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Understanding the Relationship Between Assisted Reproductive Technologies and Breastfeeding Outcomes: A Systematic Literature Review

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An abstract of
a thesis submitted to the faculty of the
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ABSTRACT

Understanding the Relationship Between Assisted Reproductive Technologies and Breastfeeding Outcomes: A Systematic Literature Review

By: Sasha M. Gambrah

Background: Breastfeeding is known to be an essential, long lasting and cost effective intervention for both the mother and child. However, many factors can influence breastfeeding initiation, exclusive breastfeeding and breastfeeding duration and these determinants may vary by context. Limited research suggests breastfeeding outcomes differ between women who conceive spontaneously or through assisted reproductive technologies (ART); however, many questions remain and there is currently no consensus in the literature.

Objectives: The purpose of this systematic literature review is to examine if women who undergo assisted reproductive technologies are more likely to have poor breastfeeding outcomes: lower breastfeeding initiation, exclusive breastfeeding and duration.

Review Methods: PubMed and Embase were used to identify peer-reviewed articles that met the inclusion and exclusion criteria. All full-text publications were entered using EndNote X8 and Covidence, and then organized into summary of findings tables using Microsoft Excel. Included articles were summarized into three breastfeeding categories: initiation, exclusivity, and duration.

Results: The literature search strategy identified 251 peer-reviewed articles related to assisted reproductive technology and breastfeeding practices. 10 full-text articles were included in this review. Overall, there is insufficient evidence to conclude an association between ART and breastfeeding initiation, exclusivity and duration. Half of the studies reported no significance for EBF, while the other half reported decreases. 3 out of 5 studies reported no significance for breastfeeding initiation, while the others were mixed (1 decrease/1 increase). Results for breastfeeding duration were very mixed with two studies reporting significant increases, two reporting significant decreases, two reporting no significant difference, and the remaining studies describing varied statistical significance at different times of their study. All included studies were conducted in developed countries: Australia (N=4), Germany, (N=2), Taiwan (N=1), United States (N=1), Canada (N=1), Italy (N=1).

Conclusion: Currently there is inadequate evidence to support the need for additional breastfeeding support for women who undergo ART beyond established risk factors like maternal age, employment, low birthweight/preterm infant, pregnancy psychological functioning and Caesarean deliveries. While there are many known factors associated with breastfeeding initiation, exclusivity, and duration of breastfeeding, there remain questions on how to best target and support mothers to reach their breastfeeding goals.

Keywords*: breastfeeding, assisted reproductive technologies, initiation, duration, exclusive, systematic review*

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ACRONYMS AND ABBREVIATIONS

ART	Assisted Reproductive Technologies
ARTC	Assisted Reproductive Technology conception
BFD	Breastfeeding duration
BFHI	Baby Friendly Hospital Initiative
BFI	Breastfeeding initiation
EBF	Exclusive Breastfeeding
EIBF	Early initiation of breastfeeding
IVF	In vitro fertilization
ISCI	Intracytoplasmic sperm injection
MeSH	National Library of Medicine's Medical Subject Headings
SC	Spontaneous conception
WHO	World Health Organization

INTRODUCTION

Background

Exclusive breastfeeding is more than simply a way to feed a baby; it is the first relationship an infant will encounter, and offers significant health benefits for both the mother and infant. For the first six months of life, breast milk alone is the ideal nourishment, providing all the nutrients, vitamins, and minerals that infants need (Butte et al, 2002). The World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) both recommend that mothers put newborns to the breast within the first hour of birth, breastfeed infants exclusively for the first six months, and continue to breastfeed for two years, with complementary foods starting in the sixth month (WHO, 2003). For the child, breastmilk provides essential vitamins and minerals and immune factors that can help fight diseases. Breastfeeding protects babies from diarrhea and acute respiratory infections, and decreases the risk of childhood leukemia, childhood obesity, asthma, and sudden infant death syndrome (SIDS) (Hanson, 2004). Continued breastfeeding beyond six months, accompanied by sufficient quantities of soft, nutritionally sufficient, appropriate complementary foods, also helps ensure good nutritional status and protects against illnesses. It has been estimated that optimal breastfeeding of children under two years of age has the potential to prevent 823,000 annual deaths in children younger than 5 years (Victora et al., 2016).

A breastfeeding mother also gains many benefits. There is a decreased risk of ovarian and breast cancer, the development of diabetes, and myocardial infarction for women who breastfed their child (Victora et al., 2016). The risk decreases even more significantly if the mother is exclusively breastfeeding without supplementation of formula and the longer the mother and

baby choose to breastfeed. Breastfeeding provides emotional satisfaction and creates a strong bond between the mother and the baby. Breastfeeding also improves the mother's health and restores her body after the pregnancy. It helps the uterus to return to normal, reduces the amount of normal vaginal bleeding, and decreases the risk of post postpartum hemorrhage. Getting the uterus back to normal also helps her to lose excess weight the mother gained during pregnancy.

Cost Benefits of Breastfeeding

Breastfeeding is one of the simplest, smartest and most cost-effective ways of ensuring that all children survive and thrive. In 2014, global sales of all baby milk formula were about US $44.8 billion, and by 2019, the market value is projected to increase to US $70.6 billion (Victora et al., 2016). Recent data from "Nurturing the Health and Wealth of Nations: The Investment Case for Breastfeeding" found that poor breastfeeding rates are responsible for roughly $1.63 billion in wage losses in Southeast Asia alone (Aguayo, 2017). According to *The Lancet* series, global wage loss could reach $300 billion annually. Country-level data show just how costly not breastfeeding can be for individual nations. India has a 55% exclusive breastfeeding rate, which is roughly $14 billion in annual losses to the country's economy (Aguayo, 2017). In Nigeria, where the exclusive breastfeeding rate is 17%, the losses are about 4.1% of their GNI ($21 billion) (Aguayo, 2017). Countries that have achieved an exclusive breastfeeding rate of 50% or higher can prevent significant economic losses by doubling efforts to improve breastfeeding practices.

The financial toll does not only fall on national economies, but also on families and individuals. With breastfeeding, a mother can save considerable time for herself and does not have to sterilize bottles or make formula. Mothers also save money, as nothing is spent for buying formula powder. The Investment Case found that the cost of purchasing formula is significant: up to one-third of a family's monthly earnings can be spent on breast milk substitutes (Aguayo,

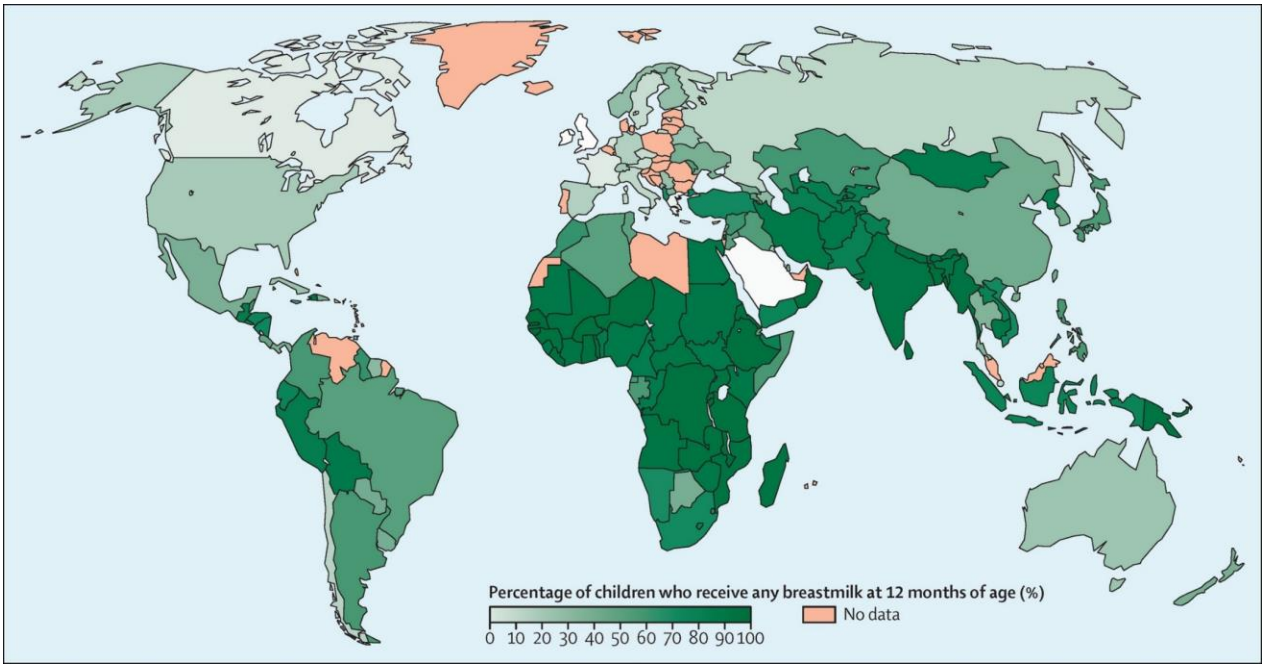
2017). Data has proven that breastfeeding is one of the most cost-effective and equitable interventions in global health and development (CDC, 2017).

