo. Importantly, it shows that SET is routine practice in surrogacy arrangements in this present study, with a resultant low rate of multiple birth as low as 2.4%. This contrasts with practice in the US, where commercial surrogacy is legal indicating almost 80% of gestational surrogate cycles between 2009 and 2013 involved MET, which was associated with about a 30% rate of multiple births (Perkins et al. 2016). These data show that MET, and its associated greater risks for gestational surrogates and offspring, could be much more common in commercial than in altruistic surrogacy arrangements. Future research should investigate the immediate and longterm health and economic implications for gestational surrogates and children born as a result of surrogacy arrangements.

It is a legislative requirement for altruistic surrogacy practice in Australia that gestational surrogates be aged at least 25 years and have previously carried a pregnancy and given birth to a live child (*Assisted Reproductive Treatment Act 2008* ; *Surrogacy Act 2008* ; *Surrogacy Act 2010* ; *Surrogacy Act 2010 No 102* ; *Surrogacy Act 2012* ; Sattaburuth 2015). As a consequence, women entering into surrogacy arrangements are, on average, older than gestational surrogates in studies which involve commercial surrogacy arrangements (Hibino & Shimazono 2013; Singha 2016). In commercial surrogacy arrangements, most gestational surrogates are reported to be aged 21 to 37 years (Cohen 2014; Hibino & Shimazono 2013; Singha 2016). Almost 60% of gestational surrogates in the US were younger than 35 years (Perkins et al. 2016). In contrast, four out of ten gestational surrogates in our study were aged between 35 and 39 years and more than one quarter were aged 40 years or more. While older maternal age is associated with lower CLBR among women using their own oocytes (Abuzeid et al. 2014; Chambers et al. 2017; Malizia, Hacker & Penzias 2009; Raz et al. 2018), advanced age among oocyte recipients or gestational surrogates does not appear to affect the chance of

a live birth (Hogan et al. 2019; Luke et al. 2012; Smith et al. 2015; Witsenburg et al. 2005). A high CLBR as 50.6% was also evident in our study. This suggests that the older age of gestational surrogates in altruistic, compared to commercial, surrogacy is unlikely to reduce the chance of a successful outcome. In our study, age group specific CLBRs were not generated due to the instability of the small population size. Further research is warranted to determine cumulative live birth success rates by age to inform health promotion and education programs.

Surrogacy remains extremely rare. Therefore observational studies, particularly on altruistic surrogacy are critical to developing evidence on treatment and pregnancy outcomes. A strength of this study is that it is population based with mandatory reporting resulting in full ascertainment of altruistic surrogacy in Victoria, a state of approximately 6.6 million (Australian Bureau of Statistics 2019). This study has some limitations, which need to be considered in the interpretation of the results. Firstly, although this population-based study included data on all gestational surrogacy arrangements in Victoria over an eight year period, the sample size is relatively small. There are a number of possible reasons for the discontinuation of treatment in gestational surrogates who have not achieved pregnancy and a live birth, which are not available from the VARTA registry. These include psychological reasons, familial relationship problems, potential financial burden and physical demands of treatment, which should all be taken into consideration in the interpretation of the CLBR (Chambers et al. 2017; Gameiro et al. 2012; Raz et al. 2018). Additionally, the variation in cycle specific rates should be interpreted with caution due to small number of gestational surrogates after second embryo transfers.

Our study was conducted in a setting where only altruistic surrogacy is legal, and thus the findings may not be generalisable to settings where commercial surrogacy is undertaken. However, the findings of this study could contribute to the evidence base across Australia and others countries where provide altruistic surrogacy arrangements. Data on whether intended parents used their own or donor gametes, and the relationship of this to resultant live births were not available in the data set. Hence, it is not known whether this influenced the CLBR. The data of live birth rates per intended parent and per

started cycle in intended parents following SET would also be useful information for surrogacy parties, but this study had limited data to analyse. Finally, the live birth rate in this study (23.5%) may be considered poor when compared to other countries such as India, where the advertised successful live birth rate of IVF is as high as 80% (Dynamic Fertility & IVF Centre n.d.). It is important to note that when this study was conducted, it was common practice in IVF to use embryo cleavage stage (58.2%) with the slow freezing technique (56%), which was claimed as a successful method and became widely used in ART following Whittingham et al.'s report of the first successful live offspring after cryopreservation (Son & Tan 2009; Testart, Lassalle & Belaisch-Allart 1986; Trouson & Mohr 1983; Whittingham, Leibo & Mazur 1972; Zeilmaker et al. 1984). The embryo transfer with cleavage stage and slow freezing technique is no longer considered best practice while many experts including the ASRM guideline recommend that the best approach to optimise higher survival and pregnancy rates is blastocyst with vitrification embryo transfer (ARSM and SART 2017; Maggiulli et al. 2019; Nagy, Shapiro & Chang 2020; Son & Tan 2009). Future research is needed to assess the advanced ART technologies in gestational surrogacy arrangements.

6.8 Conclusion

Surrogacy offers women and couples, who for medical or social reasons are unable to carry a pregnancy, the opportunity to become parents. In the present study, we conclude that the chance of delivering live births among gestational surrogates undergoing altruistic surrogacy arrangements is most successful in the first six cycles. This allows healthcare providers to better counsel intended parents and gestational surrogates to consider initiating or continuing altruistic surrogacy treatment. To minimise potential risks to gestational surrogates and offspring, a public health approach of SET is warranted in altruistic surrogacy arrangements.

6.9 Acknowledgement

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6.10 Disclosure statement

The authors thank the Victorian fertility clinics contributing database to VARTA.

6.11 References

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Chapter 7: Discussion, Recommendations and Conclusion

7.1 Chapter introduction

This chapter summarises the primary findings of this PhD thesis, describes public health perspectives, and makes recommendations towards improving safe surrogacy practices and preventing harm to gestational surrogates. The strengths and limitations of this PhD thesis and the directions for future research are also outlined herein.

7.2 Discussion

The overarching aim of this research was to investigate the risk encounters of gestational surrogates through their experiences to exemplify the risks involved in commercial surrogacy arrangements in the context of surrogacy practice in Thailand. Although risks to gestational surrogates have been debated extensively in surrogacy practice, including ethical, legal, mental well-being, physical health, and social issues, there has been no specific investigation of risks to Thai gestational surrogates in Thai gestational surrogacy practice where the jurisdiction was actively utilised for commercial surrogacy practice, which was later banned (Hibino 2020; Whittaker 2014). The novel finding of this PhD thesis could reflect the business of surrogacy practice and risk experiences of gestational surrogates, especially in the commercial surrogacy arrangement, which is now banned in the country. The overall findings of the three related studies (Chapters 4–6) provide an insight into the risks that gestational surrogates face during the process of surrogacy arrangements, particularly commercial surrogacy, linking existing and newly created knowledge to further develop guidelines for safe surrogacy practice. The findings of each study answered different research questions as laid down in Chapters 4–6, and the key findings are summarised below to aid the development of surrogacy practices, policies, and regulations to prevent harm to gestational surrogates and improve pregnancy and live birth outcomes.

7.2.1 Womb for work

The theme ‘womb for work’ answered the first question: What are the risks encountered by gestational surrogates in the process of gestational surrogacy and the related arrangements in Thailand? (Chapter 4). Thailand banned commercial surrogacy practice in 2015 (Hibino 2020), and the ban was imposed on all parties involved in commercial surrogacy arrangements. It is, therefore, illegal for Thai women to engage in commercial surrogacy arrangements as gestational surrogates, as well as for anyone else involved, including foreigners seeking commercial surrogacy arrangements in Thailand (Stasi 2017). However, there is no specification attached to the compensation that gestational surrogates receive through the surrogacy process. This makes the commercial surrogacy arrangement in Thailand extremely flexible, resulting in a manner of commercial surrogacy practice that is accepted on the condition that there is no technical issue with the documents (Hibino 2020). Consequently, the new surrogacy law remains ambiguous for Thai women if they are involved in a transnational commercial arrangement and cross-broader embryo transfer but continue their pregnancy in Thailand. The findings evidence that owing to this loophole, despite the ban, gestational surrogates in a commercial form continue to exist and commercial surrogacy arrangements are active in Thailand, thriving through the business model of a ‘womb for work’. However, the focus of this study was the gestational surrogacy practice and risk experiences of gestational surrogates in Thailand, and thus investigation of the legal issue and actions involved in the process of surrogacy arrangements was beyond the scope of this study.

This study conceptualised the business model of a ‘womb for work’ and identified risks to gestational surrogates emerging through the surrogacy business model. MET and potentially infected embryo transfer with incentives were found to strengthen the surrogacy business model to justify gestational surrogates’ decision of carrying on with ‘womb for work’, despite the risky practices with potential risks to both gestational surrogates and babies. The transnational movement of gestational surrogates from Thailand to other countries for fertility treatment and/or birth was also identified as a means to avoid the violation of Thai surrogacy law, even though this process could bear legal risks to

gestational surrogates domestically and transnationally (Kodama 2017), along with health risks and complications from air travel to the intended parents' countries during the last trimester for delivery (RANZCOG n.d.). The newly conceptualised surrogacy business model reflects the current commercial surrogacy and risky practice and describes the risks for gestational surrogates. The insights gleaned from these findings could add to the issue of commercial surrogacy arrangements in Thailand and help develop policy and regulation around surrogacy practice in the country.

7.2.2 Encapsulated risks through commitment to obligation

The thematic 'encapsulated risks through commitment to obligation' of gestational surrogates further explains the 'womb for work' theme. The findings from Study 1 (Chapter 4) demonstrate the process of commercial surrogacy arrangements in Thailand. Through the process, gestational surrogates' commitment to obligation was developed. Thai gestational surrogates showed respect and a sense of obligation toward the agency/big boss, whom they viewed as a benefactor providing them 'womb for work' jobs. Upon embarking the process of using their 'womb for work', Thai women had to sign a contract with their new employer. Upon signing this agreement, they understood that they had to accommodate the employer without resistance and comply with the expectations regardless of the actual conditions of the contract, which could disempower them and override their autonomy. This perception could be understood within the Thai cultural context. In Thai culture, it is considered respectful to avoid questioning authority figures and people in superior social positions, like healthcare professionals or employers (Pimpa 2012). Therefore, Thai gestational surrogates' commitment to obligation could present as compliance with every single instruction from the agency without asking questions or directly communicating with fertility professionals. Thai culture also emphasizes a non-confrontational attitude toward authority figures (Gunawan 2016). It follows, then, that even though Thai gestational surrogates had the chance to question fertility professionals, they simply opted to listen and comply with all their instructions and those of the surrogacy agency. Failure to seek information including that regarding the risks associated with gestational surrogacy arrangement or clarifications regarding the contract could influence Thai gestational surrogates' understanding of the

risks involved in the surrogacy process and curtail their ability to know and exercise their rights, forcing them to unintentionally accept the risks encapsulated through their commitment to 'womb for work'.

Furthermore, emphasis on a non-confrontational attitude extends to the social aspects of Thai culture. Indeed, a person's values are based on behaviour guided by cultural roles and norms and Thai cultural norms and censure uphold a conservative approach regarding a women's sexual behaviour. These norms reinforce cultural tradition, such as the preservation of women's chastity until their wedding day (Ounjit 2011). Pregnancy outside of wedlock transgresses such norms, and Thai society is thus conflicted with the notion of surrogacy. Therefore, Thai gestational surrogates fear community judgment for unacceptable sexual behaviour, and subsequently tend to isolate themselves from their communities or families, working and living on their own, including throughout the duration of the pregnancy, which is in contrast to India where surrogates were confined to the assigned surrogacy homes (Saravanan 2013). For Thai surrogates, surrogacy damages their social standing, and social devaluation can negatively impact self-esteem and increase the risk of emotional distress (Katz, Joiner & Kwon 2002). Clearly, gestational surrogates' commitment to obligation could encourage their risky attitudes and behaviours during the surrogacy process.

7.2.3 Unsafe MET practice

Following the identification of risky practice of MET in the surrogacy business model, the systematic review and meta-analysis study was conducted to answer the research question: What are the differences in surrogate pregnancy and live birth outcomes between SET and MET among gestational surrogates? (Chapter 5). This study focused on embryo transfer in surrogacy practice to present evidence regarding whether MET is far more beneficial in surrogacy practice, as it has become routine in surrogacy practice and is part of the business surrogacy model as discovered in the first study (Chapter 4). The results yielded supporting evidence that over 50% of gestational surrogates experience MET, and that it has become routine practice in commercial surrogacy arrangements (Attawet et al. 2020). This confirms the results of other studies, which also reported that MET is

common in gestational surrogacy regardless of surrogate's fertility capacity (White 2016, 2018), reflecting a gap between surrogacy practice and embryo transfer guidelines.

Although SET was introduced into practice over a decade ago to improve pregnancy and perinatal outcomes (ARSM and SART 2017), it has not been regulated in gestational surrogacy practice. The study showed that SET practice resulted in less than 1% of multiple births, but multiple births happened 52% of the times following MET. SET practice, therefore, should be encouraged in gestational surrogacy, as MET is considered risky to both the mother and the baby, and is not an acceptable practice at the community level (Norwitz 2005). MET should not be a necessity for gestational surrogates who have proved fertility capacity from having their own children. Such surrogates should be provided the chance of a successful and safe life birth through SET practice (Attawet et al. 2020).

This finding reflects the need for international consensus for SET to be the standard practice for gestational surrogacy in terms of minimising the health risk outcomes for surrogates and their babies. The results of this study may also be a new reference point for fertility professionals, policymakers, and regulators for developing surrogacy practice, guidelines, and regulations internationally.

7.2.4 The success of altruistic surrogacy use and SET practice

After understanding the risk encounters of gestational surrogates and risky practices during the arrangement of commercial surrogacy in Thailand, altruistic surrogacy arrangements are brought into attention as a valid alternative practice to answer the research question: What is the CLBR among gestational surrogates in altruistic surrogacy arrangements? (Chapter 6). The findings of this study were new evidence to estimate the chance of live birth among gestational surrogates involved in altruistic surrogacy with SET practice. It showed that CLBR increased to over 50% during the first six cycles of single and FET among gestational surrogates, which was a higher result, compared to non-surrogates (Li et al. 2018; Newman et al. 2019). The findings of this study insist on the success of SET

practice among gestational surrogates and support the use altruistic over commercial surrogacy practice.

