EXERCISE INTERVENTIONS AND FERTILITY OUTCOMES FOR WOMEN WITH OBESITY AND EXPERIENCING INFERTILIY: A NARRATIVE REVIEW

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Abstract

Introduction: Obesity negatively impacts fertility. Women with obesity and experiencing infertility may improve fertility outcomes through exercise, however there is limited evidence on exercise prescription for this population. Specifically, there is limited information on: (1) exercise interventions that are effective for women with obesity and experiencing infertility, and (2) fertility outcomes impacted by exercise interventions. **Purpose:** This narrative review will provide an analysis of current exercise interventions and the fertility outcomes reported in the literature. **Methods:** A systematic search was completed in PubMed, Embase, Cochrane, and CINAHL. Inclusion criteria for this review included quantitative studies published between 2005-2021 reporting on exercise interventions for women (aged 18-40 years), experiencing obesity (defined as BMI >28kg/m^2), and infertility (lasting >1 year). Data were extracted on exercise technique, intensity, duration, and fertility outcomes. **Results:** Out of 574 articles, 16 publications met review criteria and were included. Ten of the 16 studies demonstrated improvements in the reported primary outcome, and all studies reported benefits in at least one fertility outcome. Cyclic exercise (i.e., walking, cycling) is the technique most incorporated into the exercise intervention, though a combination of cyclic, acyclic (i.e., circuit training, bootcamp), or individualized is often used. Several fertility outcomes are reported; however, rate of conception, pregnancy, and live birth rates are the most common. **Conclusion:** There are large variations in the specific exercise prescriptions recommended to improve fertility. Most studies examined reported statistically significant positive changes in fertility outcomes after an exercise.

Keywords: Obesity, Exercise, Infertility, Review

General Summary

Introduction: Obesity negatively impacts fertility. Women with obesity and experiencing infertility may improve their fertility outcomes through exercise, however there is limited evidence on exercise prescription for this population. **Purpose:** This review provides a description and investigation into the types of exercise and fertility outcomes examined in obesity and infertility research. **Methods:** A search was completed in four databases. This review included studies published between 2005-2021 reporting on exercise programs for women with obesity and experiencing infertility. Data were extracted on information related to the exercise programs and fertility outcomes. **Results:** Out of 574 articles, 16 publications met review criteria and were included. The exercise programs examined consistently led to improvements in fertility outcomes. Cyclic exercise (i.e., walking, cycling) is the most widely used exercise technique. A range of fertility outcomes are reported however, rate of conception, pregnancy, and live birth rates are consistently explored. **Conclusion:** The exercise programs recommended to improve fertility vary widely. Most studies examined reported improvements in fertility after an exercise intervention.

Keywords: Obesity, Exercise, Infertility, Review

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List of Abbreviations

Abbreviation	Definition
ART	Assisted Reproduction Technologies
ACSM	American College of Sports Medicine
BMI	Body Mass Index
HIIT	High Intensity Interval Training
IVF	In Vitro Fertilization
IUI	Intrauterine Insemination
NL	Newfoundland and Labrador
PA	Physical Activity
PCOS	Polycystic Ovarian Syndrome
RCT	Randomized Controlled Trial
SHBG	Sex Hormone Binding Globulin
WHO	World Health Organization

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Chapter One Co-Authorship Statement

Along with my supervisors Dr. Daniel Fuller and Dr. Erin McGowan from Memorial University, direction for the aim and purpose of this study was determined. I conducted comprehensive literature reviews for this chapter both during the time of writing this thesis and prior for graduate course assignments in HKR 6000 and HKR 6001 under the supervision of Dr. Daniel Fuller and Dr. Pamela Ward, respectively. Both supervisors provided feedback and engaged in discussions pertaining to this chapter.

Chapter One: Introduction

1.1 Background

Infertility can be defined in multiple ways, such as the inability to conceive after twelve or more months of natural fertilization (Habbema et al., 2004). There are multiple ways infertility can be defined because it cannot be confirmed by pathological symptoms; rather it is the absence of being pregnant (Greil et al., 2010). Infertility may also be defined as the inability to become pregnant while "being exposed to the risk of conception" (Bushnik et al., 2012, p. 740). Definitions of infertility have evolved over time, and how infertility is defined has the potential to impact the rates of infertility reported (Bushnik et al., 2012). Given that the definition of infertility is related to the absence of conception or achieving pregnancy, fertility is the ability to do just that. By this definition, miscarriage, also known as spontaneous abortion, is not considered an infertility issue because the ability to conceive is not the problem (Statistics Canada, 2003). Therefore, for the purpose of this thesis, both fertility and infertility are directly related to one's ability or inability to conceive, respectively. There are two types of infertility, primary and secondary. The definition of primary infertility is essentially synonymous with infertility however, secondary infertility is when a woman was previously able to conceive at least once and is now unable to do so (Zegers-Hochschild et al., 2017). Throughout the literature, changes in one's fertility may be referred to as a change in fertility, fertility-related outcomes, reproductive outcomes, or fertility outcomes (Kiel et al., 2018; Maiya et al., 2008; Mutsaerts et al., 2016; Sim et al., 2014). For consistency throughout this thesis, it will be referred to as fertility outcomes. This is because there are a multitude of factors (e.g., diet, exercise, genetics, environmental factors) that may have an impact on one's overall fertility. As such, fertility can be measured in many ways. Fertility outcomes may include, but are not limited to, insulin sensitivity, hormones such as sex hormone binding globulin (SHBG), ovulation, and menstrual cyclicity (Hakimi & Cameron, 2017; Miller, 2005; Palomba et al., 2008).