Epidemiology of Global and Domestic Breastfeeding

In 1991, the Baby Friendly Hospital Initiative (BFHI) was launched to scale up ten interventions in birthing facilities to protect, promote, and support successful breastfeeding (Rollins et al., 2016). Since then, BFHI has grown with more than 152 countries around the world implementing the initiative. The initiative has measurable and proven impact, increasing the likelihood of babies being exclusively breastfed for the first six months (Rollins et al., 2016). While much effort has gone into scaling up the rates in developing countries where incidence of child malnutrition and mortality is still high, much improvement is still needed to ensure success in increasing breastfeeding levels.

Despite these initiatives being established over 25 years ago, global breastfeeding rates remain far below international targets. Recent analysis by Victora et al on the global distribution of breastfeeding at 12 months highlights that the importance of breastfeeding in low-income and middle-income countries is well recognized, but lower rates still exist in high-income countries (Victora et al., 2016). Figure 1 contains data from 153 countries between 1995 and 2013. In low-income and middle-income countries, only 37% of children younger than 6 months of age are exclusively breastfed (Victora et al., 2016). With few exceptions like the USA (27%) and Norway (35%), breastfeeding duration is shorter in high-income countries than in those that are resource-poor. In most high-income countries, the prevalence is lower than 20%. The prevalence of breastfeeding at 12 months is highest in sub-Saharan Africa, south Asia, and parts of Latin America (Victora et al., 2016).

Figure 1. Global distribution of breastfeeding at 12 months



Victora, et al., Lancet 2016; 387:475-90

Exclusive breastfeeding is important for child health and growth, but its practice is low in many developing countries, and data remains unavailable for some countries. Globally, the prevalence of breastfeeding at 12 months is highest in sub-Saharan Africa, south Asia, and parts of Latin America (figure 1).

The percentage of children who receive any breastmilk at 12 months remains low in the United States. The 2016 Breastfeeding Report Card states that more than half of states (29 states, including D.C. and Puerto Rico) have already met the Department of Health and Human Services 10-year national objective for improving the nation's health, Healthy People 2020 (HP2020) objective of 81.9% ever breastfeeding (CDC, 2016). However, breastfeeding rates remain low. In 2013, 4 out of 5 infants (81.1%) born started to breastfeed, over half (51.8%) were breastfeeding at 6 months, and almost one third (30.7%) were breastfeeding at 12 months (CDC, 2016). Rates of breastfeeding also vary across states and regions. Infants living in the southeast of the United

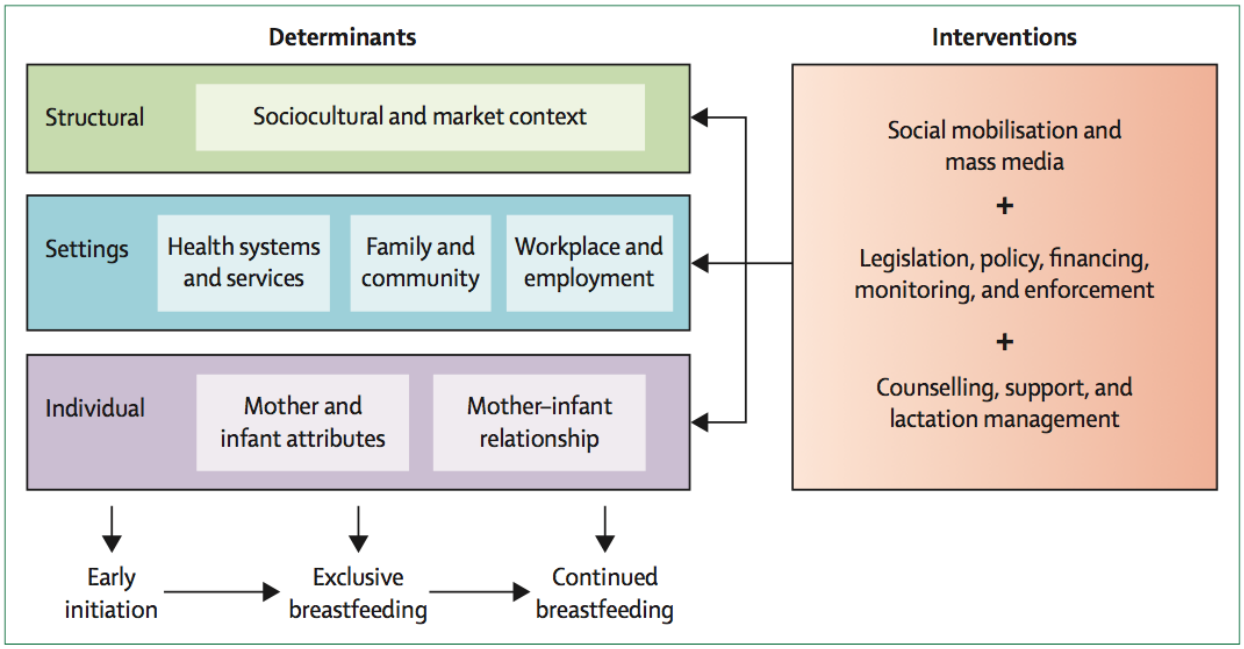
States are less likely to be breastfed at 6 months than infants living in other areas of the country. In 2014, less than 35% were breastfed at 6 months in Mississippi and West Virginia, and less than 45% in Arkansas, Louisiana, Kentucky, South Carolina, and Alabama (CDC, 2017). Fewer non-Hispanic black infants (68.0%) are ever breastfed compared with non-Hispanic white infants (85.7%) and Hispanic infants (84.8%) (CDC, 2017).

Despite high breastfeeding initiation rates and continued improvement in breastfeeding duration, most states are not yet meeting HP2020 breastfeeding duration and exclusivity targets. For infants born in 2013, 12 states met the HP2020 breastfeeding objective for 6 months duration (60.6%) (CDC, 2016). High breastfeeding initiation rates show that most mothers in the U.S. want to breastfeed and are attempting to do so. However, low breastfeeding rates among infants who are 6 and 12 months of age indicate that many mothers do not continue. These varied rates can be due to a wide range of socioeconomic, cultural, and individual factors.

Determinants of Breastfeeding: Global and Domestic Trends

A review of available studies was conducted to identify the determinants of breastfeeding. *The Lancet* 2016 recently reviewed breastfeeding and its determinants in a detailed series. The conceptual model in Figure 2 includes the determinants that operate at multiple levels and affect breastfeeding decisions and behaviors over time (Rollins et al., 2016).

Figure 2. The components of an enabling environment for breastfeeding: a conceptual model



Rollins et al., Lancet 2016; 387:491-504

Structural

Sociocultural and market context are the two components that make up the structural level, based on the conceptual model. On a market level, manufacturers are continuing to focus on appealing to consumers to buy infant milk formula. Aggressive marketing tactics of the infant formula industry undermine breastfeeding, which is clinically recommended. The promotion of infant formula to mothers can negatively influence breastfeeding (Fisher et al., 2013).

Social and cultural factors are often overlooked when encouraging mothers to choose breastfeeding as their method of infant feeding. These factors shape the structural context for breastfeeding (Rollins et al., 2016). Age, level of education and occupation are some of the facts that impact a mother's breastfeeding choice. Sexualization of the female breast can lead to embarrassment when mothers breastfeed outside the home. Negative reactions and discomfort to

breastfeeding in public, may discourage women from breastfeeding. This has a negative effect on the continuation of breastfeeding for women altogether. Fear of damaging their body shape can prevent some mothers from breastfeeding, while others see breastfeeding as desirable as it can lead to weight loss (Battersby, 2010). Knowledge of various influences can assist health professionals in their public health role and help them to give mothers advice relevant to their circumstances.

Settings

The conceptual model divides settings into three parts: health systems and services, family and community, and workplace and employment (Rollins et al., 2016). A large responsibility for advancing breastfeeding outcomes lies within health systems and services. Healthcare providers and staff play a key role in the promotion of breastfeeding. They influence and support feeding decisions at key moments before, after birth and later, when challenges occur, to maintain exclusive and continued breastfeeding (Rollins et al., 2016). However, there is still a need for more research and improved skill sets to better provide breastfeeding support for women who may or may not encounter difficulties while feeding.

Unexpected factors outside of a woman's control can also affect the rate of breastfeeding. Reasons such as high-risk pregnancies, assisted delivery and long hospital stays, maternal illness, and preterm, ill, or low-birthweight newborn babies, can all result in breastfeeding starting later or not at all (Rollins et al., 2016). Factors such as Caesarean deliveries (Fisher et al., 2013), years of infertility (Ladores & Aroian, 2015) , and milk supply (Wiffen & Fetherston, 2016) also impact breastfeeding initiation and duration.