The findings of this PhD thesis reveal that SET practice (using 97.1% of SET and 2.9% of MET) can optimise maternal and perinatal outcomes in surrogacy treatment leading to a low rate of multiple births — as low as 2.4%. The findings also show that the use of gestational (altruistic) surrogate cycles was as effective as the use of non-surrogate cycles. A study by Smith and colleagues in the UK with 156,947 women who received 257,398 IVF ovarian stimulation cycles, showed that the CLBR with a combination of SET and MET practice by the first cycle was 29.5% and it increased up to 65.3% by the sixth cycle (Smith et al. 2015). In comparison, this PhD thesis showed that the CLBR of gestational (altruistic) surrogates with SET practice was 23.5% by the first cycle and continued to increase to 50.6% by the sixth cycle. This signifies that the chance of live birth among altruistic surrogates who received SET was not much different from that for non-surrogates who received SET and MET treatment. These results could help fertility professionals have greater confidence in counselling and promoting the use of altruistic surrogacy and SET practice to parties.

This provides important new knowledge for intending commissioning parties and clinicians regarding the outcome of surrogacy treatment after the first cycle attempt fails. The results suggest that surrogacy treatment can be offered for up to six consecutive embryo transfer cycles to gestational surrogates. These findings provide significant evidence that may help surrogacy parties address important issues or guide their early attempts at surrogacy with some knowledge about the chance of live birth at each cycle attempt while using the safe practice of SET. This study also provides new evidence for policymakers to consider during any update of contemporary treatment recommendations in gestational surrogacy arrangements as well as to support the initiation of a fresh ART treatment for the maximum cycle attempts among a gestational surrogate. Such alterations in policy may prove valuable for promoting and supporting SET practice and altruistic surrogacy arrangement over commercial surrogacy arrangements.

The overall findings of this PhD thesis regarding the risks to gestational surrogates in gestational surrogacy practice in Thailand highlight the risk issues from the conceptualised surrogacy business model. The findings of risks to gestational surrogates also support the existing evidence and lead the way for further studies to provide new evidence demonstrating safe practice and effective pregnancy and live birth outcomes alternatively to commercial surrogacy practice.

7.3 Strengths and limitations of this thesis

The studies from this PhD thesis are the first evidence about commercial gestational surrogacy practice in Thailand and the impact of the business model on the lives of gestational surrogates. They provide population-based evidence of embryo transfer outcomes of SET versus MET and CLBR among gestational surrogates. The results have implications for building a consensus on the practice, guidelines, and possible advances in regulations in commercial surrogacy arrangements. However, the results need to be interpreted with caution, keeping in consideration of a number of limitations. Although the thematic analysis in the qualitative study (Chapter 4) was saturated, the number of women interviewed was considered small. Furthermore, all interview participants were recruited from a single surrogacy agency, which limits the generalisation of the findings to the Thai gestational surrogacy industry. It should be noted that this study used a qualitative descriptive design, which focused only on the gestational surrogates' risk experiences rather than investigating the phenomena's live experiences and feelings as phenomenological qualitative research. Thus, this study was limited to elucidating the gestational surrogates' lived experiences and health risk profiles during the process of gestational surrogacy rather than their experiences and feelings in relation to relinquishing the baby which have been described in previous studies. This study was the first description of the business model and gestational surrogacy arrangements in Thailand and was limited to localised practice. The insights from this study are, therefore, not generalizable to locations where commercial surrogacy is either legalised or where gestational surrogacy is practiced under dissimilar contextual situations. Risk experiences of gestational surrogates were also rooted in Thai culture, which may not be generalizable to gestational surrogates from different cultural backgrounds and countries.

Although new evidence of embryo transfer and outcomes of SET versus MET among gestational surrogates (Chapter 5) was consistent between primary results and sensitivity analysis results, this study involved a small, anonymised participant sample and the researcher was not able to identify known and unknown confounders. Moreover, the data provided for the CLBR analysis among gestational surrogates included all surrogacy arrangements with mandatory reporting in Victoria, Australia (Chapter 6). As this study utilised data from a small sample, and because IVF practices may have changed significantly since the time when this study was conducted, these limitations need to be considered when interpreting the results. Additionally, it is not known whether the limited data of the intended parents or the origin of the oocytes in relationship to live birth influenced CLBR. While this study has provided useful information of CLBR in surrogates following SET, there is limited information of live birth per intended parent and per started cycle after using the SET strategy owing to a lack of available data.

7.4 Recommendations

The purpose of this PhD thesis was to provide recommendations to promote the safe practice of gestational surrogacy and to protect the health outcomes of prospective surrogates. Public health advocacy is required to ensure international consensus on the best practices for surrogacy. Recommendations drawn from the findings of the studies in this PhD thesis are discussed in the following subsections.

7.4.1 Recommendation one: Reconsideration of surrogacy legislation

This recommendation is not intended to critique or judge the current commercial surrogacy legislation in any particular country. It brings together a range of perspectives to consider the risks encountered by gestational surrogates that need to be considered while designing or redesigning surrogacy regulations.

The identification of the risks to gestational surrogates in this PhD thesis confirms that despite the regulatory framework in place in Thailand, women may still be exploited in commercial gestational

surrogacy practice. The model used by commercial operators incentivise the use of MET. In addition, there appear to be financial incentives in place for the transfer of embryos from HIV positive and/or discordant couples. This research revealed that gestational surrogates are transported across borders and often travel overseas in the third trimester of their pregnancy to give birth in the country of residence of the intended parents. These findings indicate that exploitative commercial surrogacy operators may be able to practice despite the current surrogacy practice legislation in Thailand prohibiting such arrangements. This may suggest that the provision of further resources for monitoring compliance to legislation could be helpful in promoting current commercial surrogacy legislation. It also suggests that it may be possible to undertake further regulation of commercial surrogacy to ensure the health and safety of gestational surrogates. The business response to the banning of commercial surrogacy in specific countries has led to the movement of the industry from country to country in Southeast Asia. One of the most persuasive arguments for legalising surrogacy is that making it 'legal' could reduce the complex, unlawful, and unregulated surrogacy black market (Ekberg 2014). However, such a response would only address the legal issues related to commercial surrogacy arrangements rather than the ethical concerns based on the principle of non-maleficence.

Thailand has banned commercial surrogacy and only allows altruistic surrogacy to legally operate in the country. The findings of this thesis aim to help support altruistic surrogacy and inform the development of best practices and regulations in the Thai surrogacy industry to protect surrogates from risk and harm to their health. To prevent the exploitation of commercial surrogacy in Thailand and bring better outcomes for Thai surrogates, it may be pertinent to consider key aspects of surrogacy practice guidelines and regulations from other jurisdictions, including Australia which also only allows altruistic surrogacy. For example, mandating a minimum age limit of 25 years for surrogates could be considered, as this could help prevent very young or vulnerable women, who are not sufficiently mature to undertake the responsibility of pregnancy, from entering surrogacy arrangements (VARTA 2021). Requiring independent legal consultation for surrogates should also be considered so that surrogates can be informed of their rights, without being influenced by other parties

such as intended parents, surrogacy agents, and fertility professionals (NHMRC 2017). Although the new guideline by The Royal Thai College of Obstetricians and Gynaecologists (RTCOG) has been updated to encourage SET and limit the number of embryos being transferred at a time to two, this research found that SET may not yet be usual practice in Thailand (Attawet, Wang & Sullivan 2021; RTCOG 2017; Vutyavanich, Piromlertamorn & Ellis 2011). Mandating of SET practices, therefore, could be considered to minimise obstetric risks for surrogates as well as babies (Harbottle 2015; Practice Committee of the ASRM and the Practice Committee for the SART 2021). Furthermore, this PhD thesis identified the practice of utilising monetary incentives to attract prospective surrogates to participate in situations involving the transfer of infected embryos, such as from intended parents who are HIV positive. Thus, the introduction of legislation to proscribe increased compensation for undertaking risky surrogacies, including those involving transfer of infected embryos, and to mandate quarantining of embryos for six months may also considered as a means to protect surrogates' health and break the chain of the surrogacy business model. Regulating medical and life insurance for surrogates could also be considered as a way to enhance health equality and support for surrogates during pregnancy, and to ensure that they are financially covered for unexpected situations (Swoveland 2013). It is notable that Australia and the UK allow reasonable reimbursements for altruistic surrogates. Such reimbursements may include: covering the cost of loss of earnings, medical expenses, specialised food or supplements, additional child care or help around the house during pregnancy or after birth, maternity clothes, classes or therapies to support pregnancy, travel or accommodation relating to the pregnancy, fertility treatment, reasonable legal and counselling support, cost of making a will or buying life insurance to protect the surrogate's family. In the UK, a fixed sum of approximately 12,000 EUR to 18,000 EUR is in prescribed by relevant regulations (Hope 2020; The *Assisted Reproductive Treatment Regulations 2019*). It has been reported that such compensation of essential reimbursements is satisfactory for both intended parents and surrogates, and promotes the use of altruistic surrogacy in the UK (Mackle 2019; Norton et al. 2015). In Thailand, the development of similar regulations to ensure compensation and essential reimbursements for surrogates may be considered to help safeguard surrogates' rights, to balance out benefits and harms, and to prevent

exploitation in commercial surrogacy (Cooperman 2018; Swoveland 2013; Walker & van Zyl 2017). Policing or legalising gestational surrogacy by adopting these recommendations is expected to support the current altruistic surrogacy law and improve and control the surrogacy process that is legally permissible in Thailand.

7.4.2 Recommendation two: Establishment of health promotion programme for prospective surrogates

This recommendation is drawn from the findings of 'womb for work' experiences to the barriers in seeking further health information. Protecting gestational surrogates from health risks during the process of surrogacy should not only focus on the level of policy and regulation, but also on improving the individual health literacy of the surrogates themselves. Although surrogacy has been possible for over four decades, a discussion about the need for a healthcare programme for prospective surrogates to improve their health-related behaviour and well-being has never been conducted (Goli et al. 2019).

This recommendation borrows from the ecological model of health behaviour, and promotes the development of a health education programme to improve individual factors for surrogates. Education is a strategy for implementing health promotion programmes for the target population (Rural Information Hub 2019). Health education provides the target population with learning experiences on the relevant health topics, including the health benefits they can utilise in situations of any threats. A broad purpose of health education is to increase personal health knowledge and improve and protect personal health by encouraging supportive policies and regulations (WHO 2012). This recommendation argues that it is necessary to establish an education or health promotion programme for prospective surrogates to lay the groundwork for their understanding of health-related facts before entering the process of gestational surrogacy arrangements, as well as to promote their health.

Findings from this PhD thesis regarding risks to gestational surrogates present several considerations to address the gaps in surrogacy practice, especially through a focused health educational programme. In the surrogacy context, the literature shows that surrogates are typically poor, uneducated women,

who are less likely to understand the potential risks involved in the surrogacy arrangement (Darnovsky 2009; Hibino & Shimazono 2013; Singha 2016). However, this PhD thesis did not investigate the gestational surrogate's educational level. Reflecting on the knowledge level, low health literacy could be a barrier to surrogates' ability to access or understand the health information affecting them in terms of the health risks they might encounter. People with limited health literacy are shown to be less likely to ask questions to clinicians and seek further information (Katz et al. 2007; Rutten, Squiers & Hesse 2006), which appears to be the situation faced by gestational surrogate in this thesis finding, apart from their cultural background. Although educational level has been shown to be associated with the pathway of health literacy and health outcomes, the healthcare system should take proactive steps to promote individual health and well-being. Providing appropriately targeted health educational programmes using universal health literacy precautions is an evident strategy to improve people's understanding of health information regardless of their level of literacy or education (Adams 2010; Wittink & Oosterhaven 2018). Health education is, therefore, a programme to build individual health literacy and promote surrogates' empowerment.

Although there are many theories on how to apply pedagogy in education, this recommendation does not discuss the form or approach that the health education of gestational surrogates should adopt. Rather, this recommendation argues the urgent need for a health education programme for prospective surrogates. To date, no healthcare programmes have been available to educate surrogates in Thailand to effectively understand surrogacy treatment and the risks involved. Although information about surrogacy is available on the Internet, some information may not be reliable (Bortolotti 2009). Most of the accessible information comes from the agencies offering surrogacy services for intended parents and recruiting surrogates (Gezinski et al. 2017). Such information is provided with a focus on the benefits of using the services and becoming a surrogate, with a clear lack of information about the risks involved in the surrogacy process (Gezinski et al. 2017). Therefore, information about the risks involved in the surrogacy process should be fully presented in an educational context. Some governmental websites, such as the VARTA website of Australia (VARTA 2019), can be sources of

reliable information, but this information may not be easily accessible or may be of limited use for surrogates who are not residents in that country or whose first language is not that of the website. Customising health promotion collateral from VARTA for use by equivalent bodies in Thailand such as MOPH or RTCOG may be one means of supporting the development of more comprehensive information on a trusted website. The website could provide a fact sheet that provides a complete picture of the gestational surrogacy practice and arrangement to potential surrogates before they make a decision regarding surrogacy. This fact sheet could describe the risks involved in the process, including physical, psychological, modality of delivery, social, financial, and legal risks for surrogates. Information regarding SET practice and transfer of vitrified embryos after a period of quarantine and viral serology testing of intended parents should be also provided for a better understanding of advantages of best practice and ART outcomes.

As education is described as a primary strategy for implementing a health promotion programme, such a programme should be made available for prospective surrogates to improve their health literacy and understanding of the surrogacy process. Research by Garcia, Vassena, Prat & Vernaeve (2016) suggested that face-to-face education is the most effective approach to increase fertility knowledge among young women. This finding could also be utilised in the context of surrogacy after appropriate co-design and piloting. However, it is essential to deliver such a health educational programme formally for all women who are interested in becoming surrogates. This programme should be made available before entering the surrogacy treatment or even before meeting with the surrogacy agency. Such an approach can best ensure the optimal use of the surrogate's autonomy and avoid the influence of interested parties over the surrogate's decision making.

7.4.3 Recommendation three: Regulation of SET practice in surrogacy arrangements

This thesis is the first to engage in a systematic review and meta-analysis of embryo transfer among gestational surrogates and to strengthen the evidence regarding the overuse of MET in surrogate cycles. This recommendation is in line with guidelines from RTCOG which recommend SET for standard practice in ART (RTCOG 2017). It is suggested that it would be beneficial to extend this

practice to those undergoing surrogacy in Thailand. The findings of this PhD thesis showed that 52% of the treatment cycles were MET, which was a routine practice among gestational surrogates (Attawet et al. 2020). SET practice is well known to reduce the rate of multiple birth and associated adverse health outcomes, and is the preferred ART practice internationally. However, in surrogacy practice, SET practice guidelines and policies have not been globally adopted, including in Thailand. SET practices are only in place in Australia, New Zealand, Canada, and the UK (Harbottle et al. 2015; Newswire 2017; Reproductive Technology Accreditation Committee 2017). To provide equitable surrogacy treatment and achieve the goals of protecting surrogates' health and improving babies' health, SET guidelines should be regulated in surrogacy arrangements universally. This recommendation to mandate SET supports the current recommendation of RTCOG and may prove beneficial in protecting Thai surrogates and their babies against health risks, and curb the practice of MET in the commercial surrogacy business model.