Globally, in 2010, it was estimated that there were 48.5 million couples experiencing infertility (Mascarenhas et al., 2012). Rates of infertility increased significantly in Canada regardless of the definition used between the 1990's to 2010 (Bushnik et al., 2012). In Canada, infertility rates have doubled since the 1980's, and now impacts one in six couples (Government of Canada, 2019). In recent years, the fertility rate in Canada has been declining with the lowest being in 2020, when the fertility rate was 1.40 children per woman (Provencher et al., 2018; Statistics Canada, 2021). Canada reported record low fertility rates in both 2019 and 2020 (Statistics Canada, 2021). Fertility rate is not indicative of infertility rate; however, it is something that should be considered when looking at the bigger picture. A possible explanation for the increase in infertility reported is a delay in childbearing as women are often older when attempting their first pregnancy than they would have been in previous years (Bushnik et al., 2012). Simultaneously, there has been an increase in rates of obesity for women of childbearing age over time (Bushnik et al., 2012). The presence of obesity and increasing age have consistently been shown to negatively impact fertility outcomes (Brewer & Balen, 2010; Gambineri et al., 2002; Kelly-Weeder & Cox, 2007).

A body mass index (BMI) greater than 25kg/m^2 is considered overweight, whereas a BMI greater than 30kg/m^2 is considered obese (World Health Organization, 2020). Like many diseases, the cause of obesity is quite complex involving interactions between an individual's biological, physiological, psychosocial, and environmental factors (i.e., their environment and genotype combined) (Shook et al., 2014). Obesity is common among Canadians and has been rising since the 1980's (Statistics Canada, 2019). As of 2019, approximately one in four

Canadians reported being obese (Statistics Canada, 2019). This is important, because obesity may negatively impact fertility outcomes at many different stages of the reproductive cycle (Brewer & Balen, 2010; Jungheim et al., 2013; Silvestris et al., 2018; Talmor & Dunphy, 2015). In fact, women with obesity are three times more likely to experience infertility compared to women with a normal BMI (18.5-24.9 kg/m^2) (Brewer & Balen, 2010).

Despite the negative effect of obesity on outcomes related to fertility, there are various approaches to help women with obesity and experiencing infertility improve their fertility outcomes. Medical interventions such as pharmaceutical (i.e., metformin, clomiphene citrate) and surgical procedures (i.e., bariatric surgery, in vitro fertilization (IVF)), as well as behavioral interventions including physical activity (PA) participation, motivational counselling, diet-focused interventions, and combinations of each are all possible strategies to improve fertility outcomes (Al-Eisa et al., 2017; Hakimi & Cameron, 2017; Mutsaerts et al., 2016). Medical interventions can be quite invasive as well as costly, especially in areas where access to treatment might be limited or unavailable, such as in Newfoundland and Labrador (NL) (Maxwell et al., 2018; *Ottawa Fertility Centre*, n.d.; *Regional Fertility Program*, n.d.; *Victoria Fertility Center*, n.d.). On the other hand, PA and exercise interventions have been shown to increase menstrual regularity, several metabolic parameters important for reproduction, and ovarian function with minimal cost in comparison to various medical interventions (Miller, 2005; Silvestris et al., 2018). Additionally, improving fertility through PA and exercise could be a cost-effective way to reduce the demand on medical and pharmaceutical interventions.

Elements of PA include bodily movement resulting in energy expenditure that is positively correlated with physical fitness (Caspersen et al., 1958). The definition of exercise also includes these elements; however, exercise includes planned and structured movement completed with an objective to either improve or maintain one's physical fitness (Caspersen et al., 1958). Exercise interventions that include healthy eating can have a benefit on outcomes related to fertility, such as improved insulin sensitivity, and increased SHBG, which impact resumption of ovulation (Hakimi & Cameron, 2017). In comparison to diet interventions alone, structured exercise training programs have a greater compliance rate, and show greater improvements to outcomes related to infertility, such as ovulation and pregnancy rates (Palomba et al., 2008). Despite the benefits, it can be challenging to translate behavioural interventions into clinical practice to manage obesity (i.e., good exercise and diet habits). This challenge may be related to exercise barriers everyone faces including motivation, time, and cost. However, women experiencing obesity related infertility also have the additional challenge of experiencing weight stigma and shaming (Andajani-Sutjahjo et al., 2004; Mulherin et al., 2013; Sharifi et al., 2013). Weight stigma and weight shaming can lead to increased weight through anxiety and unhealthy eating behaviors rather than motivate the women to improve diet and exercise (O'Brien et al., 2016; Salas, 2015). In addition to the individual barriers, physicians and staff in fertility clinics may not have the resources to take an active role in providing an appropriate exercise intervention for this population (Rooney & Domar, 2014). Staff often experience high workloads and the degree of information regarding exercise prescription needed, requires the knowledge of a trained exercise specialist and is outside the scope for most physicians (Brody, 2012; Rooney & Domar, 2014). There are many challenges in both the adoption and maintenance of physically active behaviors. It is unfortunate that changing behaviours is so complex since exercise has a critical role in preventing, controlling, and reducing the impact obesity on fertility.

1.2 Purpose of Study

An exercise program for women defined as obese and experiencing infertility can have many benefits on mechanisms related to infertility, such as restoration of menstrual cycles, improving rates of both ovulation, and pregnancy (Al-Eisa et al., 2017; Conn, 2010; Duval et al., 2015). However, there is a lack of consensus on the type of exercise, frequency, intensity, and setting to prescribe to improve reproductive outcomes among this population (McLean & Wellons, 2012). There are no evidence-based guidelines on how women defined as obese and experiencing infertility can improve their fertility through exercise (Lundgren et al., 2016). The primary purpose of this study was to determine current exercise interventions used in obesity-related infertility literature. With a secondary purpose to determine how fertility outcomes are being measured in this literature. To assess the impact of exercise interventions aimed at improving outcomes related to fertility for women defined as obese, we need to understand the exercise protocols used, and the outcomes assessed in the interventions. The collective evidence on the components of the exercise interventions, and their subsequent impact on specific outcomes related to fertility have been closely examined. The review will identify knowledge gaps and provide future direction for exercise interventions aimed at improving fertility outcomes in women living with obesity-related infertility.