Within families, practices and experiences often mold the occurrence of a woman breastfeeding (Meyerink & Marquis, 2002). The level of support a mother receives from her

family can affect the incidence and possibly duration of breastfeeding. Likewise, the attitudes and preferences of fathers can also impose an affect breastfeeding. For example, women whose partners support breastfeeding breastfeed for longer (Bar-Yam & Darby, 1997; Rollins et al., 2016).

In addition to these other factors, a woman's workplace and environment can either positively, but more than often negatively influence a mother's breastfeeding decisions. Maternity leave, work-time breaks, and on site rooms for breastfeeding are necessary for the increasing numbers of women in the workplace. This is one of the leading factors for not breastfeeding or early weaning (Rollins et al., 2016). The effects of working on breastfeeding are more than just women planning to return to work after childbirth. These effects include breastfeeding discrimination at work, fatigue, and increase work load to get up speed. Short maternity leave of less than 6 weeks leads to a four-times increase in the odds of either not initiating or short duration of breastfeeding (Guendelman et al., 2009; Rollins et al., 2016)

Individual

There are many factors that influence the individual level of breastfeeding. The conceptual model identifies mother and infant attributes and the mother-infant relationship as the two subcomponents of individual level breastfeeding determinants.

Mother attributes such as mothers being the primary caregiver in the daytime (Lee, Lee, Chiang, Lee, & Lee, 2010), maternal age (Cromi et al., 2015; Ladores & Aroian, 2015; Quinn, 2012), socioeconomic status (Lee et al., 2010; Ludwig, Ludwig, & Kentenich, 2011), maternal education (Hammarberg, Fisher, Wynter, & Rowe, 2011; Ludwig et al., 2011), difficulty breastfeeding (Quinn, 2012), fatigue (Quinn, 2012), employment status, delivery method (Cromi et al., 2015), parity (Cromi et al., 2015), and smoking habits of mothers and other family

members (Ludwig et al., 2011) are known risk factors for breastfeeding initiation and duration. Infant attributes such as, factors relating to the infant are also important in breastfeeding, including preterm birth, low birth weight and multiple births (Lee et al., 2010) have an impact on breastfeeding outcomes.

Individual factors, including advice and practices that undermine maternal confidence and self-efficacy, negatively affect breastfeeding (Rollins et al., 2016). However, factors including smoking, overweight and obesity, and depression, are also important determinants because of the large number of women affected (Rollins et al., 2016). At the personal level, subjective norms and benefits of breastfeeding are the most frequently cited reasons for intending to breastfeed (Rollins et al., 2016). One of the most difficult decisions for new mothers is to decide which diet to follow with her babies. All mothers want what is best for their children, and while health care professionals encourage breastfeeding as the natural feeding choice, many mothers still choose to feed their babies with formula. Maternal reasons influencing feeding decisions include whether mothers themselves were breastfed as newborns (Castelli et al., 2015), employment, mental health (Hammarberg, Rowe, & Fisher, 2009), and successful initiation of lactation (Wiffen & Fetherston, 2016).

Factors such as perceived insufficient milk (Wiffen & Fetherston, 2016), employment (Quinn, 2012), latching, lack of support (Rollins et al., 2016), and poor positioning of breastfeeding are reasons generally discussed for shorter durations of breastfeeding. Mother-infant related issues such as infant crying and inability to calm down an infant tend to steer mothers to choosing formula for their infants, instead of carrying out breastfeeding practices.

Assisted Reproductive Technology and Breastfeeding

Global infertility prevalence rates are difficult to determine, due to limited data in

developing countries and the presence of both male and female factors which complicate estimates. Infertility is defined by WHO as failure of those of reproductive age (15-49 years) to receive clinical pregnancy after 12 months or more of unprotected sexual activity, and is estimated to affect more than 186 million people worldwide (World Health Organization [WHO], 2012). Although infertility is mostly common in aging populations and in urban areas where women have their first child at an older age, the burden of infertility and its social consequences are predominantly found in developing and transitional countries (WHO, 2012).

Advances in medicine and technology, such as assisted reproductive technology (ART), have allowed many infertile women in the world to become pregnant and deliver babies. ART is becoming an increasingly more common treatment option for women and couples who experience fertility problems. ART is the use of medical techniques to enhance fertility and increase the probability of conceiving a child. Some of the most common methods of reproductive technology include artificial insemination, gamete intrafallopian transfer (GIFT), in vitro fertilization (IVF), intracytoplasmic sperm injection (ICSI), surrogacy, and zygote intrafallopian transfer (ZIFT). It is estimated that more than half a million IVF cycles are performed annually in the developing countries, resulting in 100,000 newborns (Aleixandre-Benavent et al., 2015). The total number of successful IVF and ICSI births worldwide was reported as 5 million cases in 2012 (ESHRE, 2012). In US alone 1 million babies have been born via IVF (Fox, 2017).

With respect to worldwide recognition and increased demands for ART services, high quality research and key publications are still required to develop these technologies in developing countries.

Pregnancy with ART carries a higher risk of pregnancy-related morbidities as well as

adverse reproductive outcomes such as low birth weight, preterm birth, and multiple births (Lee et al., 2010). Michels et al report that observed differences in breastfeeding were not due to mode of conception per se, but rather to the higher proportion of preterm and low birth weight infants born to couples using ART (Michels et al., 2016) Women who conceive with ART are more likely to be first-time mothers, and are on average, older and more likely to have pregnancy complications: multiple births, operative delivery, labor induction, premature birth, and low–birth weight babies, than women who conceive spontaneously(Cromi et al., 2015). Understanding breastfeeding outcomes requires an exploration beyond maternal and newborn factors that could affect lactation success (Cromi et al., 2015). There is reason to believe that women after ART and the associated spectrum of physical and emotional challenges are less likely to commit to a long-term breastfeeding pattern (Ludwig et al., 2011). Given the importance of breastfeeding for child health and the limited research between the association of breastfeeding and ART, this literature review aims to analyze the relationship between assisted reproductive technologies and breastfeeding initiation, duration, and exclusivity.

Problem Statement

Controversial, yet limited results have been reported concerning the effects of assisted reproductive technology on breastfeeding outcomes and practices amongst mothers. The purpose of this systematic literature review is to review published studies of breastfeeding practices following conception through assisted reproductive technologies.

Objectives and Aims

The overall objective of this review is to assess the differences in breastfeeding practices among mothers who conceive spontaneously compared with those who conceive using assisted reproductive technology. The specific aims are as follows:

1. To systematically review the evidence on the association between assisted reproductive technology and breastfeeding practices.
    a. Is assisted reproductive technology associated with breastfeeding initiation?
    b. Does assisted reproductive technology impact breastfeeding duration?
    c. Does assisted reproductive technology impact exclusive breastfeeding?

Uses of This Report

The report may be used for identifying areas for promising research and setting research priorities.

METHODS

This section describes the basic methodology used to develop the review. A systematic literature review was conducted using a predefined literature search strategy, screening and data abstraction methods. Inclusion and exclusion criteria were developed prior to the literature search. Studies meeting the standards were subsequently reviewed and analyzed.

Data Synthesis

Full-text articles and publications meeting the inclusion criteria were obtained and screened. All documents included “assisted reproductive techniques” and “breast feeding”.

Articles from databases PubMed and Embase were exported into EndNote X8 and Covidence. Duplicates were removed, and titles and abstracts were reviewed for inclusion. Full-text reviews were conducted to assess the final list of articles to be included. Microsoft Excel was used to organize the documents into three summaries of finding tables used in the results section.

Search Strategy

The PubMed search strategy used the National Library of Medicine's Medical Subject Headings (MeSH) key nomenclature. Searches were limited to articles published in English. The exact search string used is provided below. Relevant reviews in the Embase Database were identified with a predefined search term, which covers all topics relevant to this report. All search strategies combined yielded a total of 251 citations.

- PubMed search terms:
    - ("reproductive techniques, assisted"[MeSH Terms] OR assisted reproductive technology OR assisted reproductive technologies OR assisted reproductive technique OR assisted reproductive techniques OR assisted reproduction OR "fertilization in vitro"[MeSH Terms] or IVF)

      AND
    - ("breast feeding"[MeSH Terms] OR breast feeding OR breast-feeding OR breastfeeding OR breastfed)
- Embase search terms:
    - ("breast feeding"/exp OR breast feeding OR breast-feeding OR breastfeeding OR breastfed)

      AND

- ("infertility therapy"/exp OR assisted reproductive technology OR assisted reproductive technologies OR assisted reproductive technique OR assisted reproductive techniques OR assisted reproduction OR in vitro fertilization OR IVF)

Screening of Abstracts

Two researchers independently reviewed abstracts and classified each as included or excluded according to project-specific criteria, which they also developed. An abstract was included for full-text review if both reviewers recommended that it be included.