An additional benefit to mandating SET in surrogacy arrangements is that such a regulation could help to control situations of financial coercion or transaction of surrogates in the business surrogacy model demonstrated through the findings of this PhD thesis. In ART, technological innovations have been designed to enhance and promote best practices, to optimise the success rate of ART and maximise patient safety by significantly improving the viability and transferability of embryo. Limiting the number of embryo transfer by SET is known to minimise multiple pregnancy. Concurrently with this advancement in IVF, other related technologies have emerged, such as preimplantation genetic testing for aneuploidies (PGT-A), oocyte preservation, and stage of embryo transfer. PGT-A, formerly known as preimplantation genetic screening (PGS), involves the process of testing all 246 chromosomes in an embryo to enable the selection and transfer of chromosomally healthy embryo to improve the chance of achieving a successful pregnancy (Griffin, Thornhill & Ogur 2018). PGT-A is also useful for testing women with multiple prior miscarriages, unsuccessful IVF cycles, or advanced maternal age to improve their chances of a successful pregnancy (Staessen et al. 2008). It has, therefore, been

advocated as an adjuvant approach following SET to select embryo to improve pregnancy and live birth rates (Staessen et al. 2008).

Cryopreservation, the process of freezing and storing embryos between zygote and blastocyst stages, has become a routine process in IVF. It is claimed to further improve the chances of pregnancy, live birth, and cumulative live birth, save embryos in the face of some medical treatments, reduce the cost of IVF or ICSI to shorten the cycle with fresh embryo transfer, reduce the chance of MET over fresh embryo transfer, and allow time for PGT (Ghobara, Gelbaya & Ayeleke 2017; Nagy, Shapiro & Chang 2020). Although there are several good reasons to cryopreserve embryos, critics argue that freezing embryos can lead to the formation of ice crystals and harm the small structures inside the cell, which could affect the survival rate of the embryo and reduce pregnancy and live birth rates (Insogna et al. 2021; Nagy, Shapiro & Chang 2020). For example, Insogna and colleagues reported that for women undergoing ART using freshly retrieved donor oocytes, fresh embryo transfer resulted in a higher live birth rate compared to cryopreserved-thawed embryo transfer (56.6% vs 44%) (Insogna et al. 2021). However, in the context of surrogacy, cryopreservation is more beneficial for surrogates, as it could minimise the risk of infection transmission.

Focusing on cryopreservation, ART technology has developed to improve the freezing technique of embryos to optimise the chance of embryo survival and live birth. Slow freezing and vitrification approaches have been introduced and investigated. Many studies have compared slow freezing and vitrification and found better results from the vitrification technique in terms of survival (post-thaw survival rate of 90–100% after vitrification and 56.9 and 91.2% after slow freezing), implantation, pregnancy, and live birth rates (over 50% pregnancy and live birth rates in vitrification versus almost 50% pregnancy and live birth rates in slow freezing) (Al-Hasani et al. 2007; Jelinkova et al. 2002; Kuwayama et al. 2005; Nagy, Shapiro & Chang 2020; Park et al. 2000; Son & Tan 2009).

Another technique, called the stages of embryo transfer, involves freezing and transfer of embryos, focused upon selecting the best quality embryo. Studies have compared cleavage stage versus

blastocyst stage embryo transfer. Although the blastocyst stage was found to be more favourable than cleavage stage of embryo transfer, and FET of blastocyst resulted in a higher chance of pregnancy and live birth compared to fresh embryo blastocyst transfer, there is no statistical difference between the CLBR in vitrified cleavage-stage and blastocyst-stage embryo transfer (De Vos et al. 2016; Glujovsky et al. 2012; Tammie et al. 2014; Wirleitner et al. 2016). Therefore, other factors in terms of time and cost efficiency and the conditions of the patient and embryo must be taken into account when considering a surrogacy arrangement.

In summary, it is recommended that SET should be mandated in the surrogacy context to optimise ART outcomes and minimise the risks of obstetric complications. Selection of vitrified blastocyst embryo with PGT-A in SET, considered eSET, has been advocated by experts including the ASRM guideline (ARSM and SART 2017; Maggiulli et al. 2019; Nagy, Shapiro & Chang 2020) for its favourable benefits to all parties involved in the surrogacy arrangements as well as for best pregnancy and live birth outcomes.

7.4.4 Recommendation four: Promoting altruistic surrogates

The results of this PhD thesis raise concerns regarding the continued practice of commercial surrogacy arrangements in Thailand. Such arrangements pose greater risks to gestational surrogates than altruistic surrogacy arrangements. As previously mentioned, the aim of this thesis is to advocate for gestational surrogates' health by discussing a range of health risk perspectives relevant to the process of gestational surrogacy arrangements and not to critique or judge legal issues related to commercial surrogacy. This recommendation supports the current ban on commercial surrogacy and advocates for the further promotion of altruistic surrogacy arrangement in Thailand. The promotion of altruistic surrogacy is important, as it sidesteps the ethical issues of exploitation from commercial surrogacy arrangements as detailed in this thesis.

Despite the Thai ban on commercial surrogacy, this PhD thesis shows that the issue of commercial surrogacy still exists in Thailand. To disrupt the existing commercial surrogacy business model, the

promotion of the altruistic surrogate model is recommended as this could be a potential driver to support the commercial surrogacy ban while advocating for the uptaking of altruistic surrogacy. Promoting altruistic surrogates can be achieved by the incorporation of legalising of gestational surrogacy as proposed in recommendations one and three with the health promotion programme suggested in recommendation two. This would require community consultation and support and is subject to cooperation between the government, MOPH and RTCOG. This could divert potential surrogates away from risky, exploitative commercial situations into a safer and better regulated gestational surrogacy system in Thailand. The recommendations that may be worthy of consideration when promoting altruistic surrogates in Thailand is summarised in Table 14.

Table 14: The recommendation to consider when promoting altruistic surrogates in Thailand

Action cooperation		**Expected outcomes**
Government: consider amendments to improve altruistic surrogacy	**Health department:** establish a health promotion programme	**Promotion of altruistic surrogates**
• Age limit at least 25 years • Independent legal advice • SET regulation • Quarantine embryo for six months • Medical and life insurance • Outlaw the risk taken from infected embryo transfer • Compensate pregnancy complications • Compensate essential reimbursements	• Fact sheet • Website • Face to face education • Full information of surrogacy process and risks involved including psychological, physical, modality of delivery, social, financial and legal risks.	• obstruction of the surrogacy business model by increasing the number of women choosing to act as altruistic surrogates and reducing the number of women choosing to act as commercial surrogates. • Prevention of exploitative commercial surrogacy • Prevention of young and vulnerable women from becoming surrogates • Minimised risks to surrogates' health • Increased surrogates' awareness of the process and risk involved in the surrogacy process • Increased surrogates' awareness of their rights • Minimised influence of other parties in surrogates' decision-making • Empowerment of surrogates • Support for surrogates during pregnancy and acceptance in the community

7.5 Directions for future research

Risks to gestational surrogates have not only been studied in this PhD thesis, but have also been investigated and debated in other studies (Jeffrey 2014; Phillips et al. 2019; Söderström-Anttila et al. 2016; Vora 2013). This PhD recommends that gestational surrogates' health can be protected by improving policy measures and the level of regulation as well as by empowering and supporting surrogates (Orfali & Chiappori 2014). Understanding the surrogates' backgrounds including their native societies and communities would help to optimise the promotion of their health and rights in the decision-making and support seeking behaviours during the process of surrogacy arrangements. Further investigation of surrogates' insights from different cultures are, therefore, needed to understand surrogates' perspectives through the surrogacy process which could be an advantage for providing their support and improving surrogacy policies, guidelines, regulations or even health planning programmes.

Not only does the surrogate's own knowledge influence health behaviour and promotion, but also research has found that families and partners also empower the surrogate's decision. For example, in India, the husband is generally dominant over the wife and often persuades her to earn what they think will be easy money (Saxena, Mishra & Malik 2012). Whereas, in Thai culture, the wife's or daughter's social role is more active, and she bears the responsibility towards other family members (Hibino & Shimazono 2013; Teerawichitchainan, Pothisiri & Long 2015), which often brings pressure on these women to find ways of earning more money. In some countries including Thailand, the concept of surrogacy may conflict with the social or community norms, which could affect the daily life of surrogates (Arvidsson et al. 2017; UNICEF Thailand 2015). To move towards a better health perspective for surrogates, support from the community and society are strongly needed. The role of the society in ensuring the health of surrogates still needs to be investigated and addressed.

7.6 Conclusion

Gestational surrogacy arrangements in the business model of commercial surrogacy were found to cause considerable risks to gestational surrogates in Thai gestational surrogacy practice. The process of gestational surrogacy arrangement adds potential legal, health, social and financial risks to gestational surrogates. MET is a common business practice in commercial surrogacy that maximises outcomes for clients while increasing health risks for gestational surrogates. The same was confirmed in this PhD thesis showing significantly high rates of multiple pregnancy in MET, with a higher rate of clinical pregnancy and live delivery than SET. However, the novel findings of this thesis suggest that altruistic surrogacy arrangements with SET are effective with a success rate of over 50% for a live birth chance at a sixth cycle. The findings of this PhD thesis support the use of SET for surrogacy arrangements and the need for a standard international approach to protect the rights and health of intending gestational surrogates by considering the reframing of surrogacy practice guidelines, policies, and regulations.

7.7 References

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Appendices

Appendix 1: Primary studies on surrogacy arrangements and outcomes

Citation	Sample/Setting	Methods	Aim	Findings
Berend 2010	Message board from www.surromomonline.com.	Qualitative online observation.	Exploring surrogates' narrative constructions of pregnancy loss and understanding of technological practice.	Surrogates define loss as the failure to give a baby to the intended parents, which ranges from the failure to conceive to miscarriage and stillbirth. The high expectation of success in ART is a contributing factor to loss. Transferring multiple embryos and early monitoring and testing are believed to maximise results in ART. Surrogates understand reproductive technology is a positive force which could make them vulnerable to loss, yet some still repeat surrogacy treatment.
Birenbaum-Carmeli & Montebruno 2019	Gestational surrogate cycles between 2010 and 2014. (US and Israel)	Quantitative retrospective study. Data collected from CDC-NASS, and the Israeli Parliament's Centre for Research and Information.	Comparing surrogacy outcomes between the US and Israel.	Domestic gestational surrogacy deliveries and infants born were higher in number in Israel than the US, but Israel only allows domestic different-sex couples to use surrogacy arrangements, while the US allows both of domestic and international different- and same-sex couples. Within five years, both settings showed

				increased rates of multiple births, up to 24% in Israel and 30.7% in the US.
Cabra et al. 2018	Includes 135 gestational surrogate cycles, 57 intended parents, and 63 gestational surrogates. (Mexico)	Quantitative retrospective study from the surrogacy program at the Centro de Cirugia Reproductiva y Ginecologia REPROGYN in Villahermosa, Tabasco, Mexico between 2007 and 2016.	Reporting on a gestational surrogacy program in Mexico.	Mexico only allows altruistic surrogacy arrangements. The average number of embryos transferred per cycle was 1.9 among surrogates. The pregnancy rate was 22.2%, and the live birth rate was 18.5%. The live birth rate per intended parent was 33.3%.
Everingham, Stafford-Bell & Hammaberg 2014	Includes 259 Australian intended parents. (Australia)	Quantitative online survey.	Investigating the characteristics of parents and intended parents in relation to planned surrogacy use.	Overseas surrogacy was considered more often than domestic surrogacy. The most common countries used for commercial surrogacy were India and US. Barriers to the use of domestic surrogacy included concerns that surrogates might keep the child (75%), the belief that the process would be complicated and prolonged (68%) and not having anyone to be an altruistic surrogate (61%).
Gezinski et al. 2017	Includes 345 commercial surrogacy websites found using Google, Yahoo and Bing search engines.	Quantitative and qualitative content analysis.	Exploring how the commercial surrogacy market targets intended parents and portrays surrogates on commercial surrogacy websites.	India and Thailand were the primary sources of advertisements for surrogacy services. Websites reassured intended parents that their surrogacy services were world-class and could solve

				their parenthood problem. Surrogates were portrayed as altruistic and conforming to strict gender roles. Websites typically ignored the issue of exploitation, structural inequalities and health risks to the surrogate or foetus.
Hibino & Shimazono 2013	Fifteen prospective surrogates. (Thailand)	Qualitative semi-structured interviews.	Exploring 'message board surrogacy' among prospective surrogates who sought surrogacy arrangements through online message boards.	Women who sought to become surrogates were as young as 24 years old. Their educational backgrounds ranged from elementary school to college. Their motivation for becoming surrogates was mainly financial need combined with various other reasons. Other motivations included compassion for infertile couples, enjoying the experience of pregnancy and merit-making (which is a Buddhist concept for ethics). Participants who had surrogacy experience stated having no attachment to the baby because it lacked their genetics. The process to enter a surrogacy arrangement involved being contacted by either a brokering agency or directly by intended parents after women posted messages on a web board. A payment agreement was then negotiated for singleton or twin delivery. Some

				surrogates agreed to discount the price if the intended parents were not wealthy. What was more important than money was how the intended parents could protect and care for the surrogate, which is what most women expected.
Imrie & Jadva 2014	Thirty-four altruistic surrogates. (UK)	Qualitative semi-structured interviews.	Examining the relationship between surrogates and surrogacy families and assessing surrogates' psychological health.	Most surrogates remained in contact with the children (77%) and mothers (85%). Surrogates felt happy with their level of contact. Over 50% of surrogates reported their motivation as 'wanting to help a childless couple'. Twenty-three per cent of surrogates reported having psychological health problems since becoming a surrogate; however, most showed no psychological problems at the time of data collection. Overall, surrogates had positive experiences with surrogacy arrangements.
Jadva et al. 2003	Thirty-four previous surrogates. (Altruistic surrogacy) (UK)	Qualitative semi-structured interviews.	Examining surrogates' motivations, experiences and psychological health.	A desire to help infertile couples was the main reason women became surrogates. Participants had positive experiences of surrogacy arrangements. No significant psychological health problems were found. Surrogates were happy to hand the baby over when it was time. The