1.3 Contributions / Significance

A critical, systematic narrative review is warranted as there is lack of consensus on the exercise intervention that may be most beneficial for improving fertility outcomes for women defined as obese and experiencing infertility. This review aims to fill this gap by synthesising the current knowledge in the literature around the impact of exercise interventions on fertility outcomes for this population. A review contributes not only to the literature but, more importantly, to improving the understanding and implication of accurate exercise prescription for this population which may maximize the benefits to fertility outcomes. Currently, there is not enough literature on exercise interventions for women experiencing obesity-related infertility to understand the dose-response for this population. The goal of a narrative review is to describe and synthesize the literature to better inform future development of exercise interventions (Kong et al., 2014). This review can help to develop evidence-based recommendations about physical activity interventions for improving fertility outcomes for women with obesity and experiencing infertility. This information may guide practitioners in the field, such as fertility physicians and exercise specialists on which types of exercise interventions are most likely to improve fertility outcomes. As well, this review has the potential to impact future fertility outcomes used by researchers, physicians, and those involved directly in the development and implementation of exercise interventions for this population. This review will identify which fertility outcomes are being explored most consistently in the literature. By identifying gaps that need further investigation this narrative review has the potential to improve the quality of obesity-related infertility research.

1.4 Thesis Format

This thesis follows a manuscript style which is organized into four main chapters consisting of an introduction, literature review, manuscript, and summary. Given that the chapters of a manuscript style thesis are “stand alone” documents, references are included at the end of each chapter. The introductory chapter includes an overview of relevant literature, how this research fits into the larger context, and outlines the objectives. The manuscript chapter consists of an introduction, methods, results, discussion, and conclusion. The summary chapter includes a summary, conclusion, and future directions. This thesis has been formatted using American Psychological Association (7th edition) referencing style.

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Chapter Two Co-Authorship Statement

I conducted comprehensive literature reviews for this chapter both during the time of writing this thesis and prior for graduate course assignments in HKR 6000 and HKR 6001 under the supervision of Dr. Daniel Fuller and Dr. Pamela Ward, respectively. Along with my supervisors Dr. Daniel Fuller and Dr. Erin McGowan from Memorial, I set the research objectives for this study. Both supervisors provided feedback and edited this chapter prior to submission.

Chapter Two: Literature Review

2.0 Introduction

Obesity is a global epidemic and a major public health concern. Defined as a body mass index (BMI) of greater than 30kg/m^2, the causes of obesity are multifactorial and complex (World Health Organization, 2020). It is well documented that obesity negatively impacts fertility outcomes and may result in experiencing infertility (Brewer & Balen, 2010; Jungheim et al., 2013; Silvestris et al., 2018; Talmor & Dunphy, 2015). Infertility can be defined as the inability to conceive after twelve or more months of natural fertilization (Habbema et al., 2004). Women with obesity are three times more likely to experience infertility compared to women with a normal BMI (18.5-24.9 kg/m^2) (Brewer & Balen, 2010). An intervention is often needed as fertility outcomes, such as ovarian function, may be negatively affected for overweight women (BMI >25kg/m^2), resulting in greater time to conceive and/or experiencing infertility (Silvestris et al., 2018). Adhering to a proper diet and being physically active is often emphasised for women with obesity (Kennedy et al., 2006). This is because, there are many known benefits of exercise participation for women with obesity and experiencing infertility (i.e., resumption of ovulation, improved live birth rates).

The following review of literature will outline existing knowledge in the field of obesity-related infertility including trends of obesity and infertility in Canada and Newfoundland and Labrador (NL), common fertility outcomes, and possible interventions for improving fertility outcomes. Barriers and facilitators to exercise participation for this population will also be examined. Lastly, exercise and diet interventions for women with obesity and experiencing infertility will be briefly summarized. Currently, despite the known benefits of exercise participation, there is no consensus on the type, frequency, intensity, and setting to prescribe to attain the most beneficial exercise to treat infertility in this population. Many factors such as diet, exercise, and smoking can play a role in the magnitude of complications a woman with obesity may experience (Pasquali et al., 2003). To better appreciate the complex relationship between obesity and infertility, we must first broaden our understanding of the multitude of factors at play for women with obesity and experiencing infertility.

2.1 Obesity

Obesity is defined as having a BMI of greater than 30kg/m^2 (World Health Organization, 2021a). The causes of obesity are multi-factorial and complex, involving interactions between an individual's biological, physiological, psychosocial and environmental factors (Shook et al., 2014). In a general sense, obesity is a disease and is developed through interactions of one's environment and their genotype (Gray et al., 2006). Obesity was first defined as a disease in 2013, however, for a while it seemed unclear whether obesity was a disease itself or a condition that leads to disease (Meldrum et al., 2017). Recent guidelines published in 2020, makes it clear that obesity is a chronic disease characterized by abnormal or excess adipose tissue that impairs health (CMAJ, 2020). Obesity effects all ages and socioeconomic groups, however, like many chronic diseases there are many factors that increase the likelihood of experiencing obesity for example race, ethnicity, age, and education (Center for Disease Control and Prevention, 2019).