The ***inclusion*** criteria consisted of:

- All geographic populations
- Studies that use only human subjects
- Articles with the following study designs: observational, case-control, cohort, longitudinal and cross-sectional
- Accessible full-text articles
    - Exceptions for two articles that only had published abstracts, where authors were contacted for full-text versions (pending inclusion in final manuscript)

and ***exclusion*** criteria consisted of:

- Articles in languages other than English due to limited resources

Screening of Full Texts

At the full-text screening stage, paired researchers independently reviewed the articles that had passed the abstract screening and indicated a decision to include or exclude them for

data abstraction. When the two reviewers arrived at different decisions about inclusion/exclusion for a given articles, a conflict reviewer was asked to reconcile the difference.

Terms and Definitions

Definitions will be provided for the following terms: exclusive breastfeeding, breastfeeding initiation, breastfeeding duration, any breastmilk, and ART. "Exclusive breastfeeding" is defined as no other food or drink, not even water, except breast milk (including milk expressed or from a wet nurse) for 6 months of life, but allows the infant to receive oral rehydration solution, drops and syrups (vitamins, minerals and medicines) (WHO, 2018). Breastfeeding initiation is the provision of mother's breast milk to infants within one hour of birth, and ensures that the infant receives the colostrum, or "first milk", which is rich in protective factors (WHO, 2018). Breastfeeding duration is the length of time for any breastfeeding, including breastfeeding through the initial stage of exclusive breastfeeding and any period of complementary feeding until weaning WHO, 2018). For this review, the term "any breast milk" is categorized under breastfeeding duration. "Any breast milk" can be defined as infants who receive some form of breast milk, whether through breastfeed feeding or bottled breast milk at a given time. Women may continue to breastfeeding for a longer duration, "any breastfeeding" just indicates the portion of women currently providing any breastmilk at that time.

ART includes all fertility treatments in which both eggs and embryos are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman (CDC, 2017). In vitro fertilization (IVF), meaning fertilization outside of the body, is the most effective and the most common form of ART. Intracytoplasmic sperm injection

(ICSI) is a type of IVF that is often used for couples with male factor infertility. With ICSI, a single sperm is injected into a mature egg. The alternative to ICSI is “conventional” fertilization where the egg and many sperm are placed in a petri dish together and the sperm fertilizes an egg on its own (CDC, 2017).

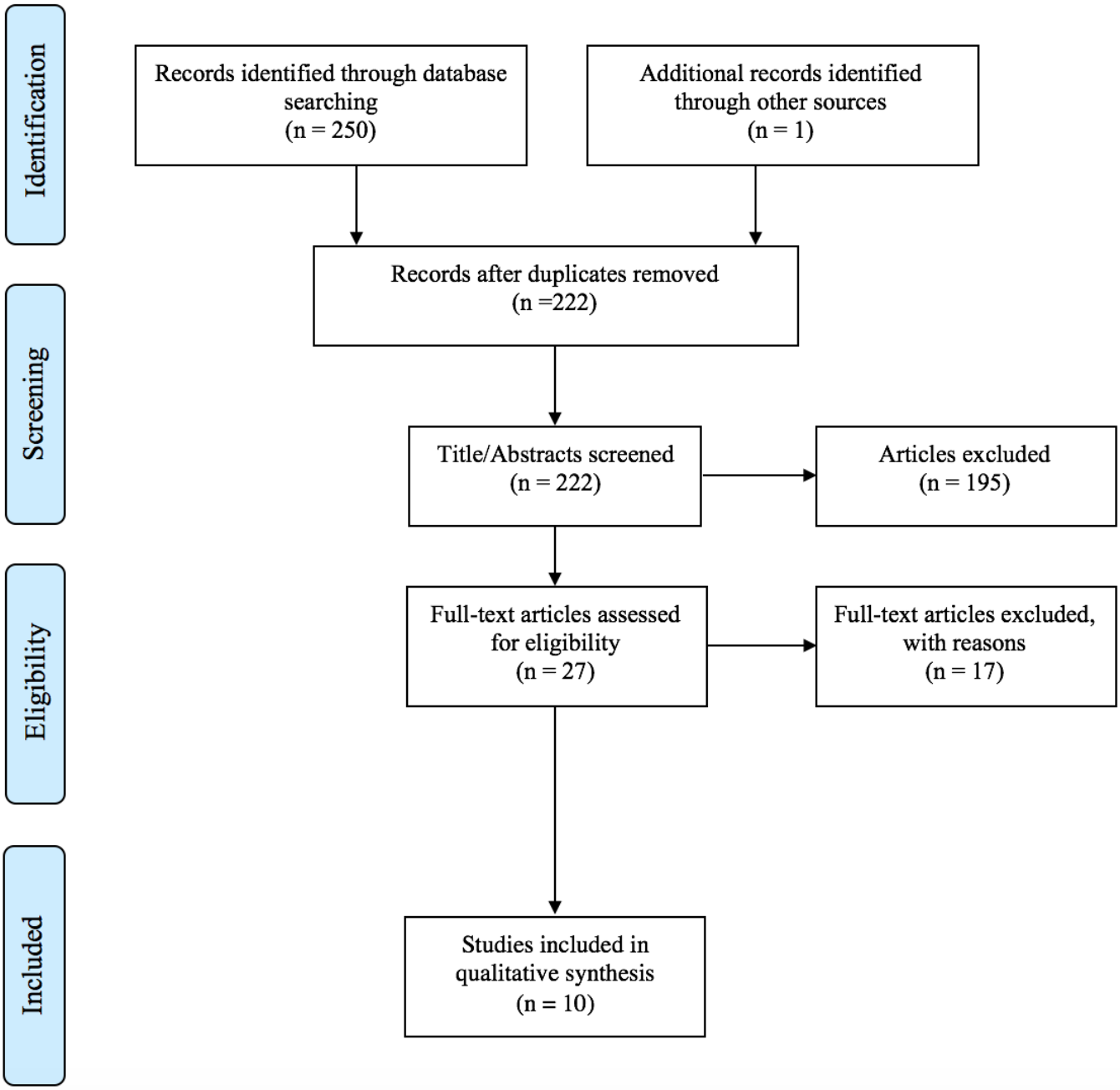
Ethical Considerations

This analysis was determined to be exempt from Institutional Review Board consideration because no human-subjects were involved and the study is a systematic review of existing literature.

RESULTS

By utilizing the search criteria, 251 articles were included in the primary analysis and dissection. Titles and abstracts of 251 articles underwent a screening process, leaving 222 articles after duplicates were removed. Of the 222 articles, 27 publications were considered for full-text review. 10 of these peer-reviewed publications fit the inclusion criteria and were relevant to ART and breastfeeding initiation, exclusivity, or duration were included in this systematic literature review (Figure 3. Literature Flow Chart). A list of excluded full-text articles with key reasons for exclusion can be found in Appendix A. All included studies were conducted in developed countries: Australia (N=4), Germany, (N=2), Taiwan (N=1), United States (N=1), Canada (N=1), Italy (N=1). There were no studies from low and middle income countries.

Figure 3. Flow chart of Literature Inclusion and Exclusion



Breastfeeding Trends in ARTC

This section presents the results of the 10 studies included in this review. Included articles were summarized into three breastfeeding categories: breastfeeding initiation (BFI), exclusive breastfeeding (EBF), and breastfeeding duration (BFD). Three tables were created to summarize the evidence and illustrate possible trends in of the association between breastfeeding outcomes and women who conceive with the assistance of ART compared to spontaneous conceptions (SC). For this review, a p-value below 0.05 is considered statistically significant.