				majority of participants were open about surrogacy arrangements with their families despite receiving negative responses when initially told. The majority of surrogates also disclosed the arrangement to their own children, receiving positive reactions.
Karandikar, Gezinski & Huber 2017	Fifteen commercial surrogates. (Gujarat, India)	Qualitative interviews.	Exploring surrogates' experiences of stress in commercial surrogacy.	Surrogates reported having experiences of physical, psychological and social stress prior, during and after pregnancy. Understanding the complexity of the social and emotional risks among surrogates must be measured.
Murugappan et al. 2018	Includes 24,269 gestational surrogate cycles and 1,313,452 non- gestational surrogate cycles. (US)	Quantitative retrospective study; data collected from 375 SART members and reported to CDC.	Comparing the clinical outcomes of all IVF cycles between gestational surrogate cycles and non-gestational surrogate cycles.	Using gestational surrogate cycles resulted in higher pregnancy and live birth rates across all IVF types when compared to non-surrogate cycles. Twin birth rates were also found to be higher in surrogate cycles.
Peters et al. 2018	Sixty intended parents and 63 gestational surrogates. (Netherlands)	Quantitative retrospective study. Data collected from the VU University Medical Centre	Investigating the 10-year experience of gestational surrogacy in the Netherlands.	Altruistic surrogacy is allowed in the Netherlands. Autologous oocytes were used in gestational surrogacy arrangements. Ninety-three IVF cycles were initiated in 60 intended mothers with 184 SET to 63 gestational surrogates, resulting in pregnancy in 55.9% and live

				births in 36.6%. There were 35 clinical singleton pregnancies and no multiple pregnancies. None of the pregnancies resulted in preterm birth. The caesarean section rate was 8.8%.
Parkinson et al. 1999	Ninety-five surrogates, 88 intended mothers and 24 oocyte donors. (US)	Multimethod. Quantitative-retrospective study of medical records. Qualitative telephone interview.	Investigating perinatal outcomes after IVF surrogacy.	An average of 4.1 +/- 0.1 embryos was transferred to surrogates. Overall, 53.8% of twin pregnancies in IVF surrogacy resulted from the transfer of five embryos. Surrogates carrying multiple pregnancies delivered substantially earlier than they did when carrying singleton infants. Incidence rates of caesarean section, pregnancy-induced hypertension, prematurity and low birthweight infants were higher among surrogates carrying multiples as opposed to singletons.
Pashmi et al. 2010	Fifteen surrogates, 15 intended mothers and 30 non-surrogates. (Isfahan, Iran)	Qualitative analytic-descriptive and causative-comparative type. Structured interview.	Evaluating surrogate mothers' and intended mothers' experiences in Isfahan.	Around 13.3% of surrogates were related to the intended mother, while 46.6% of surrogates were altruistically willing to help intended mothers rather than being motivated by a financial purpose, whereas 40% were first motivated by financial and then altruistic goals. Surrogates and intended mothers indicated they had

				good relationships during the process; however, the intended parents wanted no further relationship after delivery. Both parties were satisfied with the surrogacy arrangements.
Perkins et al. 2016	Gestational surrogate cycles between 1999 and 2013. Non-gestational surrogate cycles between 2009 and 2013. (US)	Quantitative retrospective study: data collected from CDC-NASS.	Investigating gestational surrogacy trends and outcomes in the US.	A total of 2,071,984 ART cycles were performed between 1999 and 2013, of which 30,927 used a gestational surrogate. There were 13,380 deliveries among the gestational surrogate cycles used, of which 64% were singleton and 36% were multiple births. The study found the transfer of two or more embryos was more common among gestational surrogate cycles when compared to non-gestational surrogate cycles (60.4% vs 54.6%). Clinical pregnancy and live birth rates were higher among gestational surrogate cycles using fresh oocytes (both non-donor and donor oocytes) when compared with non-gestational surrogate cycles.
Saravanan 2013	Thirteen surrogates, four intended parents, and two medical practitioners.	Qualitative ethnography. Semi-structured interview.	Examining the manifestations of exploitation in commercial surrogacy.	Asymmetries of capacity were found amongst medical practitioners, intended parents and surrogates. Medical practitioners were found to be the most powerful; intended

	(India)	Discussion. Observation.		parents also wielded power over surrogates, leading surrogates to become vulnerable. The imbalance of power among the parties created exploitation in human relationships and influenced the establishment of surrogacy rules.
Singha 2016 (Thai)	Seventeen commercial surrogates. (Phetchabun, Thailand)	Qualitative ethnography. Interview. Observation.	Examining how the lives of commercial surrogates have been constructed and depicted in the context of ART and high-anxiety maternity in relation to Marxist critical theory.	The study yielded three important findings: 1. Surrogates had less knowledge of ART and surrogacy arrangements. 2. Rhetorical practices and bodily techniques were part of everyday biomedical practices indicating successful pregnancy outcomes, which was meaningful for surrogates. 3. Acting as commercial surrogates can be a good opportunity for them to improve their lives.
Söderström-Anttila et al. 2002	Twenty-eight surrogate IVF cycles in 17 altruistic surrogates. (Finland)	Quantitative retrospective study.	Examining experiences of IVF surrogacy in Finland.	An average of 1.8 fresh and 2.1 frozen/thawed embryos were transferred to surrogates at a time. Eleven pregnancies were achieved with 10 live births (nine singletons and one pair of twins). One miscarriage was reported

				following triplet embryo transfer.
Stafford-Bell, Everingham & Hammaberg 2014	Included 259 Australian intended parents. (Australia)	Quantitative online survey.	Exploring surrogacy outcomes among Australian intended parents who engage in compensated transnational surrogacy.	India and US were the common destinations for surrogacy use for Australian intended parents. The mean number of embryos transferred was 2.9. Eighty-five percent of intended parents reported having at least one child, with 55% reporting that their surrogate had a multiple pregnancy. Forty-five percent of births were premature. Most respondents were planning to disclose the use of surrogacy and egg donation to their child.
Tanderup et al. 2015	Twenty doctors in 18 fertility clinics, five agents from four agencies, and 14 surrogates. (India)	Mixed method study using observations and semi-structured interviews.	Investigating informed consent regarding embryo transfer and foetal reduction decisions in commercial surrogacy arrangements.	Almost no surrogates were really involved in the decisions relating to embryo transfer and foetal reduction. They were unable to explain the risks involved in MET and foetal reduction. Doctors took decisions regarding MET and foetal reduction unilaterally. Intended parents were indirectly involved in the process of making the decision.
Tehran et al. 2014	Eight surrogates.	Qualitative phenomenological study.	Assessing the emotional experiences of surrogates.	Two themes were identified: experiences acquired in pregnancy and consequences of surrogacy. Surrogates

	(Iran)			revealed that although they worried about the baby's health during surrogate pregnancy, they did not feel attached to it. Surrogates were afraid of informing their families, relatives and friends about their surrogate pregnancies. They also worried about their marital relationships as a result of being surrogates. One surrogate experienced complications and ended up hospitalised. Surrogates preferred to keep their pregnancies secret as they were not sure about the religious legitimation and social acceptability thereof. Surrogates hoped that their financial problems would be resolved through surrogacy arrangements.
Wang et al. 2016	Included 169 intended parent cycles and 388 gestational surrogate cycles. Altruistic surrogacy. (Australia)	Quantitative retrospective study. Data collected from ANZARD between 2004 and 2011.	Exploring gestational surrogacy and perinatal outcomes in Australia 2004-2011.	Ninety-one percent of embryo transfers were cryopreserved and 69% were SET. There were no significant differences between pregnancy and live birth rates between SET (27% and 19%) and MET (25% and 19%). Rates of preterm birth and low birthweight were higher following MET (31% and 20%) when compared to SET (13% and 11%).

White 2016	All IVF cycles, including gestational surrogate cycles. (Canada)	Quantitative retrospective study. Data collected from CARTR between 2001 and 2012.	Investigating gestational surrogacy practices and outcomes in Canada.	Eight hundred and three IVF-conceived infants were born to gestational surrogates between 2001 and 2012. The average age of the gestational surrogates was found to be younger (31.7 years) than the average age of intended mothers (38.2 years). Gestational surrogates were found to be at risk of receiving a MET despite their younger age. Higher rates of MET were also found when intended mothers' oocytes were used in gestational surrogates. The rate of multiple births was found to be up to 41% among gestational surrogates by 2009. Although the multiple birth level began to drop in gestational surrogates in 2010, the rate of multiple births was still higher than it was for non-surrogates.
White 2017	All IVF cycles, including gestational surrogate cycles.	Quantitative retrospective study. Descriptive statistics – data collected from CDC-NASS between 2003 and 2014.	Examining embryos transferred to gestational surrogates in the US over a 12-year period (2003–2014).	From 2003 to 2014, gestational surrogates showed consistently higher multiple birth rates (41%–25%) even though other forms of IVF witnessed a decline in multiple births. Gestational surrogates experienced a greater risk of receiving MET compared to other IVF patients (RR = 1.027). The number of embryos

				transferred to gestational surrogates rose with the age of the surrogates and when embryos contain intended mothers' oocytes.
White 2018	All gestational surrogate cycles from 2010 to 2014. (US and Canada)	Quantitative retrospective cohort study. Data collected from CDC, NASS and CARTR	Comparing surrogacy outcomes in two different settings of commercial (US) and altruistic (Canada) surrogacy arrangements.	The trend of multiple births in the US and Canada was similar. Although the level of multiple births among surrogates declined from 2010 to 2014, gestational surrogates continued to have a higher rate of multiple births compared with non-surrogates. However, there was a higher rate of multiple births in the US than in Canada. Overall, gestational surrogates in the US experienced a 7% higher relative risk of receiving MET than Canadian gestational surrogates. The results showed that 42% of surrogacy practice in the US adhered to embryo transfer guidelines while 48% did so in Canada.
Woo et al. 2017	Included 124 gestational surrogates. (US)	Quantitative retrospective cohort study. Data collected from two surrogacy agencies in California and the University	Examining perinatal outcomes following surrogate and spontaneous pregnancies in the same gestational surrogates.	One hundred and twenty-four gestational surrogates achieved 494 pregnancies, of which 312 were spontaneous and 182 were surrogate. Of 494 clinical pregnancies, there were 352 single live births: 103 were achieved through surrogate pregnancies and 2499 conceived

	of Southern California Fertility Center.	spontaneously. The result of multiple births was more likely in surrogate pregnancies (33% vs 1%). The lower mean gestational age at delivery was also higher in surrogate pregnancies (38.8 +/- 2.1 vs 39.7 +/- 1.4), with a higher rate of preterm birth (10.7% vs 3.1%) and low birthweight (7.8% vs 2.4%). Surrogate pregnancy also had significantly higher rates of obstetrical complications when compared with spontaneous pregnancies.

Appendix 2: Other peer-reviewed literature about surrogacy arrangements and outcomes

Citation	Article Type	Aim	Conclusion	Notes
Serafini 2001	Report review.	Addressing surrogacy outcomes.	IVF surrogacy resulted in a higher birth rate (37.2%) when compared to conventional IVF. The birthweights for singletons following IVF surrogacy and conventional IVF were similar. Birthweights of multiple births born to IVF surrogates were found to be heavier than those delivered from conventional IVF mothers.	Surrogacy arrangements would provide potentially beneficial outcomes for the infant.
Söderström-Anttila et al. 2016	Systematic review.	Analysing surrogacy outcomes.	The search returned 1795 articles, of which 55 met the inclusion criteria. The results showed that hypertensive disorders in pregnancy and placental complications in IVF surrogacy were similar to conventional IVF. The preterm birth rate in surrogacy singletons varied between 0%–11.5% as compared with 14% for conventional IVF singletons. Low birthweight occurred in between 0% and 11.1% of surrogacy singletons, while it occurred in 13.6%–14% of conventional IVF singletons. However, PTB and LBW rates in multiple births in gestational	

			surrogates were high, from between 30% and 100%. The multiple pregnancy rate among gestational surrogates was found to be as high as 75%. Other assessments like the psychological well-being of children born to surrogates from 1 to 10 years of age were no different when compared to children conceived naturally.	
Brinsden 2003	Literature review.	Reviewing gestational surrogacy.	Clinical pregnancy and live birth rates in IVF surrogacy were equivalent to or better than conventional IVF.	The review also included the patient selection, method of surrogacy arrangements and ethical and legal complications associated with gestational surrogacy.
Duffy et al. 2005	Case study.	Reporting two cases of severe complications in gestational surrogacy pregnancies.	Ten couples with 13 gestational surrogate cycles were analysed. Clinical pregnancy rates were 69%. Two cases of gestational surrogates were reported with placenta accrete and uterine rupture following 3 ET, with hysterectomy as the consequence. One gestational surrogate had multiple pregnancies with one set of triplet infants who died from complications related to prematurity. A second gestational surrogate delivered a singleton with cerebral palsy as a complication.	

Appendix 3: Qualitative study tools

UTS UNIVERSITY OF TECHNOLOGY SYDNEY

1. DISTRESS AND SAFETY PROTOCOL

Research project: Experiences of gestational surrogates in Thailand

The sufficient information regarding the risks and benefits of the research will be provided to participants for their decision to accept or decline participation. The information about counselling services or psychological supports, should it be required, will be also provided to participants prior to the commencement of the interview. Counselling services provided will be according to the suggestion of the Department of Mental Health, Ministry of Public Health which will be upon on the participant's residency. Should participants become distressed during the actual interview, this protocol will be put strictly in place and the following actions will be taken by the interviewer:

1. The researcher will suggest that it is appropriate for the interview be terminated.
2. If the participant show the sign of distress or feeling upset when answering the questions such as silence or halfalogues which can be a sign that things are going awry, the researcher will discontinues the interview process and immediate assess their feeling and safety.
3. The participants will be encouraged to call Mental Health Hotline 1323 immediately which is a free service.
4. The researcher or the representative will also take an action to contact and arrange the service and will be responsible for the fee service if the participant is required further therapy.
5. The participants will be contacted by the next day to ensure their feeling and safety and to determine feasibility of a follow up interview if one wishes.

2. LETTER OF INVITATION TO PARTICIPATE IN A RESEARCH PROJECT

Project Title: Experiences of gestational surrogates in Thailand
Investigator: Jutharat Attawet, Faculty of Health, University of Technology Sydney (UTS)
Supervisors: Associate Professor Alex Wang, Faculty of Health, UTS
Professor Elizabeth Sullivan, Faculty of Health, UTS

We are writing to invite you to participate in the research project, Experiences of gestational surrogates in Thailand. This research project aims to investigate experiences of gestational surrogates in Thailand which is most beneficial to help the healthcare system to provide patients the safe practice and maximise the health advantage to both mother and baby.

The research team are inviting other gestational surrogates to tell us their experiences and treatments about surrogacy arrangements. We would like to invite you to tell us your experience in a one-off interview with a researcher, taking approximately 30 minutes. The interviewed information will not be passed to any organisation or company. This research is for academic purposes and is not connected with the government.

The information people give us in interviews will be used to help the research team to explain the results of the study more fully, and to guide the healthcare system as well as other people in the same position as yourself in relation to the surrogacy treatment. There are no right or wrong answers to this – we are keen to gain a wide variety of opinions. Your decision on whether or not to tell us your experience does not effect your participation in this research project, or the relationships between the researcher or the surrogacy agent. You will be contacted by the local research representative, Ms. Pairin Suwaruksorn for your follow ups if you agree.