Globally, rates of obesity have been increasing since the 1980's in both developed and developing countries (Ng et al., 2014). It has been estimated that there are 671 million people worldwide who are defined as obese (Ng et al., 2014). The World Health Organization (WHO) has referred to this as "globesity", a global epidemic of overweight and obesity (World Health Organization, 2021b). Indeed, the prevalence of overweight and obesity has become a global health challenge and has said to be one of the biggest threats to global public health today

(World Health Organization, 2010). The obesity epidemic, however, is often considered the result of an “obesogenic” environment where technologies, and structures of communities regularly reduce physical activity in combination with cheap high calorie, highly processed foods (Meldrum et al., 2017; Swinburn et al., 1999).

The prevalence of obesity worldwide is troublesome given that it is causally related to a wide range of diseases and can impact many health conditions (Janssen, 2013). Obesity has been linked to major diseases such as cardiovascular disease, some cancers, and diabetes (Brewer, 2017). Various other well-known diseases and conditions relating to obesity include, but are not limited to, osteoarthritis, hypertension, gout, chronic obstructive pulmonary disease, metabolic syndrome, and dyslipidemia (Janssen, 2013). Experiencing obesity does not mean inevitability experiencing the development of such diseases, however, it is a predisposing factor (Janssen, 2013). The relationship between weight and mortality is usually illustrated as a U- or J-shaped curve in that there is increased risk for mortality at both extreme lower and upper ends of the BMI spectrum (Janssen, 2013). In addition to the impact of obesity on an individual’s health, there are both individual and societal economic costs associated with obesity. Indirect economic impacts of obesity include healthcare expenditure, lost productivity, and permanent disability (Tremmel et al., 2017). More direct impacts on the individual may include inpatient and outpatient costs, ambulance, administration, research, education, bariatric surgery, nutrition, and weight loss counselling (Lehnert et al., 2015; Tremmel et al., 2017; Wang et al., 2015).

2.1.1 Obesity in Canada

In Canada, obesity has been steadily rising since the 1980’s with steep increase in excessive weight categories between 1985 and 2011 (Statistics Canada, 2019). Obesity has been and continues to be common among Canadians (Statistics Canada, 2019). In 2019, approximately one in four (26.8%) Canadians over the age of 18 reported being obese, and 36.3% of adults reported being overweight (Statistics Canada, 2019). In combination, 63.1% of Canadians are considered to have excess weight and therefore, are at risk for health complications (Statistics Canada, 2019). Over the last few decades there has been no real change in the quality of diets in Canada, and limited improvement or change in the prevalence of obesity (Bélanger-Ducharme & Tremblay, 2005; Nardocci et al., 2019; "Predicting the Future: Obesity in Canada," 2014). Additionally, the fitness levels of Canadians over the last decade has remained stable, however, at low levels given the substantial decline in fitness levels between 1981-2007 and 2009 (Doyon et al., 2021). In Canada, obesity is a common health problem as many diseases are related to or exacerbated by obesity (Bélanger-Ducharme & Tremblay, 2005; Meldrum et al., 2017). It has been shown that as BMI went up in Canada, so too did the prevalence of hypertension, heart disease and diabetes (Jiang et al., 2007). This is not surprising as individual health risks rise with increasing excess weight (Jiang et al., 2007).

Unfortunately, with the rising of chronic disease comes the increased costs on the healthcare system. A systematic review on the cost of obesity in Canada concluded that the economic burden is substantial (Public Health Agency of Canada, 2013; Statistics Canada, 2011). More specifically, the Public Health Agency of Canada reported that the economic burden of obesity, including both direct and indirect costs, was estimated to increase from 3.9 billion in 2000 to 4.6 billion in 2008 (Janssen, n.d., as cited in Statistics Canada, 2011). In comparison, in 2017, the direct healthcare costs alone of obesity in Canada was estimated to be between 4.6 billion to 7.1 billion and rise to 8.8 billion by 2021 (Anis et al., 2010; Canadian obesity network-Réseau Canadien en obésité, 2017; Nadeau et al., 2013). A systematic review focusing on the costs of obesity in Canada cautioned not to focus on direct costs as indirect costs can account for

40-60% of total cost (Public Health Agency of Canada, 2013). Therefore, emphasis on direct medical costs only, without information incorporated on costs and benefits from a societal perspective could leave out a big piece of the puzzle (Public Health Agency of Canada, 2013). Overall, obesity and the chronic diseases consistently associated with obesity significantly impact the Canadian economy (Canadian obesity network-Réseau canadien en obésité, 2017; Public Health Agency of Canada & Canadian Institute for Health Information, 2011).

2.1.2 Newfoundland and Labrador Context

Newfoundland and Labrador (NL) is the easternmost province in Canada. Newfoundland is an island situated in the Atlantic Ocean, separated from Labrador by the Strait of Belle Isle. Labrador, often called "The Big Land" shares a border with the province of Quebec, as well as a small border with Nunavut at its most northern tip. Both the island of Newfoundland and mainland Labrador have many areas of sparsely populated land with the majority of the province's population being in and around the capital city of St. John's. As of January 2021, the population was 520,438 people over 370,510 square kilometers for a population density of 1.4 people per square kilometer (Government of Newfoundland and Labrador, n.d.). In comparison, the population density of Canada is 3.9 people per square kilometer (Statistics Canada, 2012).

Larger communities on the Newfoundland Island are located along the Trans-Canada Highway whereas smaller fishing villages are found along the coastlines (Simms & Greenwood, 2015). In Labrador, communities span from their southern border, all the way to the northern tip where there are isolated, remote, indigenous communities only accessible by plane. Additionally, there are 12 ferry services in the province which gives access to many remote communities otherwise inaccessible (Butler, 2021). This geography of NL contributes to the difficulty with supplying resources to many parts of the province, especially since groceries for example, enter

Newfoundland via ferry service. Given the delay in time arriving in the province to the time hitting the shelfs in many rural and remote communities, the price of groceries is quite high and unfortunately, the quality can be low. Additionally, NL often experiences many snowstorms throughout the winter with high winds halting ferry routes resulting in delayed delivery of goods (CBC News, 2019). The winter weather creates challenges with access to medical care as many people outside of the major centers travel long distances to medical appointments. Further complicating the matter of accessibility in the province, in 2019, one in five people in NL did not have a family doctor (Newfoundland and Labrador Medical Association, 2019).