Exclusive Breastfeeding

Table 1. Summary of Findings for Exclusive Breastfeeding

Key: ↓: statistically significant decreases in EBF in women who conceive via ART vs SC, ↑: statistically significant increases in EBF in women who conceive via ART vs SC, – not statistically significant

Table 1. **Summary of Findings for Exclusive Breastfeeding**								
Author/Year	Study Design	Sample Size	Country	Maternal Age (mean age, y)	Confounder	Main Outcome	Statistical Measure	Outcome Summary
Ludwig,2011	retrospective analysis; case-control study	472 women; ARTC= 236 SC= 236	Germany	ART =35.7y SC = 33.1y	parenting commitment, addictive behavior and sociodemographic factors (educational level, income)	EBF duration	ARTC = 6.5 mo SC = 6.1 mo; p = 0.096	–
Hammarberg, 2011	prospective cohort study	183 women	Australia	ART = 35y SC = 30y	anxiety, education, number of babies, quality of breastfeeding advice	EBF at 6 wks. EBF at 3mo	ARTC: 6 weeks = 77% 3 months =46% Australian pop. At 3 mo:57.3%; p = 0.004	↓ EBF
Fisher, 2013	cohort study	549 women (ART = x), (SC = x)	Australia	ART = 35.3y SC = 32.0y	Caesarean deliveries, education, anxiety, intention to breastfeed	EBF at hospital discharge EBF at 4 mo	At discharge: ARTC = 63.6% SC = 76.5% At 4 mo: ARTC = 41.3% SC = 53.8% p < 0.001	↓ EBF
Cromi,2015	matched case-control study	188 women (ART=94, SC=94)	Italy	ART= 35.7y SC = 35.4y	maternal age, parity, type of delivery, gestational age	EBF at 6 mo	ARTC = 42% SC = 48.9% p = 0.48	–
Quinn,2012	prospective cohort study	1296 women (ART =76)	Canada (Non-Caucasian ART=21, SC=30; Caucasian ART =55, SC=122)	ART = 32.9y SC = 30.8y	difficulty breastfeeding, fatigue, maternal age, income, marital status, first pregnancy	EBF at 4 mo	ARTC = 54.1% SC = 59.7% p = 0.99	–
Hammarberg, 2009	prospective longitudinal & cohort study	166 women	Australia	35-39y	pregnancy psychological functioning (mental health, stress, anxiety, depression), age over 25, higher level of education	ARTC EBF at 3 months compared to 1995 Australian National Health Survey	ARTC = 45% SC = 62% p = 0.0001	↓ EBF

A total of six studies discussed exclusive breastfeeding. None of the studies reported a statistically significant increase in EBF among the ARTC group. However, three of the studies did report a statistically significant decrease in EBF in ARTC. Fisher et al found that exclusive breastfeeding rates at hospital discharge (63.6%) and 4 months postpartum (41.3%) were lowest amongst ARTC women who experienced Caesarean prior to labor ($p < .001$), compared to SC at discharge (76.5%) and 4 months (53.8%) (Fisher et al., 2013). Similarly, Hammarberg et al described that a smaller proportion of participants at 3 months (46%), compared to the Australian population (57.3%) were exclusively breastfeeding ($p = 0.004$) (Hammarberg et al., 2011). In another study by Hammarberg et al, the proportion of the ARTC group (45%) breastfeeding their infants exclusively at 3 months were smaller than among women in the 1995 Australian National Health Survey (62%); p value = 0.0001 (Hammarberg et al., 2009).

On the other hand, three of the six studies could not conclude that a significant difference exits. In a study conducted by Cromi et al, EBF rates at 6 months for ARTC and SC were 42% and 48.9%, respectively ($p = 0.48$) (Cromi et al., 2015). In another study, Ludwig et al stated that there was no significant difference in the duration of the exclusive nursing period. The ARTC EBF rate was 6.5 months, while the SC EBF rate was 6.1 months ($p=0.096$). (Ludwig et al., 2011). Comparably, Quinn et al assessed EBF rates in ARTC and SC at four months postpartum. EBF ARTC and EBF SC were 54.1% and 59.7%, respectively with a p value of 0.99. (Quinn, 2012).

Although a trend of statistically significant decreases was observed in half of studies, there is insufficient evidence to compare the association between ARTC and EBF.

Breastfeeding Initiation

Table 2. Summary of Findings for Breastfeeding Initiation

Key: ↓: statistically significant decreases in BFI in women who conceive via ART vs SC, ↑: statistically significant increases in BFI in women who conceive via ART vs SC, – not statistically significant

Table 2. **Summary of Findings for Breastfeeding Initiation**								
Author/Year	Study Design	Sample Size	Country	Maternal Age (mean age, y)	Confounder	Main Outcome	Statistical Measure	Outcome Summary
Hammarberg/2009	prospective longitudinal & cohort study	166 women	Australia	35-39y	pregnancy psychological functioning (ex: mental health, stress, anxiety, depression), maternal age over 25, higher level of education	A third of participants either did not initiate breastfeeding or breastfed for <6 weeks	ARTC= 79% SC= 93% P = 0.04	↓ initiation
Hammarberg/2011	prospective cohort study	183 women	Australia	ARTC= 35y SC= 30y	anxiety, education, number of babies, quality of breastfeeding advice	Participants more likely than general population to initiate breastfeeding	ARTC = 89% SC = 83.3% P = 0.05	↑ initiation
Cromi/2015	matched case-control study	188 women (ART=94, SC=94)	Italy	ARTC= 35.7y SC = 35.4y	age, obesity, parity, breastfeeding experience, education, employment, maternal smoking during pregnancy, mode of delivery, birth weight, admission to the neonatal intensive care unit, gestational age at birth	Cases were as likely as controls to initiate breastfeeding	ARTC = 89.4% SC = 90.4% P = 1.0	–
Quinn/2012	prospective cohort study	1296 women (ART=76)	Canada (Non-Caucasian ART=21, SC=30; Caucasian ART =55, SC=122)	ARTC mean age = 32.9y SC mean = 30.8y	difficulty breastfeeding, fatigue, maternal age, income, marital status, first pregnancy	No significant differences in terms of breastfeeding initiation	ARTC = 97.3% SC = 93.3% P = 0.60	–
Fisher/2013	cohort study	549 women	Australia	ARTC = 35.3y SC= 32.0y	Caesarean deliveries, education, anxiety, intention to breastfeed	Not significant at discharge	ARTC= 93.8% SC = 94.9%	–

A total of five included articles reviewed breastfeeding initiation. One of the studies reported that there was a statistically significant decrease in BFI among ARTC women. Hammarberg et al conducted a study among a population of 166 Australian women. Many factors are associated with a higher rate of initiation and longer duration of breastfeeding including maternal age over 25, higher level of education, being partnered and having higher socioeconomic status (Hammarberg et al., 2009). Most of the participants in this study had these characteristics, but despite these, the rate of initiation of breastfeeding was not higher and the proportion breastfeeding at 3 months was significantly lower than among the general population of childbearing women. Almost a third of participants either did not initiate breastfeeding or breastfed for less than 6 weeks. The rate of initiation for ARTC (79%) compared to the general population of SC women in Australia (93%); $p = 0.04$) (Hammarberg et al., 2009). However, another study by Hammarberg reported a statistically significant increase in BFI among a population of 183 Australian women. Intention to breastfeed is an important determinant of initiation of breastfeeding (Hammarberg et al., 2011) and it may have been expected that those who initiated breastfeeding would continue to do so, at least for the first 6 weeks. Participants in this study were more likely than the general population of SC women in Australian to initiate breastfeeding at discharge. The ARTC and SC breastfeeding initiation rates were 89% and 83.3% ($p = 0.05$) (Hammarberg et al., 2011).

The three remaining studies reported no significant difference in breastfeeding initiation between women conceiving via ARTC or BFI in SC. In a study by Fisher et al, the rate of any breastmilk at discharge was reported. At discharge, no statistical significance could be determined. 93.8% of the ARTC group and 94.9% of the SC group were providing any breastmilk (Fisher et al., 2013). Cromi et al states that the cases (89.4% BFI) in their study were

as likely as their controls (90.4% BFI) to initiate breastfeeding (p=1.0) (Cromi et al., 2015). Likewise, among a population of 228 Canadian women, Quinn et al reported that while the ARTC BFI was 97.3% and SC BFI was 93.3%, there was also no significance in terms of breastfeeding initiation (p=0.60) (Quinn, 2012).

Overall, there is insufficient evidence to conclude an association between ARTC and BFI. Results were very mixed with one study reporting a significant increase, one a significant decrease and two studies reporting no difference

Breastfeeding Duration

Table 3. Summary of Findings for Breastfeeding Duration

Key: ↓: statistically significant decreases in BFD in women who conceive via ART vs SC, ↑: statistically significant increases in BFD in women who conceive via ART vs SC, – not statistically significant

Table 3. **Summary of Findings for Breastfeeding Duration**

Author/Year	Study Design	Sample Size	Country	Maternal Age	Confounder	Main Outcome	Statistical Measure	Outcome Summary
Michels/2016	population-based cohort study	4591 mothers included, (30% = 1361 mothers conceived with fertility treatments)	United States	28-30y	maternal age, race/ethnicity, body mass index (BMI), education, marital status, private insurance status, previous births, morbidities	Relative risk of breastfeeding cessation at 4, 8 and 12 months	4 months RR = 0.82 (0.66-1.03) 8 months RR = 0.93 (0.67-1.31) 12 months RR = 0.47 (0.25-0.88)	– BFD at 4 months – BFD at 8 months ↑ BFD at 12 months
McMahon/1997	controlled clinical study	ART = 70, SC= 63	Australia	greater than or equal to 28yr	psychosocial adjustment to early motherhood	Any breastfeeding at 4 months	ARTC = 68.8% SC = 74.6% P=X?	↓ BFD
Ludwig/2011*	retrospective analysis; case-control study	472 women (236 = ARTC, 236 = SC)	Germany	ARTC= 35.7y SC= 33.1y	parenting commitment, addictive behavior and sociodemographic factors (educational level, income)	Breastfeeding duration in months	ARTC = 11.5 months SC = 10.0 months p = 0.028	↑ BFD
Lee/2010	cohort study	21,248 mother and children pairs	Taiwan	ARTC= 33.2y SC= 28.8y	multiple gestation, having mother as caregiver in the daytime, socio-demographic	Any breastfeeding at 18 months	ARTC =5.9% (N=21) SC = (6.4%) (N=1262) p = 0.64	–
Fisher/2013	cohort study	549 women	Australia	ARTC=35.3y SC= 32.0y	Caesarean deliveries, education, anxiety, intention to breastfeed	Any breastmilk at 4 months	ARTC = 64.5% SC= 69.8%	↓ BFD