Before you decide whether or not you would like to tell us your experience, it is important for you to understand why we are doing this research project and what it would involve for you if you decide to participate. Please take time to read the enclosed information sheet carefully and take time to think about whether or not you would like to take part.

The recruitment of potential participants for this research project will aim at experienced gestational surrogates who age between 20-40 years old, and not currently pregnant. If you meet the criteria and interested to participate, please feel free to contact Ms. Pairin Suwaruksorn directly on +66 [redacted] (same LINE ID) or [redacted]@hotmail.com.

If you have any questions about the research project then please do contact us on +66 [redacted] or [redacted]@hotmail.com or [redacted]@student.uts.edu.au and I will be happy to discuss with you any questions you may have.

Thank you very much for reading this letter,

Yours sincerely,

Jutharat Attawet

UTS UNIVERSITY OF TECHNOLOGY SYDNEY

2. จดหมายเชิญชวนเข้าร่วมในโครงงานวิจัย

โครงงานวิจัย: ประสบการณ์แม่อุ้มบุญในประเทศไทย

นักวิจัย: Jutharat Attawet, Faculty of Health, University of Technology Sydney (UTS)
อาจารย์: Associate Professor Alex Wang, Faculty of Health, UTS
Professor Elizabeth Sullivan, Faculty of Health, UTS

ขอเชิญชวนแม่อุ้มบุญเข้าร่วมโครงงานวิจัย โครงงานวิจัยนี้จัดทำขึ้นเพื่อส่งเสริมพัฒนาระบบการแพทย์ในประเทศไทย การร่วมแชร์ประสบการณ์ของคุณจะเป็นประโยชน์อย่างยิ่งในโครงงานวิจัยนี้

โครงงานวิจัยนี้ได้เชิญชวนแม่อุ้มหลายคนในการเข้าร่วม งานวิจัยนี้จะสัมภาษณ์แม่อุ้มบุญที่ สนใจเข้าร่วมโครงการ โดยการสัมภาษณ์จะใช้เวลา 30 นาที เกี่ยวกับประสบการณ์ตรงของคุณ บทสัมภาษณ์จะถูกนำมาใช้เพื่อประกอบงานวิจัยเพียงเท่านั้น และจะไม่มีการเปิดเผยต่อหน่วย งานใดๆ ทั้งสิ้น

ก่อนที่คุณจะตัดสินใจเข้าร่วมโครงงานวิจัยนี้ เราขอให้คุณอ่านเอกสารที่แนบมาเพื่อความเข้าใจยิ่งขึ้นของการวิจัยนี้ การวิจัยนี้เราต้องการผู้เข้าร่วมที่มีประสบการณ์ตรง และอยู่ในช่วงอายุ 20-40 ปี และไม่กำลังตั้งครรภ์ หากคุณสนใจเข้าร่วมโครงงานเพื่อประโยชน์การพัฒนาทางการแพทย์ คุณสามารถติดต่อ

Ms.Pairin Suwaruksorn โทรศัพท์ +66 [redacted] (LINE ID) หรืออีเมล [redacted]@hotmail.com.ได้โดยตรง

หากคุณมีข้อสงสัยสามารถสอบถามโดยตรงได้ที่ +66 [redacted] หรือ [redacted]@hotmail.com หรือ [redacted]@student.uts.edu.au เรายินดีตอบคำถามคุณทุกข้อ

ด้วยความเคารพ

จุฑารัตน์ อรรถาเวช

Jutharat Attawet

UTS UNIVERSITY OF TECHNOLOGY SYDNEY

3. PARTICIPANT INFORMATION SHEET

PhD project: Experiences of gestational surrogates in Thailand

WHO IS DOING THE RESEARCH?

My name is *Jutharat Attawet* and I am a student at UTS. My supervisors are *Associate Professor Alex Wang and Professor Elizabeth Sullivan*

WHAT IS THIS RESEARCH ABOUT?

This research is to investigate gestational surrogates' experiences in Thailand

WHY HAVE I BEEN ASKED?

You have been invited to participate in this study because you are experienced gestational surrogates, age 20-40 years old and not currently pregnant who can share your experiences regarding surrogacy arrangements. You can directly contact the local research representative for your sharing experiences. Ms. Pairin Suwaruksorn directly on +66 [redacted] (same LINE ID) or [redacted]@hotmail.com.

IF I SAY YES, WHAT WILL IT INVOLVE?

If you decide to participate, I will invite you to *answer questionnaires that will take approximately 20-30 minutes to complete via the telephone. It will be in the format of a semi-structured interview that will be audio recorded and transcribed.*

ARE THERE ANY RISKS/INCONVENIENCE?

Yes, there are some risks/inconvenience that you might be asked sensitive questions.

DO I HAVE TO SAY YES?

Participation in this study is voluntary. It is completely up to you whether or not you decide to take part.

WHAT WILL HAPPEN IF I SAY NO?

If you decide not to participate, it will not affect your relationship with the researchers or the University of Technology Sydney or the organisational agency for infertility arrangements. If you wish to withdraw from the study once it has started, you can do so at any time without having to give a reason, by contacting the, Jutharat Attawet via email [redacted]@student.uts.edu.au. Alternatively, you can contact the local researcher representative, Pairin Suwaruksorn on +66 [redacted] or [redacted]@hotmail.com.

If you withdraw from the study, your recorded interviews and transcripts will be destroyed.
However, it may not be possible to withdraw your data from the study results if these have already had your identifying details removed.

CONFIDENTIALITY

By signing the consent form you consent to the research team collecting and using personal information about you for the research project. All this information will be treated confidentially. All details and records will be kept in the electronic file with locked password. Only the researcher and supervisors can access this file. Your information will only be used for the purpose of this research project.

We would like to store your information for future use in research projects that are an extension of this research project. In all instances your information will be treated confidentially.

We plan to submit the results with your de-identification in the dissertation, which is a part of my degree to the University of Technology Sydney. In any publication, information will be provided in such a way that you cannot be identified.

WHAT IF I HAVE CONCERNS OR A COMPLAINT?

If you have concerns about the research that you think, the local research representative can help you or you can contact the UTS ethic secretaries on research.ethics@uts.edu.au.
You will be given a copy of this form to keep. **Please see the page for translation to Thai language**

Translation to Thai language

ใครทำโครงงานวิจัยนี้?

นางจุฑารัตน์ อรรถาเวช ซึ่งเป็นนักศึกษาของมหาวิยาลัย University of Technology Sydney ภายใต้การดูแลของ รองศาสตราจารย์ Alex Wang และ ศาสตราจารย์ Elizabeth Sullivan

โครงงานวิจัยนี้เกี่ยวกับอะไร?

แม่อุ้มบุญและผลลัพธ์ของการอุ้มบุญในประเทศไทย

ทำไมฉันถึงถูกทาบทามในโครงงานวิจัยนี้?

เนื่องจากโครงงานวิจัยนี้เกี่ยวกับแม่อุ้มบุญและประสบการณ์โดยตรง และคุณอยู่ในช่วงอายุ 20-40 ปีและไม่กำลังตั้งครรภ์ คุณจึงถูกเชิญชวนเพื่อเข้าร่วมในโครงงานวิจัยนี้ คุณสามารถติดต่อ ตัวแทนนักวิจัยได้โดยตรง หากคุณสนใจในการเข้าร่วมโครงงานนี้ Ms. Pairin Suwaruksorn directly on +66 [redacted] (same LINE ID) or [redacted]@hotmail.com.

ถ้าฉันตกลงเข้าร่วมในโครงงานวิจัยนี้ จะเกิดอะไรขึ้น?

นักวิจัยจะโทรสัมภาษณ์คุณเกี่ยวกับประสบการณ์การอุ้มบุญ ซึ่งใช้เวลาประมาณ 20-30 นาที บทสัมภาษณ์จะถูกบันทึกเพื่อนำมาแปลเป็นภาษาอังกฤษ

จะมีความเสี่ยงอะไรไหมจากการเข้าร่วมในโครงงานวิจัยนี้?

อาจจะมีคำถามที่อาจทำให้คุณรู้สึกอ่อนไหวหรือไม่สบายใจในการตอบคำถาม

จำเป็นไหมที่จะต้องเข้าร่วมโครงงานวิจัยนี้?

ทั้งที่คุณอยู่กับความเต็มใจและการตัดสินใจของคุณ

จะเกิดอะไรขึ้นถ้าฉันไม่อยากเข้าร่วมโครงงานวิจัยนี้?

จะไม่มีผลกระทบใดๆทั้งสิ้นเกิดขึ้น คุณสามารถเพิกถอนได้ตลอดเวลาโดยไม่ส่งผลใดๆทั้งสิ้น และข้อมูลทุกอย่างจะถูกทำลายลง คุณสามารถติดต่อนักวิจัยโดยตรงที่ [redacted]@student.uts.edu.au or Pairin Suwaruksorn +66 [redacted] or [redacted]@hotmail.com.

ปลอดภัยและเชื่อถือได้ไหม?

ข้อมูลบทสัมภาษณ์ทุกอย่างจะถูกเก็บไว้อย่างดี ปลอดภัย ไม่เปิดเผยต่อสาธารณะ จุดประสงค์ ในการทำโครงงานวิจัยนี้เป็นส่วนหนึ่งของปริญญาเอกเพื่อใช้ประกอบผลวิทยานิพนธ์ ข้อมูลจะ ไม่มีการเปิดเผยชื่อบุคคลที่แท้จริง

หากฉันกังวลหรือต้องการร้องเรียน?

คุณสามารถติดต่อตัวแทนนักวิจัย Ms. Pairin Suwaruksorn directly on +66 [redacted] (same LINE ID) or [redacted]@hotmail.com. หรือ หน่วยงานจริยธรรม UTS ที่ research.ethics@uts.edu.au.

*โปรดเก็บแผ่นนี้ไว้

UTS UNIVERSITY OF TECHNOLOGY SYDNEY

4. CONSENT FORM

PhD project: Experiences of gestational surrogates in Thailand

I_____agree to participate in the research project "***Experiences of gestational surrogates in Thailand***" Ethic approval number_____being conducted by Jutharat Attawet from University of Technology Sydney, Faculty of Health 15 Broadway, Ultimo NSW 2007, telephone +61 2 95141222.

I have read the Participant Information Sheet, which is attached in Thai language.

I understand the purposes, procedures and risks of the research as described in the Participant Information Sheet.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time without affecting my relationship with the researchers or the University of Technology Sydney.

I understand that I will be given a signed copy of this document to keep.

I agree to be: Audio recorded

I agree that the research data gathered from this project may be published in a form that: Does not identify me in any way and May be used/not used for future research purposes

I am aware that I can contact *Jutharat Attawet, Associate Professor Alex Wang, Professor Elizabeth Sullivan or Pairin Suwaruksorn* if I have any concerns about the research.

_____ ____/____/____

Signature of participant Date

_____ ____/____/____

Signature of researcher/ representative Date

Please see the next page for translation to Thai language before you sign

Translation to Thai language

ใบอนุญาตให้เก็บข้อมูลในโครงงานวิจัยนี้

ดิฉัน_____ยินดีที่จะเข้าร่วมในโครงงานวิจัยนี้ เรื่องแม่อุ้มบุญและ ผลลัพธ์ของการอุ้มบุญในประเทศไทย (Ethical approval number:_____) ของ นักศึกษา จุฑารัตน์ อรรถาเวช จากมหาวิยาลัย University of Technology Sydney คณะสาธารณสุข ที่อยู่ 15 Broadway, Ultimo NSW 2007, โทรศัพท์ +61 2 95141222.

ฉันได้อ่านข้อมูลในการเข้าร่วมโครงงานวิจัยนี้ในฉบับภาษาไทย และเข้าใจดีทุกอย่าง ถึงจุดประสงค์ในการทำโครงงานวิจัยนี้ และยินดีในการเข้าร่วมโครงงานวิจัยนี้ และหากฉันต้องการเพิกถอนสามารถทำได้ตลอดเวลาโดยจะไม่มีผลกระทบใดๆทั้งสิ้น

สำเนาของเอกสารฉบับนี้จะถูกมอบให้ฉันเพื่อเก็บไว้ ฉันยินดีให้อัดบทสัมภาษณ์นี้และใช้เพื่อจุดประสงค์ของการทำวิทยานิพนธ์ โดยไม่ระบุชื่อจริงของดิฉัน

ฉันเข้าใจดีว่าฉันสามารถติดต่อนักวิจัย จุฑารัตน์ อรรถาเวช และทีมวิจัย หรือ คุณไพริน สุวรักษร ได้ตลอดเวลา

_____ _____

ชื่อและลายเซ็นผู้เข้าร่วมโครงงานวิจัย **วันที่**

_____ _____

ชื่อและลายเซนนักวิจัยหรือตัวแทน **วันที่**

INTERVIEW QUESTIONS

1. Getting to know surrogate carriers

Probe: Age of surrogate carriers

Probe: How many times have been a surrogate carrier?

2. Please describe your family background

Probe: what is your marital status?

Probe: How many children do you have?

Probe: Do you want to have any more children?

3. Reasons for your decision to become a surrogate carrier

Probe: Why did you decide to become a surrogate carrier?

Probe: Does anyone know about your decision?

4. What is your surrogacy experience?

Probe: Have you ever been a surrogate carrier before?

Probe: How many IVF attempts (or cycles) did you try in order to achieve a pregnancy?

Probe: How did you cope with your pregnancy?

Probe: What is your experience during and after surrogate pregnancy and relinquishing the child?

Probe: What sort of support system during surrogate pregnancy?

5. What is information received for your surrogacy arrangement?

Probe: the number of embryo transfer, stage of embryo transfer and types of embryo transfer

Probe: Risk of communicable disease and infections during transfers

Probe: Any options for your treatment or can you say NO to the treatment?

Probe: Awareness of risks involved in the process of surrogacy arrangements

6. Are you aware of any complications from surrogate pregnancy?

Probe: What are you feelings on pregnancy with twins or triplets?

Probe: What are you feeling on selective reduction? (Reducing the number of fetuses in a multiple pregnancy)

Probe: Any travel involved in the process and are you aware of any complications during travelling?

Probe: Have you experienced any complication during surrogate pregnancy, such as high blood pressure, diabetes, preeclampsia, preterm birth?

Appendix 4: Abstract publication, conference at ASRM 2020 Scientific Congress & Expo Goes Virtue

CONCLUSIONS: Use of donated embryos can provide a successful means to parenthood, particularly for those with diminished ovarian reserve. In the absence of PGT-A, FET of donated embryo was associated with a high live birth rate. Single embryo transfer should be recommended in order to minimize twin gestations.