In addition to impacting transportation and medical services, weather can negatively affect PA participation. In general, Canadians are more physically active in the summer in comparison to winter months (Merchant et al., 2007). Interestingly, seasonality is not a strong predictor of PA participation in NL (Merchant et al., 2007). This has been attributed to the much higher amounts of precipitation even in the summer. For example, the average temperature in St. John's is 16.1◦ C with 100mm of precipitation in August in comparison to Vancouver, where the average is 18.0◦ C and 36.7mm (Environment Canada, 2021). Participating in PA and maintaining that participation over time can be quite challenging when NL weather causes significant interruptions no matter the season. Geography and weather are two of the many factors which contribute to the challenges Newfoundlanders and Labradorians face with regards to maintaining their health and engaging in PA.

2.1.3 Obesity in Newfoundland and Labrador

Newfoundland and Labrador is among the Atlantic provinces in Canada, which, are known for low levels of leisure time PA, low consumption of fruits and vegetables and high rates of obesity (Vanasse et al., 2006). The prevalence of obesity in NL is much higher than the national average (Hakimi & Cameron, 2017; Mutsaerts et al., 2016; Tarabusi et al., 2004). In 2012 in St. John's, NL, which, is a census metropolitan area, 33.2% of the population aged 18 and older reported being obese (Navaneelan & Janz, 2014). It was predicted in 2014 that 70% of the population in NL would be overweight by 2019 (Twells et al., 2014). In 2019, NL reported 40.2% of adults were obese, which, is the highest percentage in the country (Statistics Canada, 2019). This is unfortunate because as mentioned, obesity greatly impacts the development and progression of chronic diseases (Luo et al., n.d.). Additionally, obesity has the potential to negatively influence fertility of both males and females (Craig et al., 2017; Silvestris et al., 2018). There are numerous reproductive issues associated with obesity at many different points in the reproductive process (e.g., oocyte fertilization, spermatogenesis) (Craig et al., 2017; Jungheim et al., 2013).

2.2 Fertility in Canada

Fertility relates to the ability and quality to reproduce whereas infertility relates to experiencing difficulty or the inability to do so. There is no clear definition of infertility. In Canada, experiencing infertility often means the inability to conceive after one year of regular intercourse without contraception for women under 35 years of age (Government of Canada, 2019). For women over 35, the timeframe changes to six months (Government of Canada, 2019). The fertility rate in Canada has been declining since 2009 with the lowest being in 2020 when the fertility rate was 1.40 children per woman (Provencher et al., 2018; Statistics Canada, 2021). In 2019 and 2020, Canada reported the lowest fertility rates in history (Provencher et al., 2018; Statistics Canada, 2021). In addition to this decline in fertility rate, infertility rates in Canada have been increasing over the past few decades (Bushnik et al., 2012). In 2010, the prevalence of infertility was between 11.5-15.7%, meaning up to one in six couples experience infertility in

Canada (Bushnik et al., 2012; Government of Canada, 2019). Two decades earlier in 1992, 8.5% of women aged 18-44 living married or common law were considered to be infertile (Dulberg & Stephens, 1993). Despite this considerable change in infertility over time, we must be cautious when making comparisons given the definition of infertility has changed over time (Bushnik et al., 2012).

2.2.1 Fertility in Newfoundland and Labrador

Just as NL's obesity rate is higher than the national average, the fertility rate is also lower than the national average (Government of Newfoundland and Labrador, 2020; Provencher et al., 2018). As of 2019, the fertility rate in NL is 1.30 children per woman, which is the lowest rate in the country (Government of Newfoundland and Labrador, 2020). Currently, there is only one fertility clinic in the province located in St. John's (Planned Parenthood - NLSHC, 2017). Unfortunately, no data specific to the prevalence of infertility in NL is available. However, the COVID-19 pandemic negatively impacted fertility services in the province as fertility appointments were cancelled and deemed non-urgent (White, 2020). Since this happened, there has been an increased commentary on social media platforms, in local newspapers, and on news outlets expressing concern and the need for such services. Specifically, a Facebook page titled "Faces of Fertility" has gathered attention as it aims to raise awareness and share stories of people experiencing fertility issues in NL (Mercer, 2020). The page aims to express frustration with the government of NL, and more specifically the premier and minister of health. In response to this outcry, the Government of Newfoundland released in January 2021 that they would work to increase access to fertility treatments and open a clinic offering specific fertility treatments in the province such as in vitro fertilization (IVF) (Jackson, 2021). IVF is a treatment option for women experiencing infertility which, will be discussed further in the section outlining medical interventions. The premier said that in the interim, he would try to ease the financial burden for those having to travel elsewhere for fertility treatment (Jackson, 2021; Liberal Party of NL, 2021). This is important for the province, however, there was no mention of changes to funding for fertility services in the 2021 budget reports and publications (Government of Newfoundland Labrador, 2021).