Cromi/2015	matched case-control study	188 women (ART=94, SC=94)	Italy	ART = 35.7 y SC = 35.4 y	age, obesity, parity, breastfeeding experience, education, employment, maternal smoking during pregnancy, mode of delivery, birth weight, admission to the neonatal intensive care unit, gestational age at birth	Any breastmilk at 6 weeks and 6 months	6 weeks ARTC = 20.2% SC = 5.3% p = 0.0035 6 months ARTC= 35.1% SC = 43.6% p = 0.28	↑ BFD at <6 weeks – BFD at > 6 months
Ludwig/2012*	matched-case control study	472 women (ARTC=236, SC= 236)	German	ARTC = 35.7y SC = 33.1 y	maternal age and education	breastfeeding duration in months	ARTC=11.9 months +/- 5.56 SC= 9.44 months +/- 3.84 p= 0.025	↑ BFD
Quinn/2012	prospective cohort study	1296 women (ART=76	Canada (Non-Caucasian ART=21, SC=30; Caucasian ART =55, SC=122)	ARTC= 32.9y SC= 30.8 y	difficulty breastfeeding, fatigue, maternal age, income, marital status, first pregnancy	infant currently receives some breast milk at 4 mo	ARTC = 71.6% SC = 79.3% p = 0.20	–

* indicates that full-text article was not available

Eight studies examined the association between ARTC and BFD. Of those eight, two studies showed a statistically significant increase in BFD among ARTC women. Ludwig et al found that women who had conceived by an IVF/ICSI-treatment nursed on average 1.5 months longer in comparison to participants with spontaneous conception (11.5 months +/- 4.9 (ARTC) vs. 10.0 months +/- 4.0 (SC), with a p value of 0.028) (Ludwig et al., 2011). Similarly, another report by Ludwig et al using the same number of participants, supported a longer breastfeeding duration for ARTC women compared to spontaneous conception. The ARTC BFD rate was 11.9 months +/- 5.56, while the SC BFD was 9.44 months +/- 3.84 (p= 0.025) (Ludwig, Ludwig, & Kentenich, 2012).

Two studies described varied statistical significance at different times of their study. Michels et al reported any breastfeeding rates at 4 months, 8 months, and 12 months. At 4 months and 8 months, there were no significant differences between groups (risk ratio (RR) of 0.82 (95% CI = 0.66–1.03) and 0.93 (95% CI = 0.67–1.31), respectively). However, at 12 months the ARTC group was 53% less likely to continue breastfeeding compared to the SC group (RR 0.47 (95% CI = 0.25–0.88), (Michels et al., 2016). The final study conducted by Cromi et al, reported a significant increase in the proportion of infants receiving any breastmilk at 6 weeks, 20.2% in the ARTC group and 5.3% (p=0.0035) in the SC group. However, at 6 months postpartum, no differences were found in mothers providing any breastmilk between women who used ART (35.1%) and women who conceived spontaneously (43.6%); p=0.28) (Cromi et al., 2015).

Two studies reported a statistically significant decrease in BFD. In a study by Fisher et al, the promotion of infants receiving any breastmilk at 4 months was 64.5% of the ARTC group and 69.8% of the SC group (Fisher et al., 2013). McMahon et al reported that at 4 months, the

ARTC group had a lower breastfeeding rate than the SC group. 68.8% of the IVF-ET group and 74.6% of the control group were still breastfeeding their infants (McMahon, Ungerer, Tennant, & Saunders, 1997).

In a study with Lee et al among a Taiwanese population, there was no significant difference in the proportion of infants receiving any breastmilk at 18 months (ARTC group (N=21) was 5.9% and the SC group (N=1262) was 6.4% (p= 0.64) (Lee et al., 2010). Similarly, no significance was reported in a study by Quinn et al (Quinn, 2012). The reported rates of the ARTC and SC groups with infants that were currently receiving some breast milk at four months postpartum were 71.6% and 79.3%, respectively with a p value of 0.20.

Overall, there is insufficient evidence to conclude an association between ARTC and BFD.

Other Breastfeeding Outcomes

Table 4. Summary of Findings for Other Outcomes

Table 4. **Summary of Findings for Other Outcomes**

Author/Year	Study Design	Sample Size	Country	Maternal Age	Confounder	Main Outcome	Statistical Measure
Wiffen/2016	observational study	16 women (ARTC=8, SC=8)	Australia	ARTC= 33y SC= 31y	antenatal steroids, polycystic ovarian syndrome, thyroid disease, caesarean birth, skin-to-skin	total milk volumes on day 4 and day 7	day 4 ARTC= (191 mL, SD= 110) SC=(285mL±225) day 7 ARTC= (374 mL, SD= 238) SC (601 mL, SD =243)
Castelli/2015	longitudinal nonexperimental cohort study	73 women	France	mean age= 32.7y	duration of infertility greater than 2 years, cesarean delivery, and history of formula feeding as newborns	higher breastfeeding rate of women who were breastfed as newborns than the rate of formula fed women	76% of breastfed women, chose breastfeeding 41% formula fed women, chose breastfeeding p=0.03
Castelli/2015	longitudinal nonexperimental cohort study	73 women	France	mean age= 32.7y	duration of infertility greater than 2 years, cesarean delivery, and history of formula feeding as newborns	in IVF population, the breastfeeding initiation rate was like that in the general French population	IVF breastfeeding initiation = 63% (n = 46)

Quinn/2012	prospective cohort study	1296 women (ART=76	Canada (Non-Caucasian ART=21, SC=30; Caucasian ART =55, SC=122)	ARTC= 32.9y SC= 30.8 y	difficulty breastfeeding, fatigue, maternal age, income, marital status, first pregnancy	Experienced any breastfeeding difficulties	ARTC = 88.2% SC = 90.1% p = 0.65
Ladores/2015	Qualitative secondary analysis	12 women	United States	mean maternal age= 34.33y	years of infertility prior to first child	Less than half of the participants still breastfeeding exclusively at 3 mo	n = 5, or 42%

*indicates that full-text article was not available

While some of articles reviewed for other outcomes did not fit the inclusion criteria, the results in these studies reported outcomes of interest. Four articles observed breastfeeding outcomes outside of initiation, exclusivity, and duration. Two of the four articles did not have SC control groups.

First, articles that looked at other breastfeeding outcomes like maternal reasons influencing feeding decisions and milk production, were observed. Castelli et al reported breastfeeding decisions among 73 French women who gave birth after ART. Among the women who gave birth after IVF, 63% (n = 46) chose breastfeeding. In the study population, 46 women were breastfed as newborns. Among them, 76% (N= 35) chose breastfeeding, and this rate was significantly higher than the breastfeeding rate (41%) of the women who were formula-fed as newborns (n = 27) (p = 0.03) (Castelli et al., 2015). They also found that in the IVF population, the breastfeeding initiation rate (N= 46, 63%) was like that of the general French population (60.2%) (statistical significance not reported). In another study, Wiffen et al measured 24-hour milk production on days 4 and 7 postpartum to examine any potential relationships that may exist between mode of conception and successful initiation of lactation in late preterm mothers. Although the mean total milk volumes were clinically lower on day 4 for the ARTC group (191 mL, *SD* = 110) compared to the SC group (285mL, *SD*=225) and on day 7 (374 mL, *SD* = 238) and (601 mL, *SD* =243) respectively, the differences were not statistically significant (day 4, p= 0.304; day 7, p = 0.079). (Wiffen & Fetherston, 2016). One study reported by Quinn et al (Quinn, 2012) was mentioned previously for EBF and BFI, however, this study also observed breastfeeding difficulties and infants that were currently receiving any breastmilk at four months postpartum. There were no significant differences in these outcomes. The reported rates of

ARTC and SC mothers who experienced any breastfeeding difficulties were 88.2% and 90.1%, respectively with a p value of 0.65.