P-416 4:30 PM Sunday, October 18, 2020

DOES ELEVATED PROGESTERONE ON DAY OF TRIGGER ASSOCIATE WITH BLASTOCYST PLOIDY IN EGG DONOR CYCLES? Priscilla Caldeira, MD,[1] Aline R. Lorenzon, PhD,[2] Ana Paula Aquino, MD,[3] Bruna Barros, BSc,[3] Eduardo L. A. Motta, MD, PhD,[4] Thais S. Domingues, MD, PhD.[5] [1]School of Medicine - University of São Paulo, Brazil; [2]Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil; [3]Huntington Medicina Reprodutiva, São Paulo, Brazil; [4]Department of Gynecology, Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil; [5]Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OBJECTIVE: Evaluate if high progesterone levels on day of trigger influences blastocyst ploidy and embryo quality parameters in egg donors cycles.

DESIGN: Retrospective cohort study from ICSI cycles using frozen donated oocytes that underwent embryo biopsy at blastocyst stage performed between April/2013 and February/2019 at Huntington Medicina Reprodutiva. Two groups were set according to progesterone (P4) level on day of trigger: group A if P4 <1.5 ng/mL (n=75 cycles: 57 donors – 69 recipients) and group B if P4 ≥1.5 ng/mL (N=184 cycles: 115 donors – 163 recipients).

MATERIALS AND METHODS: Donors were women under 35 years old, with regular menstrual cycles, no gynecological or other health diseases, IMC under 30 Kg/m^2 and normal karyotype. They received standard ovarian stimulation protocol with GnRH antagonist. Clinical parameters such as antral follicular count, FSH basal, total gonadotrophins dose and estradiol (E2) at trigger were analyzed. Number of eggs retrieved, mature oocytes (MII), number of ICSI, fertilization rate, number of blastocysts, number of top quality blastocyst, number of euploid/aneuploid blastocysts, euploid/aneuploid embryo rate and clinical pregnancy were compared between group A and B. T and Fisher tests were used for statistical analysis.

RESULTS: Group A mean age was 25.15±3.59 and group B 24.46±3.73 years old (p=0.19). Total gonadotropins used and basal FSH were not different between group A and B (2777.83±526.02 vs 2814.54±538.78, p=0.7363; 5.19±1.51 vs 5.22±1.47, p=0.3035). Antral follicular count was higher in group B than in A (22.95±10.65 vs 19.60±7.08, p=0.0301) and estradiol at trigger was higher in group A than in B (5255.00±6405.77 vs 5252.83±4346.33 vs, p=0.0340). Number of eggs retrieved, MII and number of ICSI performed were higher in group B than A (33.96±1.76 vs 28.01±11.78, p=0.0014; 24.84±11.74 vs 21.12±10.56, p=0.0082; 8.08±1.74 vs 7.61±1.63, p=0.0025). There were no differences between groups in oocytes post-thaw survival rate, fertilization rate, number of blastocysts and number of top-quality embryos (0.95±0.10 vs 0.98±0.17, p=0.2626; 0.83±0.14 vs 0.82±0.13, p=0.854; 3.60±1.52 vs 3.68±1.52, p=0.6671; 2.27±1.59 vs 2.28±1.43, p=0.8019). The mean of blastocyst biopsied per group were similar (3.15±1.33 versus 3.06±1.29, p=0.6998; n=236 group A and 563 group B). There was no difference between groups when comparing number of euploid embryos and euploid embryo rate (1.92±1.25 vs 1.92±1.13,p=0.9542; 0.31±0.20 vs 0.30±0.18, p=0.6257). Number of aneuploid embryos and aneuploid embryo rate were not different between groups (1.23±1.01 vs 1.14±0.94,p=0.5927; 0.21±0.19 vs 0.18±0.15, p=0.4363). There was no difference in clinical pregnancy rate (0.73 vs 0.82, p= 0.4765). Seminal parameters were similar between groups.

CONCLUSIONS: Our data showed that elevated progesterone levels on trigger's day is not associated with blastocyst aneuploidy rates or worst embryo quality parameters in egg donors cycles, in which the cofounder of maternal age is excluded from the analysis.

P-417 4:30 PM Sunday, October 18, 2020

PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY IN DONOR OOCYTE IVF CYCLES: A MATCHED, SIBLING OOCYTE COHORT STUDY. Devora Aharon, MD,[1] Dmitry Gounko, MA,[2] Joseph A. Lee, BA,[2] Tanmoy Mukherjee, MD,[1] Alan B. Copperman, MD,[1] Lucky Sekhon, MD[2] [1]Icahn School of Medicine at Mount Sinai, New York, NY; [2]Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: The use of preimplantation genetic testing for aneuploidy (PGT-A) has been shown to improve live birth rate per embryo transfer (ET) and reduce pregnancy loss.[1] Whether PGT-A is beneficial in donor oocyte recipient cycles, with lower expected rates of aneuploidy, is less clear.[2-4] A major concern is the possible lower positive predictive value of PGT-A when the technology is used to screen young donor-oocyte derived embryos, which may reduce the number of healthy embryos available for transfer and/or cryopreservation. This study aims to compare the overall IVF cycle efficacy and efficiency in recipients of sibling donor oocytes who did and did not utilize PGT-A.

DESIGN: Retrospective, matched cohort study.

MATERIALS AND METHODS: The study included single embryo transfers in recipients of sibling oocytes from the same donor in which one recipient utilized PGT-A ("PGT-A" group) and the other recipient did not ("unscreened" group) from September 2016 to March 2020. Donors underwent controlled ovarian hyperstimulation and the retrieved oocytes were divided equally among the recipients. PGT-A was performed using Next Generation Sequencing. Baseline characteristics including age, BMI, endometrial thickness, use of donor sperm, fresh vs. frozen embryo transfer, embryo age, and embryo quality were compared between the groups. Outcomes included cycle efficiency, defined as percentage of fertilized oocytes that were transferred and/or cryopreserved, as well as clinical pregnancy, live birth, and pregnancy loss rates. Comparative statistics and linear and logistic regression were used for analysis.

RESULTS: The study included a total of 50 matched pairs, or 100 oocyte recipient cycles. Average oocyte age was 26.5±2.7 years. The groups were similar in terms of recipient age and BMI. The PGT-A group had a significantly lower endometrial thickness, lower rate of donor sperm use, higher proportion of frozen-thawed embryo transfers, and lower proportion of day 5 vs. day 6 embryos transferred compared to the unscreened group. With regards to embryo quality, the PGT-A group had significantly higher expansion grades, similar inner cell mass morphology grade, and a higher proportion of trophectoderm grade B. Cycle efficiency was similar between the groups (60.7±0.2% vs. 56.5±0.2%, p=0.44). On multivariate logistic regression, no significant differences were seen between the PGT-A and unscreened groups in clinical pregnancy rate (OR 0.85, 95% CI 0.26-2.73, p=0.79), live birth rate (OR 1.93, 95% CI 0.51-7.35, p=0.33), or pregnancy loss rate (OR 0.65, 95% 0.11-3.69, p=0.63) when controlling for confounders.

CONCLUSIONS: Our study which utilized a sibling donor oocyte matched model failed to demonstrate alterations in cycle outcome in cases with embryos that had undergone PGT-A. We did not observe a reduced number of embryos available for transfer or cryopreservation, suggesting that the use of PGT-A does not reduce treatment efficiency. Recipients who desire the use of PGT for sex selection or aneuploidy screening can be reassured that this technology is safe and will not reduce the number of embryos available for treatment.

REFERENCES:

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SUPPORT: None

P-418 4:30 PM Sunday, October 18, 2020

UNDERSTANDING SELF-PERCEPTIONS AND RISK EXPERIENCES OF GESTATIONAL SURROGATE MOTHERS IN GESTATIONAL SURROGACY ARRANGEMENTS, THAILAND. Jutharat Attawet, PhD candidate. University of Technology Sydney, Sydney, NSW, Australia.

OBJECTIVE: This study aims to explore gestational surrogate mothers' self-perceptions and risk experiences during the process of gestational surrogacy arrangements in Thailand.

DESIGN: Qualitative descriptive design

MATERIALS AND METHODS: Fifteen Thai women who had gestational surrogacy experience were interviewed by telephone. An approximately 30-minute semi-structured interview was conducted per individual. During the interview, audio tape was used to record the conversation for the purpose of transcription and translation. Thematic analysis was applied to analyze the translated interviews.

RESULTS: 'Womb for work' was an overarching theme for Thai women deciding to become gestational surrogate mothers. Thai women perceived that their wombs could be turned into money and simultaneously assist a childless couple to complete their family. In doing this, Thai women were able to justify the exchange of 'womb for work.' For entry into commercial surrogacy arrangements, Thai women had to sign a contract, which they perceived as outlining their obligations and having to be followed without deviating. Thai women mostly entered the surrogacy process through a surrogacy agency, who they called a 'big boss.' Thai women perceived that the 'big boss' was a powerful person in the surrogacy arrangement, with whose instructions they had to comply during the process of the gestational surrogacy arrangement. The women reported that they mainly communicated with the 'big boss' and obtained surrogacy treatment information from the 'big boss.' Communicating between the Thai women and fertility professionals could be described as a 'triangle communication,' meaning they received surrogacy treatment information from the 'big boss' rather than directly communicating with the fertility professionals. Through the process, it was identified that some details, such as risks associated with multiple or potential infected embryo transfer, or complications of multiple pregnancy, were omitted. According to cultural norms, asking questions of a powerful person, such as the 'big boss' or fertility professionals, was an inappropriate behavior. Consequently, these self-perceptions of being inadequately empowered to ask questions about surrogacy treatment and their own health among the Thai women were creating a barrier to further knowledge about potential health risks involved in gestational surrogacy arrangements. It was therefore found that Thai women had limited understanding and knowledge of potential health risks involved in the process of gestational surrogacy arrangements, which could possibly have contributed to their experiences of making decisions regarding surrogacy treatment and accepting risks unintentionally.

CONCLUSIONS: Self-perceptions were found to be the barrier limiting gestational surrogate mothers from further seeking information from reliable sources—fertility professionals—which affected their understanding of health risks and decision-making in the process of surrogacy treatment.

SUPPORT: N/A

P-419 4:30 PM Sunday, October 18, 2020

SUBJECTIVE PSYCHOLOGICAL FACTORS ASSOCIATED WITH EGG DONORS UNDERGOING ADDITIONAL DONATIONS AFTER THEIR FIRST OOCYTE DONOR CYCLE.

Diane Tober, PhD,[1] Kevin S. Richter, PhD,[2] Shannon Kokjohn, MSc,[3] Christina M. Garibaldi, MS,[4] Raquel Cool, BA,[5] Kezia Mostak, MS,[4] Natalia Villegas, BS,[4] Cris Zubizarreta, BA,[4] Katarina Cook, BS,[4] Said Daneshmand, MD.[3]
[1]UCSF Institute for Health and Aging, San Francisco, CA; [2]Fertility Science Consulting, Silver Spring, MD; [3]San Diego Fertility Center, San Diego, CA; [4]University of California, San Francisco, San Francisco, CA; [5]We Are Egg Donors, Santa Cruz, CA.

OBJECTIVE: To determine psychological factors that influence egg donors' decisions to undergo repeat donation cycles.

DESIGN: Survey.

MATERIALS AND METHODS: Oocyte donors (n=318) in the US were surveyed regarding subjective psychological assessments of their experience as first-time donors, and the subsequent probability that they undergo additional donations after their first. Donors providing eggs to a friend or relative were excluded.

RESULTS: Egg donors were more likely to donate oocytes again if they considered their first experience with donation to be rewarding, if their expectations regarding egg donation were met, if potential short-term and long-term risks of donation were adequately explained by their clinic before treatment, and if they were satisfied with their clinic (Table). Donors who reported feeling regret (53.5% vs 84.8, $p<0.0001$, C^2), fear or anxiety (63.2% vs 87.9%, <0.0001, C^2), depression (61.4 vs 85.9%, <0.0001, C^2), or mood swings (68.3 vs 84.7%, $p=0.0012$, C^2) during or after their first donation were significantly less likely to undergo a second oocyte donation.

Proportion of egg donors choosing to do additional oocyte donations after their first donation, according to their subjective experiences of their first donation rated on a Likert scale, assessed using Kendall's test for significant association

CONCLUSIONS: Oocyte donors reporting comprehensive informed consent and high satisfaction with patient care were more likely to donate again.

SUPPORT: This study was supported by the University of California, San Francisco, Institute for Health and Aging; UCSF Individual Investigator Grant (#7501159); and funding from the National Science Foundation (#1828783).

P-420 4:30 PM Sunday, October 18, 2020

6 YEARS OF DONOR OOCYTE TRANSFERS IN A SINGLE PROGRAM: WHAT HAVE WE LEARNED?.

Alexandra Peyser, M.D., Nicole Noyes, MD, Stephanie R. Brownridge, M.D., Mary Rausch, MD. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Advances in IVF & oocyte cryopreservation technology have allowed for newer modalities in the field of donor oocyte (DE) such as the use of frozen oocytes purchased from banks (COM-O) & genetic testing of resultant embryos. The objective of our study was to analyze our program's DE data over a 6-year period to assess DE usage efficiency & trends over time & whether these changes have positively impacted pregnancy outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: From 2014-2019, our program completed 462 DE transfers in 241 recipients (REC; avg 2-embryo ET/REC) using embryos derived from a total of 163 donors. We analyzed the data for the following: freshly-retrieved oocytes (FRESH-O) vs. COM-O, FRESH-ET (in retrieval or egg-thaw cycle) vs. FROZEN-ET of resultant frozen thawed embryos; SOLE (all oocytes to 1 REC) vs. SHARED (oocytes split between 2 REC) cycles, & usage of PGT-A or not. In addition, donor age & duration of freeze were analyzed. Primary outcome was ongoing pregnancy (>8 wks) + live birth rate (OP/LB). Chi Square was used with significance at $p<.05$.

RESULTS: A total of 368 FRESH-O (80%) and 94 COM-O (20%) were performed. Overall, FRESH-O ETs yielded a significantly higher OP/LB compared to COM-O ETs (44% vs. 30%, p=.01). Within the FRESH-O group, OP/LB was not different when comparing FRESH-ET vs. FROZ-ET (51% vs 41%, p=.08). Within FRESH-ETs, those using FRESH-O had a higher OP/LB compared to COM-O (51% vs. 27%, p=.0007). When comparing SOLE ETs (n= 169; avg # eggs: 17 MII) vs. SHARED ETs (n= 147; avg # eggs: 10 MII), OP/LB rates were 53% vs. 40% (p=.02); of note, 60/75 (80%) SOLE & 28/30 (93%) SHARED donors produced at least 1 OP/LB. The use of PGT-A did not positively impact OP/LB in DE cycles as a whole (p=.9). When excluding PGT-A cycles, SOLE ETs yielded a significantly higher OP/LB than SHARED (59% vs. 40%, p=.002). Length of freeze as well as donor age (21-32y) did not impact OP/LB outcomes (p=.15 and p=.3, respectively).