2.3 Fertility Outcomes

Though a successful pregnancy is often the most desired fertility outcome by women, measuring fertility is multifaceted. Given that improvements to fertility are related to physical and mental health, there are a wide range of outcomes that have been used to measure fertility in the literature (Hakimi & Cameron, 2017; Mutsaerts et al., 2016; Tarabusi et al., 2004). To further complicate things, infertility is not directly measurable as it is essentially the absence of fertility (Greil et al., 2010). For example, infertility cannot be confirmed by altered reproductive hormones, rather it is confirmed by the inability to conceive. However, the altered hormones could be a contributing factor to this inability, and therefore are considered fertility outcomes. Admittedly, the wide range of fertility outcomes can be confusing, this is expected as there is no true gold standard for fertility markers at this time.

2.3.1 Reproductive Related Hormones

Hormonal panels are used as a measure of fertility in the majority of studies exploring obesity-related infertility in women (Al-Eisa et al., 2017; Almenning et al., 2015; Nybacka et al., 2011; Palomba et al., 2008). As mentioned, though there is no 'gold standard' of fertility outcomes in the literature, studies often aim for a successful pregnancy as the primary outcome of the intervention. However, given low numbers in such interventions, insulin sensitivity is often used as the primary outcome (Kiel et al., 2018; Palomba et al., 2008). Insulin sensitivity is a very common marker of fertility used in the literature, as will be examined further when discussing the use of pharmacological, and exercise interventions for women with obesity and experiencing infertility (Almenning et al., 2015; Bruner et al., 2006; Miller, 2005). Improvements in insulin are related to resumption of ovulation and are important for metabolic and reproductive health (Kiel et al., 2018; Kuchenbecker et al., 2011). Other reproductive hormones that may be considered a fertility outcome include luteinizing hormone, follicule stimulating hormone, prolactin, adiponectin and anti-Mullerian hormone (Al-Eisa et al., 2017; Miller, 2005).

Leptin, though not commonly reported on in obesity-related infertility literature, is an important hormone related to reproductive function (Blüher & Mantzoros, 2007). The mechanism of how leptin is important is not entirely understood, however, it includes complex interactions with the hypothalamus-pituitary-gonadal axis (Moschos et al., 2002). For example, leptin stimulates the hypothalamus to secrete gonadotropin-releasing hormone (Comninos et al., 2014). Varying levels of gonadotropin-releasing hormone at different phases of menstruation are necessary for regular cycles (Gore, 2002). Additionally, high serum leptin levels have been found to directly inhibit ovarian steroidogenesis and subsequently, resulting in ineffective follicular maturation (Moschos et al., 2002). Without proper follicular maturation, there is potential for many downstream effects such as improper oocyte development and therefore, the possibility of experiencing infertility. Despite the role leptin plays in the physiology of normal reproductive health, it does not seem to be considered a primary fertility outcome in current obesity-related infertility literature (Moschos et al., 2002). Nevertheless, the relationship between leptin and obesity is important and requires further investigation and explanation which, will be further discussed in the next section on obesity.

2.3.2 Improvement in Ovulation and Menstrual Regularity

A common outcome reported in reproductive health studies for women is improvement in ovulation or menstrual cyclicity (Mena et al., 2019; Nybacka et al., 2011; Palomba et al., 2008). To define improvements in menstrual cyclicity, a forward progression of the following would be considered an improvement: amenorrhea, irregular cycles, oligomenorrhea, and eumenorrhea (Miller, 2005). Respectively, this is progression from no menstruation, irregular cycles, infrequent periods, and normal cycles. Ovulation, on the other hand can be confirmed based on elevated levels of progesterone measured during the menstrual cycle (Nybacka et al., 2011). Improvements in either of these outcomes is considered to be a good indication of improvements in one's overall fertility (Edison et al., 2016; Nybacka et al., 2011).

2.3.3 Rates of Conception, Pregnancy and Live Birth

More traditional measures of fertility and arguably the targeted primary outcome of much of the literature on reproductive health include conception, pregnancy, and live birth rates (Espinós et al., 2017; Kiel et al., 2018; Palomba et al., 2008). Understandably, the birth of a healthy child is the only meaningful fertility outcome for women experiencing infertility (Morin-Papunen et al., 2012). Pregnancy is often defined as sonographic evidence of fetal cardiac activity and an intrauterine gestational sac at seven weeks, or a positive pregnancy test result (Kiel et al., 2018; Morin-Papunen et al., 2012; Palomba et al., 2008). Despite these definitions, such early indications of pregnancy could suggest rates of conception rather than the ability of the woman to remain pregnant and carry to term. On the other hand, live birth rates are defined as when a baby is born and shows evidence of life irrespective of gestation (World Health Organization, n.d.).

2.4 Obesity and Infertility

Obesity has consistently been shown to negatively impact fertility outcomes (Brewer & Balen, 2010; Jungheim et al., 2013; Silvestris et al., 2018; Talmor & Dunphy, 2015). However, not all women with obesity will experience infertility, as factors such as diet, exercise, and smoking can play a role in the magnitude of complications (Pasquali et al., 2003). The effect of obesity on fertility is multifactorial.

2.4.1 Biochemical Effects of Obesity on Fertility

Adipose tissue impacts the steroid pool of a woman defined as obese, which, affects the delivery of both androgens and estrogens (Brewer & Balen, 2010; Gambineri et al., 2002). Particularly, increased adipose tissue in women is known to negatively affect sex hormone production, such as an increase in estrogens and a decrease in sex hormone binding globulin (SHBG) (Talmor & Dunphy, 2015). According to Talmor and Dunphy (2015), this results in an increase in free estradiol and testosterone which further decreases the production of SHBG. In turn, they reported that there is an increase in stimulation of ovarian androgen production and luteinising hormone. The concentration of SHBG is also significantly impacted by the distribution of body fat with central obesity stimulating a greater reduction in SHBG (Brewer & Balen, 2010). Though the hormonal impact of obesity is much more complex than described, the overall altered endocrine environment negatively impacts folliculogensis which, is the development of an ovarian follicule (Talmor & Dunphy, 2015). The negative consequences of impaired folliculogensis can be far reaching as ovarian follicles are the basic units of a women's reproductive biology.