Ladores et al (Ladores & Aroian, 2015) conducted a study among 12 first-time mothers in the United States as part of a larger phenomenological study. These mothers conceived their first-born child within the past 3 years after undergoing fertility treatment. All the participants initiated breastfeeding after birth. Participants reported that they wanted to breastfeed because of breast milk's health benefits for their infants and the bonding experience that breastfeeding facilitated. 10 of the 12 participants believed that breastfeeding embodied motherhood, and placed immense pressure on themselves to breastfeed exclusively. However, despite their desire to breastfeed, only a few of them met their goal. This study found that less than half of the participants (n=5, 42%) verified that they were still breastfeeding exclusively at 3 months postpartum (Ladores & Aroian, 2015).

DISCUSSION

Summary of Results

In this review, we investigated initiation, exclusivity, and duration of breastfeeding in women who have conceived with the help of ART. Currently it is still uncertain if mothers who conceive through ART will have different breastfeeding outcomes compared to those who conceive spontaneously. We identified 10 studies that discuss fertility treatment and breastfeeding practices. The limited evidence about the potential impact of an ART treatment history on breastfeeding capacity is inconclusive and contradictory, mainly because of significant methodological limitations in the studies to date, including recruitment strategies, inadequate sample sizes, lack of appropriate comparison groups, and failure to control for known risk factors for lactation difficulties (Cromi et al., 2015). Limited inference can be made as to why differences exist between mode of conception and breastfeeding outcomes, owing to small sample sizes, incomplete control for confounding by socioeconomic factors, and inappropriate adjustment for potential causal intermediates such as low birth rate and preterm birth.

Exclusive breastfeeding has many health benefits, both in the short term and the longer term, to infants and their mothers. Breastfeeding also promises cost savings compared to formula feeding. However, lower breastfeeding rates still exist in high-income countries, where women can afford ART treatments. Despite high breastfeeding initiation rates and continued improvement in breastfeeding duration, most states are not yet meeting HP2020 breastfeeding duration and exclusivity targets in the United States, where some of the lowest breastfeeding rates lie. With the growing number of infants born through ART, there is a need for future research to better understand breastfeeding implications. This systematic review aimed to provide awareness of the currently known factors that contribute to lack of initiation or short

duration of breastfeeding among women who give birth after ART to better promote assistance with breastfeeding practice.

A wide range of socioeconomic, cultural, and individual factors affect breastfeeding rates. Factors such as age, level of education, occupation, family and community, pregnancy psychological functioning and mode of delivery were all discussed as determinants of breastfeeding for both mothers who conceived spontaneously and with the use of fertility treatments. Women who conceive with ART are more likely to be first-time mothers; they are, on average, older and more likely to have pregnancy complications, multiple births, operative delivery, labor induction, premature birth, and low birth weight babies than women who conceive spontaneously (Cromi et al., 2015). Duration of exclusive breastfeeding has been associated with socio-economic advantage, higher level of education, lower levels of depression and anxiety, a more resilient personality and intention to breastfeed. Data indicates that even when these factors are controlled, older women are more likely than younger women to maintain breastfeeding (Fisher et al., 2013). Women who are older than 35 experience higher rates of Caesarean births than those who are younger, but are the group most likely to initiate and maintain exclusive breastfeeding (Fisher et al., 2013). ARTC women have the highest rates of Caesarean births, which has unfavorable consequences for breastfeeding, especially when conducted prior to labor. Although relationships between stress and anxiety during the postpartum period and implications for breastfeeding remain poorly characterized, evidence suggests a relationship between early postpartum maternal anxiety and reduced exclusivity and continuation of breastfeeding (Hammarberg et al., 2009). Maternal anxiety and depression has been suggested to undermine breastfeeding through physiological stress responses and reduced confidence and self-efficacy.

These data demonstrate that the relationships between factors such as age, mode of conception, birth and breastfeeding are complex. Furthermore, fertility treatment classifications, definitions of breast feeding duration, and selection criteria across studies are quite heterogeneous. Overall, included studies demonstrated varied significance between mode of conception and breastfeeding outcome. 3 out of 5 studies reported no significance in breastfeeding initiation, 1 reported an increased significance and 1 reported a decreased significance. Likewise, with exclusive breastfeeding, 3 out of 6 studies reported no significance. The remaining 3 studies reported a significant decrease in exclusive breastfeeding. For breastfeeding duration, 3 out of 8 studies reported a significant decrease, 2 out of 8 studies reported a significant increase, 2 studies described varied statistical significance at different times of their study, and 1 study reported no significance. There was no specific trend in significance depending on timing.

There is insufficient evidence to conclude an association between ARTC and breastfeeding initiation, exclusivity and duration. or BFI.

There were inconsistent results in breastfeeding initiation, exclusivity, and duration. Some of these differences across studies may be due to differences in breastfeeding outcome definitions, timing of assessment, sample sizes, healthcare/lactation support access and population demographics. However, even within the context results varied. For example, two similar Australian studies that had opposing results due to the timing of the assessment.

One Australian cohort of 166 women, who conceived with ART, found that one third of participants did not initiate breastfeeding or breastfed for less than 6 weeks. The proportion exclusively breastfeeding at three months (45%) was less than the Australian national average of 62% (Hammarberg et al., 2009). Hammarberg et al. found that anxiety in late pregnancy was an

independent risk factor for early cessation of breastfeeding in mothers who used ART. Although relationships between anxiety and stress during the postpartum period and implications for breastfeeding remain poorly characterized, evidence suggests a relationship between early postpartum maternal anxiety and reduced exclusivity and continuation of breastfeeding (Hammarberg et al., 2009). The women in this study completed telephone interviews and postal questionnaires 3 months postpartum.

Another Australian cohort study had opposing results showing that women who conceived using ART were more likely to initiate breastfeeding 89% vs. 83.3%, although by 3 months postpartum a smaller proportion were exclusively breastfeeding 46% versus 57.3% compared with the general population of childbearing Australian women (Hammarberg et al., 2011). The women in this study completed telephone interviews and postal questionnaires in pregnancy and 3, 8 and 18 months after the birth. Leaving much room for recall bias and error.

Other studies have shown no difference between women who conceived spontaneously versus though who conceived through ART. A Canadian study (Quinn, 2012) and an Italian study (Cromi et al., 2015) found no difference in breastfeeding initiation and exclusivity between SC and ARTC. McMahon, et al. (McMahon et al., 1997) also found no difference in breastfeeding outcomes when comparing primiparous women in Australia with no history of infertility and those who had IVF-ET.

The reports demonstrated inconsistent results in breastfeeding trends across modes of conception but small sample sizes and use of unadjusted analyses for comparisons (e.g., chi-square tests) are problematic. Outliers that may have been present in the data sets would have be removed as they have a large impact on the calculated means of small populations.

Strengths and Limitations

This review has several limitations. 100% (N=14) of the studies included in this review were reported in developed countries, with 35.7% (N=5) of those studies reported in Australia. none of the studies reported were in developing countries. Global research on ARTs has been highly concentrated among the world's richest countries while developing countries have indicated the least contribution to the research on ARTs and reproductive technologies. As research on ARTs and breastfeeding has been distributed disproportionately among countries, further investigations are needed to explore these patterns between and within countries.

We used standard electronic searching strategies, using appropriate key words in a specific search string. At conflicting stages of the review process, a conflict resolver decided whether an article was included or excluded. However, it is possible that some relevant articles may not have been identified in our search, and that the results of these articles would have changed the recommendations and conclusions. To mitigate this risk, two reviewers independently identified records in Covidence retrieved from the databases, and independently selected articles for full-text review based off inclusion criteria.

We limited the search to English-language articles. No articles were excluded based on English language. This does not seem like a limitation to our study. Another potential limitation of this review is the inclusion of articles that used retrospective designs, which introduces the possibilities of reporting errors and recall bias, as breastfeeding outcomes were based on self-report of recalled practices. ART has a variety of fertility methods. Further research to explore other modes of ART and ARTC in developing countries is needed.

This review provides global insight into the breastfeeding practices among women who undergo ART. It is also the first systematic review to look at breastfeeding outcomes and ART.

Another strength is that this review had no specific geographic scope. However, very few studies explore the factors of breastfeeding determinants and ART in developing countries. This review also had the advantage of having two reviewers, as opposed to one. This may have limited the exclusion of abstracts or full-text articles with important results.

Further Research Needs

Small sample sizes, such as 102 mothers in Italy (Cromi et al., 2015), 166 (Hammarberg et al., 2009) mothers in Australia and 183 (Hammarberg et al., 2011) in another Australian cohort, may have insufficient power to detect associations between mode of conception and breastfeeding outcomes. A smaller sample will give a result which may not be sufficiently strong enough to detect a difference between the groups.