	Strongly agree	Somewhat agree	Neutral	Somewhat disagree	Strongly disagree	*P*-value
Donation was rewarding	87.1%	76.1%	75.0%	40.0%	40.0%	<0.0001
Expectations were met	88.5%	81.0%	73.3%	72.3%	40.9%	<0.0001
Short-term risks explained	89.0%	77.9%	70.6%	78.0%	64.7%	0.0009
Long-term risks explained	91.7%	87.0%	76.9%	78.3%	70.7%	0.0005
Satisfaction with clinic	90.1%	78.1%	77.3%	65.7%	56.7%	<0.0001

Appendix 5: Poster presentation at ASRM 2020 Scientific Congress & Expo Goes Virtue

Understanding self-perceptions and risk experiences of gestational surrogate mothers in gestational surrogacy arrangements, Thailand

Jutharat Attawet, PhD candidate

Faculty of Health, University of Technology Sydney, Australia

Objectives

1. Explore gestational surrogate mothers' self-perceptions.
2. Explore risk experiences of gestational surrogate mothers during the process of gestational surrogacy arrangements in Thailand.

Materials and Methods

Qualitative descriptive study design:

Fifteen Thai women who had gestational surrogacy experience were interviewed by telephone. An approximately 30-minute semi-structured interview was conducted per individual. During the interview, audio tape was used to record the conversation for the purpose of transcription and translation. Thematic analysis was applied to analyze the translated interviews.

Results

- 'Womb for work' was an overarching theme for Thai women deciding to become gestational surrogate mothers.
- Entry into commercial surrogacy arrangements, Thai women had to sign a contract, which they perceived as outlining their obligations and having to be followed without deviating.
- Thai women called a surrogacy agency as a 'big boss' and perceived that the 'big boss' was a powerful person in the surrogacy arrangement.
- Thai women indirectly communicated to fertility professionals.
- According to cultural norms, asking questions of a powerful person, such as the 'big boss' or fertility professionals, was an inappropriate behavior.
- Thai women had limited understanding and knowledge of potential health risks involved in the process of gestational surrogacy arrangements.
- Unintentionally accepting the risks e.g. multiple embryo transfer

Conclusion

Self-perceptions were found to be the barrier limiting gestational surrogate mothers from further seeking information from reliable sources—fertility professionals—which affected their understanding of health risks and decision-making in the process of surrogacy treatment.

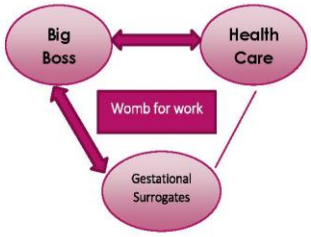

Figure: Illustration of the surrogacy relationship of three parties

Appendix 6: Published article by Human Fertility: 'Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand

HUMAN FERTILITY
https://doi.org/10.1080/14647273.2021.1937716

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ORIGINAL ARTICLE

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'Womb for work' experiences of Thai women and gestational surrogacy practice in Thailand

Jutharat Attawet[a], Alex Wang[a] and Elizabeth Sullivan[a,b]

[a]Faculty of Health, University of Technology Sydney, Ultimo, Australia; [b]College Health, Medicine and Wellbeing, University of Newcastle, Callaghan, Australia

ABSTRACT

Risks to gestational surrogates became a concern for public health. In commercial gestational surrogacy arrangements, gestational surrogates are commonly recruited from low- to middle-income countries. Thailand is well known as a surrogacy hub in this regard. However, little is known concerning Thai surrogacy practice and the risks that Thai gestational surrogates experiences. The semi-structured interviews with fifteen Thai women who had been gestational surrogates were conducted over the telephone in Thai between March and May 2020 and lasted approximately 30 minutes. Thematic analysis was applied to analyse the translated interviews. The findings indicated that 'womb for work' was perceived as a surrogacy career among Thai women. 'Womb for work' was defined as a superordinate theme that consisted of three subthemes: (i) gestational surrogacy arrangements in Thailand; (ii) the business model of gestational surrogacy arrangements in Thailand; and (iii) risk experiences of gestational surrogates. Clear deficiencies in surrogacy practice and regulations were identified, which put gestational surrogates at risk, including those associated with embryo transfer, transnational gestational surrogacy, and unsupported pregnancies. This study shows the urgent need to introduce regulations to protect women's health transnationally in this domain more effectively.

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Oral Presentation Session 2

Male and Female Infertility

Friday, 12 April 2019

OR06: Evaluating the prevalence, management, and the psycho-social impact of premature ovarian insufficiency on patients attending an academic hospital reproductive endocrine clinic

Mmaselemo Tsuari, Tygerberg Academic Hospital, Cape Town, South Africa; Thabo Matsaseng

Background: Primary Objective: To measure the prevalence of premature ovarian insufficiency (POI); Secondary Objective: To determine the etiology, review the management process and approach and to assess the impact of the diagnosis on patients with POI; Design: Cross-sectional study; Setting: Reproductive Endocrine Clinic in an academic hospital; Patients: Patients living with a diagnosis of POI.

Methods: Materials and Methods: Patients interviews, review of medical records including bone scans, clinical evaluation of patients as they present at the clinic. The study was undertaken over 12 months from August 2016 to July 2017. Primary Outcome Measure: The prevalence of POI in our Reproductive Endocrine Clinic; Secondary Outcome Measures: The management of POI, and impact of the diagnosis on the women.

Results: There were 47 patients living with a diagnosis of POI and the total number of all patients seen during this period at the above clinic was 561. The prevalence of POI in our setting is 8,4% (Confidence interval 6.28%-11.06%).

The etiology of POI in 32% of the patients was idiopathic, 19% genetic syndromic disorder, all of which were Turner Syndrome, 10% were non-syndromic genetic disorders. A familial disorder was found according to family history and accounted for 2% of the causes.

Auto-immune causes accounted for 6%, infective causes 6%, cancer and chemotherapy 6%, obstetric complications 6%, iatrogenic 4% and endometriosis 2%.

A dual energy X-ray absorptiometry (DEXA) scan was done of which 32% had osteopenia, 11% had osteoporosis 21% patients a DEXA scan was requested but not done. Patients with normal DEXA scans were re-assessed 5 years later and patients with osteopenia and osteoporosis were re-assessed every 2 years while on treatment. Eighty-one percent (81%) of patients with osteoporosis were treated with bisphosphonates.

There were 55% of patients with depression and they were treated with various antidepressant.

Conclusion: The prevalence of POI in our clinic is reported to be 8.4%, which is much higher than the prevalence quoted in literature of 1%. This large difference may be due to a bias caused by a smaller sample size relative to the total number of patients seen. All patients received the standard treatment protocol and various specific treatment modalities.

Funding: Budget requirements: There was no budget allocated to the study.

OR07: Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review

Jutharat Attawet, University of Technology Sydney; Alex Wang; Cindy Farquhar; Elizabeth Sullivan

Background: The likelihood of livebirth following assisted reproductive technology (ART) is increased when more than one embryo is transferred. However, with the transfer of more than one embryo there is also an increased risk of multiple pregnancy and subsequent adverse maternal and perinatal outcomes. This is particularly important for gestational carriers as they may potentially have long term complications following a surrogacy pregnancy. As a result in Australia, New Zealand and Canada, single embryo transfer (SET) is strongly recommended for gestational surrogacy. Nonetheless, there is limited evidence that systematically evaluates pregnancy outcomes between single and multiple embryo transfers (multiple ET) for gestational carriers.

Methods: This study is a systematic review. Electronic databases were searched from CINAHL, Medline, Embase, Scopus and ProQuest for studies from 1980 to 2017. Cross-references and national ART reports were also manual searched. Articles without restriction of English language and study types were accessed. The key words for searching were surrogacy, gestational carriers, embryo transfer, SET and multiple ET. The primary outcomes were live delivery and multiple delivery per gestational carrier, and compared between SET and multiple ET. Mantel-Haenzel risk ratios (RRs) with 95% confidence intervals (CIs), using the numbers of outcome events in SET and multiple ET of each study were calculated suing RevMan5.3.

Results: The search returned 97 articles. Of which five met the inclusion criteria where articles focused on SET and MET carrier cycles along with primary outcome measures. Of the five studies there were 898 carriers aged from 21 to 52 years. There were 885 gestational carrier cycles with embryo transferred, 48% (432) of SET and 52% (463) of MET. The live delivery rate was not significantly different between SET and MET with RR = 0.88 (95% CI: 0.61-1.30, n = 4, I2 = 67%). There were 105 sets of twins and one set of triplets following MET. There was one set of twins following SET. The multiple delivery rate per gestational carrier was significantly lower following SET than MET (RR = 0.04, 95% CI: 0.01-0.26, n = 3, I2 = 37%). The clinical pregnancy rate was not significantly different between SET and MET (RR = 0.89, 95% CI: 0.66-1.19, n = 5, I2 = 62%).

Conclusion: SET should be strongly recommended among gestational carriers to prevent multiple pregnancy and subsequent adverse outcomes for both carrier and baby.

Funding: N/A.


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Richard Kennedy, MD
President, IFFS
Joe Leigh Simpson, MD
2019 Scientific Committee Co-Chair, IFFS
Zi-Jiang Chen, MD, PhD
2019 Scientific Committee Co-Chair, IFFS
2240

Appendix 8: Published article by Human Fertility: Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis

HUMAN FERTILITY
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ORIGINAL ARTICLE

Pregnancy and birth outcomes of single versus multiple embryo transfer in gestational surrogacy arrangements: a systematic review and meta-analysis

Jutharat Attawet[a], Alex Y. Wang[a], Cindy M. Farquhar[b], Vanessa Jordan[b], Zhuoyang Li[a] and Elizabeth A. Sullivan[a,c]

[a]Faculty of Health, University of Technology Sydney, Ultimo, Australia; [b]Faculty of Medical and Health Sciences, the University of Auckland, Auckland, New Zealand; [c]Faculty of Health and Medicine, University of Newcastle, Callaghan, Australia

ABSTRACT

Multiple embryo transfer (MET) is associated with both an increased risk of multiple pregnancy and of live birth. In recent years, MET has become standard practice for most surrogacy arrangements. There is limited review of the use of MET versus single embryo transfer (SET) in surrogacy practice. The present review systematically evaluated the pregnancy outcomes of surrogacy arrangements between MET versus SET among gestational carriers. A systematic search of five computerized databases without restriction to the English language or study type was conducted to evaluate the primary outcomes: (i) clinical pregnancy; (ii) live delivery; and (iii) multiple delivery rates. The search returned 97 articles, five of which met the inclusion criteria. The results showed that clinical pregnancy (RR = 1.21, 95% CI: 1.06–1.39, n = 5, I^2 = 41%), live delivery (RR = 1.29, 95% CI: 1.10–1.51, n = 4, I^2 = 35%) and multiple delivery rates (RR = 1.42, 95% CI: 6.58–69.73, n = 4, I^2 = 54%) were statistically significantly different in MET compared to SET. Adverse events including miscarriage, preterm birth and low birthweight were found following MET. Our findings support the existing evidence that MET results in multiple pregnancy and subsequently more adverse outcomes compared to SET. From a public health perspective, SET should be advocated as the preferred treatment for gestational carriers.

ARTICLE HISTORY
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Surrogacy; embryo transfer; multiple pregnancy; assisted reproductive technology; gestational surrogacy; pregnancy outcomes

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Supplemental data for this article can be accessed here.

Appendix 9: Abstract publication, conference at ESHRE Virtual 36th Annual Meeting

P-730 High prevalence of Mycoplasma /Ureaplasma in asymptomatic oocyte donors

P.L. Aldama González[1], M. Lacarcel[1]

[1]*Eva Fertility Clinics, EvaBank, Madrid, Spain*

Study question: What is the current prevalence of Sexually Transmitted Infections (STIs) in asymptomatic oocyte donors?
Summary answer: The current prevalence of STIs in asymptomatic oocyte donors is higher than expected, especially for Mycoplasma and Ureaplasma Urealyticum.
What is known already: Sexually transmitted infections (STIs) are related to infertility worldwide. The impact of STIs such as Mycoplasma hominis, Ureaplasma Urealyticum and Chlamydia Trachomatis on fertility has been debated for several decades without being able to reach definitive conclusions due to isolating difficulties and absence of symptoms.
Study design, size, duration: This is a retrospective observational study including all the asymptomatic oocyte donors with complete STIs detection report between July and December of 2019.
Participants/materials, setting, methods: A total of 72 donors (18 to 29 years old) were included in the study. Samples from each donors were cultured for Mycoplasma Hominis, Ureaplasma Urealyticum and Ureaplasma Parvum. Chlamidya Tracomatis antigen and Neisseria Gonorrhoeae antigen in cervical sample, Pallidum Antitreponema and Herpes 1/2 antibodies were analyzed. General vaginal microbiological culture was performed also for each donor. The statistical analysis was performed using measures of central tendency, and Pearson's Chi2, using the SPSS version 25
Main results and the role of chance: STIs were found in 58% of asymptomatic oocyte donors (n =42). Therewas no correlation between STIs with age, race, occupation, or marital status. However, STIs were significantly associated with low education (p=0.045). Mycoplasma hominis was founded in 39%of the cases (n=16), Ureaplasma Urealyticum in 56% (n=23), Ureaplasma Parvum 14% (n=6). Chlamydia Trachomatis 9% (n=4). Mycoplasma hominis and Ureaplasma Urealyticum was founded together in 24% (n=10), and Ureaplasma spp in 14% (n=6).
Limitations, reasons for caution: This is an small observational study based on a retrospective data analysis. Better extrapolation of the results could be validated by performing an extensive prospective study.
Wider implications of the findings: The young healthy population must be targeted with preventive educational programs. Although STI is not investigated routinely but in long run, it can might have negative impact on fertility rate in society.
Trial registration number: Not Applicable

P-731 The impact of body mass index on in vitro fertilization performance in infertile women

A. Albu[1], D. Albu[2]

[1]*Carol Davila University of Medicine and Pharmacy, Endocrinology, Voluntari, Romania ;*
[2]*Carol Davila University of Medicine and Pharmacy, Obstetrics and Gynecology, Voluntari, Romania*