Leptin is an adipocyte-secreted hormone discovered in 1994 which circulates at levels proportionate to the amount of adipose tissue (Zhang et al., 1994). Leptin levels are correlated with absolute fat mass and, modern-day obesity is associated with hyperleptinemia – elevated leptin levels (Blüher & Mantzoros, 2007; Duval et al., 2015; Farr et al., 2015; Lindheim et al., 2000). The elevation of leptin levels due to a higher body fat percentage often results in leptin resistance and subsequently, the inability to modulate weight due to failure to control hunger (Farr et al., 2015; Lustig et al., 2004). Therefore, obesity influences leptin and likewise, leptin levels impact fertility, as previously mentioned. For example, it has been reported that women who are overweight or obese not only have increased leptin levels in their peripheral blood but in their follicular fluid as well (Lin et al., 2017). Results from this study suggest that high leptin levels may promote apoptosis and inhibit cell growth which has potential to weaken the development of the embryo (Lin et al., 2017). Together, this can contribute to one of the many mechanisms why women with obesity can experience infertility.

2.4.2 Effect of Obesity on the Oocyte

In comparison to women with a normal BMI (18.5-24.9 kg/m^2), the follicular fluid of women with obesity have alterations in both the metabolites and hormones which affect fertilization, oocyte maturation, and preimplantation embryo development (Purcell & Moley, 2011; Song et al., 2020; Talmor & Dunphy, 2015). Follicular fluid is defined as a fluid which surrounds an oocyte and provides nourishment for its development (Mariani & Bellver, 2018; Selvam et al., 2019). Given this, altered follicular fluid composition may result in diminished oocyte maturation, and therefore influence the ability to conceive. Obesity has been shown to impact oocyte quality further contributing to impaired fertility (Robker et al., 2009). Weakening oocyte quality translates to negatively effecting an oocytes ability to first be fertilized, and secondly, support the development of an embryo (Purcell & Moley, 2011).

2.4.3 Effect of Obesity on Ovulation and Uterine Receptivity

Obesity affects neuroendocrine mechanisms which impact ovarian function, including ovulation rate, and uterine receptivity (Silvestris et al., 2018). Alterations in the neuroendocrine environment can include interfering with the regulation of the hypothalamic-pituitary-ovarian axis (Silvestris et al., 2018). Both ovulation rate and uterine receptivity; defined as the ability of the blastocyst to implant in the endometrial lining, are essential components of conception. As previously mentioned, obesity may alter the physiology of an oocyte which, can have downstream effects on uterine receptivity and implantation (Silvestris et al., 2018). For example, negatively impacting implantation can affect pregnancy and live birth rates (Bellver et al., 2013). These findings are the result of ovum donation models which are considered the best human model for determining impaired reproductive outcomes originating from embryonic or uterine factors (Bellver et al., 2013).

2.4.4 Effect of Polycystic Ovarian Syndrome (PCOS) on Fertility

Polycystic ovarian syndrome (PCOS) is the leading cause for anovulatory infertility (Almenning et al., 2015). Anovulatory, is when there is no release of an ovum due to no rupture of a follicle (ESHRE Capri Workshop Group, 1995). PCOS is a very complex reproductive disorder with signs and symptoms including menstrual disturbances, anovulation associated with primary or secondary infertility, increased pregnancy loss, and pregnancy complications (Rekha et al., 2019). Obesity, and in particular increased visceral fat (i.e., abdominal fat), has been recognized as a common feature in PCOS (Kirchengast & Huber, 2001; Sam, 2007). The relationship between the two is not well understood, but it is noted that many of the reproductive and metabolic abnormalities associated with PCOS are exacerbated by obesity (Sam, 2007). Weight loss has been emphasized as the first and most important option for women with PCOS who are overweight and experiencing infertility (Crosignani et al., 2003; Galtier-Dereure et al., 1997). However, it has been argued that it is not necessarily weight loss, rather the beneficial impacts of exercise itself such as improved insulin sensitivity that may positively impact a woman's fertility (Kiel et al., 2018).

2.4.5 Psychological Effects of Obesity on Fertility

Obesity is a modifiable risk factor that can affect a woman's fertility. Physicians should therefore strongly encourage exercise as a part of their patient education as it has potential to impact obesity and fertility (Talmor & Dunphy, 2015). However, doing so is a delicate process as many

may already feel anxiety related to their infertility (Chen et al., 2004). The inability to achieve a desired role in society associated with infertility can negatively impact one's mental health (Greil et al., 2010). Infertility-related anxiety can negatively affect fertility outcomes and reducing stress and anxiety has been shown to have a beneficial impact on conception rates (Tarabusi et al., 2004). In addition, women with obesity have been found to have higher rates of anxiety and poorer psychological functioning in comparison to overweight and normal weight women (Davis et al., 2005). Noting that infertility is often described as a stressful situation for couples, these factors create a complex situation for both the women and their healthcare teams (Cousineau & Domar, 2007).

Women with obesity and experiencing infertility may also experience weight stigma (Mulherin et al., 2013). Weight stigma is built on the premises that weight is a result of the commitment, or lack thereof of the individual, and that their weight is entirely in their control (Ward & McPhail, 2019). Literature has suggested that weight stigma can trigger a chain reaction in that "calling people out on their fatness" has shown to cause increased eating whether that be emotional or uncontrolled eating (O'Brien et al., 2016; Ward & McPhail, 2019, p. 227).