Beyond demographics, obstetrics, and facility-level factors, for breastfeeding failure in mothers conceiving through ART, should be researched. Future research should therefore concentrate on identifying potential modifiable factors, like breastfeeding intention (Fisher et al., 2013), breastfeeding self-efficacy (Rollins et al., 2016) and social support (McMahon et al., 1997), that contribute to breastfeeding failure among women who give birth after ART. Mothers who conceived through ART did not differ from control mothers on measures of anxiety, postnatal depression, marital satisfaction, or use of support services. However, in one study they reported lower self-esteem and lower maternal self-efficacy (McMahon et al., 1997). With the increase of ART fertility treatment, future research should concentrate on expanding sample sizes by using data from more than one birthing facility, unlike the study designed by Cromi et al (Cromi et al., 2015). With larger sample sizes, generalizability may be minimized or eliminated. Research should also focus on that customized breastfeeding support strategies can be developed to address these factors in the clinical setting.

There is also a need for a more comprehensive control of confounders in the further study on the effect of breastfeeding, and for research on the associations between mode of conception and breastfeeding outcomes in developing countries. Some confounders identified in this review included Caesarean deliveries (Fisher et al., 2013), maternal age (Ludwig et al., 2012; Michels et al., 2016; Quinn, 2012), education (Ludwig et al., 2012), pregnancy psychological functioning such as stress and anxiety (Hammarberg et al., 2009), and employment (Ludwig et al., 2011; Quinn, 2012). ART increases the risk of mothers undergoing a Caesarean birth, which negatively impacts breastfeeding initiation and duration. In a study by Ludwig et al., there was no relevant difference in breastfeeding outcomes between ARTC and SC groups when factoring only the educational level. However, there was a statistically significant increase of ARTC breastfeeding duration when factoring for maternal age (Ludwig et al., 2012). Pregnancy psychological functioning was reported to have a negative breastfeeding effect on both BFI and EBF (Hammarberg et al., 2009).

Future Recommendations

This review found that there is insufficient evidence of breastfeeding trends in ARTC. Larger, longer term studies of breastfeeding outcomes in both the United States and internationally are needed. Larger cohort studies that can be matched on attitude with intention or mode of delivery with initiation, and adjusted for ART fertility treatment are recommended. While most mothers who turn to ART due to infertility fall around the mean age of 35 years old, these mothers are usually first time mothers. ART is one of many factors that should be considered in comprehensive strategy to improve breastfeeding rates. It is recommended that healthcare providers should offer and encourage breastfeeding support strategies to their patients. Despite the known health benefits of breastfeeding, in many countries, a considerable

proportion of newborns are not breastfed within 1 hour after birth in accordance with the WHO recommendation. Breastfeeding support should include facilitation to motherhood, learning to read and understand the baby's cues, and building up confidence to breastfeed. Support should also focus on mother who encounter similar factors that may contribute to early cessation of breastfeeding, such as pain, child latching issues, and lack of lactation. As highlighted in *The Lancet* (Rollins et al., 2016), future strategies should focus on enhancing the determinants that operate at multiple levels and affect breastfeeding decisions and behaviors over time. Strategies should focus on positively influencing social norms to support recommended breastfeeding practices. Future efforts should take the approach to address health systems, close family members, including fathers, as well as places of employment on the benefits of optimal breastfeeding practices.

CONCLUSION

Currently there is inadequate evidence to support the need for additional breastfeeding support for women who undergo ART beyond established risk factors like maternal age, employment, low birthweight/preterm infant, pregnancy psychological functioning and Caesarean deliveries. While there are many known factors associated with breastfeeding initiation, exclusivity, and duration of breastfeeding, there remain questions on how to best target and support mothers to reach their breastfeeding goals.

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APPENDIX A: LIST OF EXCLUDED STUDIES

All excluded studies listed below were reviewed in their full-text version. Following each reference, in italics, is the reason for exclusion. “Excluded,” in this context, means “not included for data abstraction.” Reasons for exclusion signify only the usefulness of the articles for this study and are not intended as criticisms of the articles.

1. Thatcher, S (2006): Pregnancy outcome in infertile patients with polycystic ovary syndrome who were treated with metformin – *wrong patient population*
2. Gilling-Smith, C (2006): Fertility management of HIV couples - *wrong patient population*
3. Fisher, J (2012): Admissions for early parenting difficulties among women with infants conceived by assisted reproductive technologies: A prospective cohort study – *wrong outcomes*
4. Fisher, J (2002): Health and social circumstances of women admitted to a private mother baby unit. A descriptive cohort study – *wrong outcomes*
5. Boivin, J (2009): Associations between maternal older age, family environment and parent and child wellbeing in families using assisted reproductive techniques to conceive – *wrong outcomes*
6. Berlin Jr, C (2007): “Exclusive" breastfeeding of quadruplets – *wrong study design*
7. Barnes, M (2013: Experiences of birth and breastfeeding following assisted conception – *wrong study design*
8. Barnes, M (2012): Outcomes for women and infants following assisted conception: implications for perinatal education, care, and support – *wrong study design*
9. Bajoria, R (2009): Current perspectives of fertility and pregnancy in thalassemia – *wrong outcomes*

10. Azim, H (2011): Motherhood after breast cancer: searching for la dolce vita – *wrong patient population*
11. Applegarth, L (1995): Families created through ovum donation: a preliminary investigation of obstetrical outcome and psychosocial adjustment – *wrong outcomes*
12. Wiffen, J (2016): Relationships between assisted reproductive technologies and initiation of lactation: Preliminary observations – *wrong study design*
13. Cuello, J (2017): Multiple sclerosis and pregnancy: a single-centre prospective comparative study – *no control group*
14. Scholefield, H (2002): A wise baby knows its mother! Do babies born after ovum donation successfully breast-feed? – *no control group*
15. Castelli, C (2015): Maternal factors influencing the decision to breastfeed newborns conceived with IVF – *no control group*
16. Zegers-Hochschild, F (2010): Reproductive performance in oocyte donors and their recipients: Comparative analysis from implantation to birth and lactation – *no control group*
17. Ladores, S (2015): First-Time Mothers with a History of Infertility: Their Internalized Pressure to Breastfeed

APPENDIX B: DATA EXTRACTION SHEET

Author/Year	Study Design	Confounders	Sample Size	Maternal Age	Type of ART	Country	What did they control for?
Michels. 2016	population-based cohort study	maternal age, race/ethnicity, body mass index (BMI), education, marital status, private insurance status, previous births, morbidities	4591 mothers included, (30% = 1361 mothers conceived with fertility treatments)	28-30y	ovulation induction, and artificial insemination	United States	direct effects of fertility treatment on feeding, independent of preterm birth
McMahon, 1997	controlled clinical study	psychosocial adjustment to early motherhood	ARTC= 70, SC= 63	greater than or equal to 28y	IVF-ET	Australia	women with no previous history of infertility
Ludwig, 2012*	matched case-control study	maternal age and education	472 women (236 = ARTC, 236 = SC)	ARTC = 35.7y SC = 33.1y	IVF/ICSI treatment	Germany	maternal age and education
Ludwig, 2011*	retrospective analysis; case-control study	parenting commitment, addictive behavior and sociodemographic factors (educational level, income)	472 women (ARTC=236, SC=236)	ARTC= 35.7y SC= 33.1y	IVF/ICSI treatment	Germany	psychosocial factors
Lee, 2010	cohort study	multiple gestation, having mother as caregiver in the daytime, socio-demographic	21,248 mother and children pairs	ARTC= 33.2y SC= 28.8y	various fertility treatments	Taiwan	growth in children born after ART
Hammarberg, 2009	prospective longitudinal study of consecutive cohort of women	pregnancy psychological functioning (ex: mental health, stress, anxiety, depression), maternal age over 25, higher level of education	166 women	35-39y	embryo transfer	Australia	admissions rates to residential early parenting services (REPSs) after assisted conception vs spontaneous

Hammarberg, 2011	prospective cohort study	anxiety, education, number of babies, quality of breastfeeding advice	183 women	ARTC= 35y SC= 30y	not specified	Australia	the general population of childbearing Australian women to initiate breastfeeding vs. ART conceiving participants
Fisher, 2013	cohort study	Caesarean deliveries, education, anxiety, intention to breastfeed	549 women	ARTC = 35.3y SC= 32.0y	not specified	Australia	Caesarean birth to breastfeeding initiation and duration
Cromi, 2015	matched case-control study	age, obesity, parity, breastfeeding experience, education, employment, maternal smoking during pregnancy, mode of delivery, birth weight, admission to the neonatal intensive care unit, gestational age at birth	188 women (ART=94, SC=94)	ART = 35.7y SC = 35.4y	IVF and embryo transfer (ET); ovulation induction or artificial insemination	Italy	matched control cohort of women who gave birth with no history of ART
Quinn, 2012	prospective cohort study	difficulty breastfeeding, fatigue, maternal age, income, marital status, first pregnancy	1296 women (ART=76)	ARTC mean age = 32.9y SC mean = 30.8y	Fertility-enhancing drugs and invasive procedure: artificial insemination; IUI: intrauterine insemination; IVF: in vitro fertilization; ICSI: intracytoplasmic sperm injection	Canada	breastfeeding rate in women who conceived with ART vs spontaneously

* indicates that full-text article was not available