Study question: Which is the relationship between the entire spectrum of body mass index (BMI) and in vitro fertilization (IVF) parameters?
Summary answer: Both low BMI and overweight BMI seem to be associated with oocytes and zygotes number and the responder type.
What is known already: The association between BMI and IVF outcome is widely debated, the results of the available studies being divergent. While higher BMI seems to have a negative impact on reproductive outcome, the data regarding the connection between low BMI and reproductive parameters are limited.
Study design, size, duration: We performed a retrospective study in the Department of Reproductive Medicine of a private hospital. The medical records of all consecutive patients who underwent IVF between January 2015 and December 2018 with all causes of infertility were reviewed.
Participants/materials, setting, methods: One thousand three hundred thirty-seven patients were included in the study (mean age 34.7±4.2 years). Patients were divided according to BMI in underweight (n=116, BMI<18.5kg/sqm), normal weight (n=971, BMI 18.5-24.99 kg/sqm), overweight (n=195, BMI 25-29.99 kg/sqm) and obese (n=55, BMI>30 kg/sqm). The number of oocytes obtained at egg collection and the zygotes number were recorded. Patients were also categorized according to the type of responder: poor responder, low responder, normal responder and hyper responder.
Main results and the role of chance: BMI was positively correlated with age (rho = 0.141, p < 0.0001) and negatively with oocytes (rho = - 0.068, p = 0.014) and zygotes number (rho = - 0.080, p = 0.004). In a multivariate regression model, after adjustment for age and AMH serum level, being underweight was positively associated with oocytes number (beta = 0.072, p = 0.002) and with zygotes number (beta = 0.059, p = 0.02) and being overweight was negatively associated with oocytes number (beta = - 0.051, p = 0.028). In a multinomial regression model, after adjustment for age and AMH serum level, underweight patients had an increased chance of being normal responder in comparison with normal weight patients (OR 1.4, CI 1.2-2), while overweight patients had decreased odds of being normal responder in comparison with normal weight patients (OR 0.56, CI 0.29-0.8)
Limitations, reasons for caution: The main limitation of the study is the relatively small number of patients included in the obese and underweight category, probably affecting the statistical analysis.
Wider implications of the findings: Our study showed the association between low and high BMI and oocytes and zygotes number, which were reported to be significant predictors of live birth, therefore offering possible ways to influence IVF outcome by modifying body weight.
Trial registration number: NA

P-732 Cumulative live birth rates among gestational carriers in altruistic surrogacy arrangements

J. Attawet[1], A. Wang[1], Z. Li[1], K. Hammarberg[2], L. Johnson[3], E. Sullivan[4]

[1]*University of Technology Sydney, Public Health, Sydney, Australia ;*
[2]*Monash University, Public Health, Melbourne, Australia ;*
[3]*Victoria Assisted Reproductive Treatment Authority, varta, Melbourne, Australia ;*
[4]*University of Newcastle, Health and Medicine, Callaghan, Australia*

Study question: What is the cumulative live birth rate (CLBR) among gestational carriers in altruistic surrogacy arrangements?
Summary answer: The CLBR among gestational carriers ranged from 23.5% after the first embryo transfer cycle to 50.6% after six consecutive embryo transfer cycles.
What is known already: CLBR is a measure of the success of assisted reproductive technology (ART) which demonstrates how each additional treatment adds to the chance of having a live birth. It is commonly used in the context of autologous treatment where women have used their own eggs.
Study design, size, duration: This was a population-based retrospective cohort study of all intended parents and gestational carriers who had at least one embryo transfer cycle in the state of Victoria, Australia between 2009 and 2016. Pregnancy and birth outcomes were followed until a live birth was achieved or until June 30, 2017, whichever came first.
Participants/materials, setting, methods: Data collected by the Victorian Assisted Reproductive Treatment Authority (VARTA) on all gestational surrogacy arrangements in Victoria between 2009 and 2017 were analysed. The primary outcome was cumulative live birth, which was defined as live deliveries with at least one live born baby resulting from initiated stimulated cycles and associated thaw cycles. Life-table was used to calculate the CLBR.
Main results and the role of chance: There were 66 intended parents and 81 gestational carriers. Of the 170 embryo transfer cycles, the majority were single embryo transfers (97.1%), using frozen/thawed embryos (97.6%) which had been fertilized by intracytoplasmic sperm injection (ICSI) (77.6%). The cumulative live birth rate was 23.5% (95% CI, 15.6-33.8%) after the first cycle and increased to 50.6% (95% CI, 40.0-61.2%) after the sixth cycle. Of the 41 deliveries, 40 were singletons and one was a twin delivery. Two of the 42 babies were preterm, two were low birthweight and one was small for gestational age.
Limitations, reasons for caution: Although this population-based study included all gestational surrogacy arrangement in Victoria, the sample size is small. The study was conducted in a setting where only altruistic surrogacy is legal, and the findings may not be generalizable to settings where commercial surrogacy is undertaken. .

Wider implications of the findings: Altruistic surrogacy arrangement is unlikely to reduce the cumulative live birth rate. Among gestational carriers, surrogacy treatment can be offered up to six consecutive embryo transfer cycles without reducing the chance of a live birth. This estimate can be used in counselling and decision-making for all parties involved in surrogacy.
Trial registration number: not applicable

P-733 Childless by circumstance – the fertility experiences of women who wanted children

J. Harper[1], D. Chauhan[1], E. Jackson[2]

[1]Institute for Women's Health, EGA Institute for Women's Health, London, United Kingdom ;
[2]London School of Economics, Law, London, United Kingdom

Study question: What reproductive experiences did childless women go through and how do they feel about being childless?
Summary answer: Women experienced social infertility, miscarriages, and if they went through IVF, they mainly stopped for emotional reasons. The majority felt negatively about being childless.
What is known already: Childlessness is increasing across many middle- and high-income countries, for a wide variety of reasons, including increasing gender equality, greater respect for reproductive autonomy, infertility and, in some cases, an inability to find a partner. Many women have postponed childbearing and the age of first birth is increasing annually. Europe has the lowest fertility rate on record, as well as a record number of women being permanently childless.
Study design, size, duration: An online survey study was developed and validated with help from childless women. The survey consisted of questions with quantitative-answer formats as well as open-text qualitative answer formats. It was promoted through social media. The survey remained open online for 15 days.
Participants/materials, setting, methods: The survey was only completed by women who were aged 46 years of age and above, who had wanted children but were childless. In total 303 survey responses were collected, 176 of which were complete surveys. The data was explored through the survey platform's data reporting function. The qualitative data was analysed with a qualitative descriptive analysis approach.
Main results and the role of chance: 16.3% (n=27) of women who wanted children reported that they did not try to have children, most commonly due to the lack of a partner (40%, n=11). Of the women who tried to have children (n=139), 70.5% (n=98) had used calendar-based menstrual cycle tracking methods to identify their fertile window and many had fertility checks including hormone tests (75.5%) and ultrasound scans (71.2%). A significant proportion of women had experienced a miscarriage (38.8%). Many women decided not to have any fertility treatments (43.2%, n=60). For those that did undergo fertility treatments, many had tried in vitro fertilization (42.4% (n=59), and this was mainly privately funded. The most common reason women gave for stopping fertility treatment was due to emotional reasons (42.4%, n=59). When asked how women felt about their childlessness, the most common emotions identified were sadness (53.1%, n=85), gradual acceptance (36.3%, n=58), and ostracism (33%, n=53).
Limitations, reasons for caution: The use of the word childless was discussed. 'Childless by circumstance' was agreed in order not to presuppose reasons for women's childlessness, or to assume that women's attitude towards their childlessness was fixed. 127 participants started but did not complete the survey. The survey was only advertised on social media.
Wider implications of the findings: This study has listened to the self-reported experiences of women who wanted children, but who are childless. Support for unsuccessful fertility patients and other childless women should be expanded, and emphasis on fertility education should be established in order to ensure that women are better informed about their fertility.
Trial registration number: Not applicable

P-734 Cost-effectiveness of medically assisted reproduction or expectant management for unexplained subfertility: when to start treatment?

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Study question: Over a time period of three years, which order of expectant management (EM), IUI-OS and IVF is the most cost-effective for couples with unexplained subfertility?
Summary answer: The most cost-effective scenario depended on the monetary value assigned to a live birth: EM-EM-IVF (if assigned <€32,000) or EM-IUIOS-IVF when assigned more.
What is known already: IUI-OS and IVF are commonly used for unexplained subfertility although these couples can still conceive naturally. Few countries have guidelines on when to proceed with medically assisted reproduction (MAR) but there is a lack of evidence to support these strategies. The increased uptake of IUI-OS and IVF over the past decades and costs related to reimbursement of these treatments are pressing concerns to health service providers. For MAR to remain affordable, sustainable and a responsible use of public funds, guidance is needed on the cost-effectiveness of treatment strategies for unexplained subfertility.
Study design, size, duration: We developed a cost-effectiveness model that follows couples with unexplained subfertility for a total of 3 years from diagnosis onwards, divided into three periods of 1 year each. The model was based on contemporary evidence i.e. the dynamic prediction model for natural conception and the network meta-analysis on RCTs in MAR for unexplained subfertility. We changed the ordering of the three options, EM, IUIOS and IVF to yield different treatment scenarios.
Participants/materials, setting, methods: The main outcomes were the probability of live birth and aveage costs. We chose the Dutch societal perspective. The probabilities of live birth after EM were taken from the dynamic prediction model for natural conception. The relative effects of IUI-OS and IVF were taken from the network meta-analysis and applied to probabilities of live birth after EM. We applied discounting. Uncertainty was taken into account using probabilistic sensitivy analyses, replicating the simulation model 20,000 times.
Main results and the role of chance: From IVF-EM-EM to EM-IUIOS-IVF, the probability of live birth varied from approximately 54% to 64% and the average costs from approximately €4000 to €9000. The scenarios IVF-EM-EM and EM-IVF-EM were dominated by EM-EM-IVF as the latter yielded a higher cumulative probability of live birth at a lower cost. The scenario IUIOS-IVF-EM was dominated by EM-IUIOS-IVF as the latter yielded a higher cumulative probability of live birth at a lower cost. After removal of scenarios that were dominated, the incremental cost-effectiveness ratio (ICER) for EM-IUIOS-IVF was approximately €31,000 compared to EM-EM-IVF. The range of ICER values between the lowest 25% and highest 75% of simulation replications was broad.

The net benefit curve showed that when we assume a live birth to be worth approximately €32,000 or less, the scenario EM-EM-IVF had the highest probability to achieve the highest net benefit. When we assume a monetary value per live birth over €32,000, the scenario with the highest probability to achieve the highest net benefit was EM-IUIOS-IVF. Results for subgroups with different baseline prognoses were similar to the primary analysis but yielded different threshold values for the assumed monetary value per live birth.
Limitations, reasons for caution: Our model was at the population level and thus based on average statistics. We also assumed certain model parameters and assessed the influence of these assumptions on our results. The change in relative effectiveness of IVF over time was found to be highly influential on results and their interpretation.
Wider implications of the findings: Two scenarios, EM-EM-IVF and EM-IUIOS-IVF, were the most cost-effective at different monetary values for a live birth with a threshold of €32,000. Our results can be used in determining sustainable MAR protocols for couples with unexplained subfertility that avoids unnecessary treatment.
Trial registration number: Not applicable

Appendix 10: Poster presentation at ESHRE Virtual 36th Annual Meeting

Cumulative live birth rates among gestational carriers in altruistic surrogacy arrangements

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Background

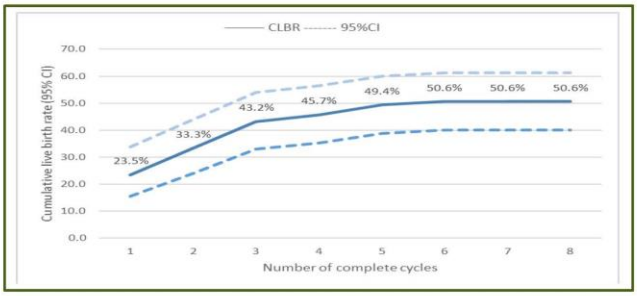
Understanding the likelihood of a live birth is important for fertility treatment planning, particularly when one cycle fails and further treatment may be contemplated. To date no published study has reported the cumulative live birth rate (CLBR) for gestational surrogacy arrangements.

Methods

This was a population-based retrospective cohort study of all intended parents and gestational carriers who had at least one embryo transfer cycle in the state of Victoria, Australia between 2009 and 2016. Pregnancy and birth outcomes were followed until a live birth was achieved or until June 30, 2017, whichever came first. The primary outcome was cumulative live birth, which was defined as live deliveries with at least one live born baby resulting from initiated stimulated cycles and associated thaw cycles. Life-table was used to calculate the CLBR.

Results

There were 66 intended parents and 81 gestational carriers with 170 embryo transfer cycles. Of the 170 embryo transfer cycles, the majority were single embryo transfers (SETs) (97.1%), using frozen/thawed embryos (97.6%) which had been fertilized by intracytoplasmic sperm injection (ICSI) (77.6%). The cumulative live birth rate was 23.5% (95% CI, 15.6-33.8%) after the first cycle and increased to 50.6% (95% CI, 40.0-61.2%) after the sixth cycle.



Conclusion

The findings imply that surrogacy treatment can be offered up to six consecutive embryo transfer cycles to gestational carriers. These estimates can be used in counselling and decision-making for intended parents and gestational carriers to continue a surrogacy treatment, and informing public policy on assisted reproductive technology treatment.

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5 to 8 July 2020

This is to certify that

Attawet, Jutharat - Australia

gave a poster presentation with title:

" Cumulative live birth rates among gestational carriers in altruistic surrogacy arrangements"

during the **36th virtual Annual Meeting of the European Society of Human Reproduction and Embryology** from 5 to 8 July 2020.

Cristina Magli
Chairman of ESHRE

Appendix 11: Published article by Human Fertility: Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements

HUMAN FERTILITY
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ORIGINAL ARTICLE

Cumulative live birth rates among gestational surrogates in altruistic surrogacy arrangements

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ABSTRACT

Understanding the likelihood of a live birth is important for fertility treatment planning, particularly when one cycle fails and further treatment may be contemplated. This study aims to estimate the chance of live birth among gestational surrogates undergoing altruistic surrogacy arrangements between 2009 and 2016 in Victoria, Australia. A total of 81 gestational surrogates with 170 embryo transfer cycles were included. Of the 170 embryo transfer cycles, the majority were single embryo transfers (SETs; 97.1%), using frozen/thawed embryos (97.6%) which had been fertilized by intracytoplasmic sperm injection (77.6%). The cumulative live birth rate was 23.5% (95% CI, 15.6–33.8%) after the first cycle and increased to 50.6% (95% CI, 40.0–61.2%) after the sixth cycle. Of the 41 deliveries, 40 were singletons and one was a twin delivery. Two of the 42 deliveries were preterm, two were low birthweight and one was small for gestational age. The findings imply that surrogacy treatment can be offered up to six consecutive embryo transfer cycles to gestational surrogates. SET is encouraged in surrogacy practice to improve perinatal outcomes. These estimates can be used in counselling and decision-making for intended parents and gestational surrogates to continue a surrogacy treatment and informing public policy on assisted reproductive technology treatment.

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Altruistic; assisted reproductive technology; cumulative live birth rate; gestational carrier; surrogates; surrogacy

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