Ward and McPhail (2019) report that weight stigma is essentially placing blame on the women for their size, and often leads to feelings of humiliation and frustration. In keeping with this knowledge, they have recommended that healthcare professionals take a more holistic and health centered, not weight centered, approach for women planning to have children. This is due to the fact that overall diet and exercise levels are major contributing factors to one's overall health (Ward & McPhail, 2019). Such an approach would minimize the negative psychological effects of weight stigma and blame while still encouraging exercise and healthy eating.

2.5 Medical Interventions for Women with Obesity and Experiencing Infertility

Although obesity has the potential to negatively impact a multitude of reproductive factors, women with obesity and experiencing infertility can avail of interventions to improve their chances of conceiving (Jungheim et al., 2013). Medical interventions can range from low-cost pharmaceuticals such as metformin, to very costly and invasive surgical interventions such as, bariatric surgery followed by IVF (Mitchell & Fantasia, 2016; Patel et al., 2009). It is important to note that interventions for women with obesity and experiencing infertility often include aspects of various medical interventions as well as advocating for proper diet and exercise prescription (Espinós et al., 2017; Kiel et al., 2018; van Oers et al., 2016). For example, an exercise intervention followed by a medical intervention such as IVF (Espinós et al., 2017).

2.5.1 Pharmaceutical Interventions

Metformin and Clomiphene appear to be the two most widely used pharmaceutical treatments to improve fertility for women with PCOS, as well as for women with obesity (Mitchell & Fantasia, 2016). Letrozole, an aromatase inhibitor has been used as a fertility treatment for women with PCOS (Legro et al., 2014). In Canada, these are termed ovulation inducing drugs, better known as fertility drugs (Government of Canada, 2019). Much of the research on pharmaceutical interventions for fertility involve women with PCOS and not necessarily those defined as obese, however, obesity is a common feature in this population (Sam, 2007). Metformin has been shown to have a more beneficial effect on improving both live birth and pregnancy rates for women experiencing infertility, diagnosed with PCOS, and with obesity in comparison to those who were not defined as obese (Morin-Papunen et al., 2012)

Metformin is the most commonly used drug to treat type 2 diabetes as it decreases hepatic glucose production and acts to decrease insulin resistance through increasing insulin sensitivity (Bailey & Turner, 2007; Mitchell & Fantasia, 2016; Patel et al., 2009). Early research on the use of metformin to treat women with PCOS discovered that those who had taken metformin had higher rates of spontaneous ovulation in comparison to those given the placebo (Nestler et al., 1998). This is imperative as without ovulation, there is no ovum released to be fertilized and therefore, the women would experience anovulatory infertility (ESHRE Capri Workshop Group, 1995).

In recent years a larger study reported that Clomiphene alone or in combination with Metformin is better at improving live birth rates than Metformin alone (Legro et al., 2009). Legro et al. (2009) conducted this study with over 600 participants and determined that women with PCOS taking only Clomiphene had significantly improved rates of conception, pregnancy, and live birth rates. These women were randomly assigned to receive Clomiphene plus placebo, Metformin plus placebo, or a combination of both drugs for up to 6 months (Legro et al., 2009). Despite improved birth rates, such protocol allowed researchers to show that serious adverse events relating to pregnancy were more likely to occur to women receiving Clomiphene either alone or in combination with Metformin (Legro et al., 2009). Letrozole, on the other hand, has been found to be even more effective at improving live birth rates than Clomiphene (Legro et al., 2014). Though the sample size of this study was too small to detect a significant difference, there appeared to be an increase in major congenital abnormalities for babies conceived with Letrozole (Legro et al., 2014).

2.5.2 Surgical Interventions

2.5.2.1 Assisted Reproductive Technology. Assisted reproductive technology or treatment (ART), sometimes called assisted human reproduction are medical procedures with the main objective of achieving a pregnancy (Government of Canada, 2019). ART involves manipulating the egg, sperm or both outside of the human body by healthcare providers with specialized training (Allen et al., 2006; Government of Canada, 2019). In Canada, ART consists of IVF and intrauterine insemination (IUI) (Government of Canada, 2019). In short, standard IVF procedures include fertilizing the egg with sperm in a laboratory, allowing the two to interact and culture for two to five days before inserting the embryo, if fertilized, into the uterus (Allen et al., 2006). On the other hand, IUI involves depositing prepared sperm into the uterine cavity at the time of ovulation (Allen et al., 2006). There are additional procedures and pharmaceuticals that can be used in both IVF and IUI to further increase the chances of a successful pregnancy. For example, women may receive injections of gonadotropin to promote maturation of their eggs before sperm is deposited, sometimes called ovarian stimulation IUI (Allen et al., 2006). Unfortunately, it has been reported that women with obesity have lower live birth rates when undergoing ART likely due to factors previously discussed, such as decreased implantation and obstetric complications (Bellver et al., 2006; Brewer & Balen, 2010).

2.5.2.2 Bariatric Surgery. Bariatric surgeries, such as a gastric sleeve or gastric banding, may be used to facilitate improvements in conception through decreasing BMI and subsequently improving ovulation (Mitchell & Fantasia, 2016). However, studies on this type of intervention have limitations such as a very small number of participants, and long periods of time between bariatric surgery and later fertility procedures such as IVF (Tsur et al., 2014). Additionally, results and methods vary widely as some studies investigate women who were unable to conceive after having undergone IVF both before and after bariatric surgery (Tsur et al., 2014). On the other hand, one study examined five women who had previous bariatric surgeries and four of these women successfully conceived and delivered their children (Doblado et al., 2010). In this situation, it is difficult to say whether these women would have successfully conceived with IVF alone irrespective of their previous weight loss.

2.6 Exercise as an Intervention for Women with Obesity and Experiencing Infertility

Exercise has been shown to positively impact fertility by improving ovulation rate, and restoration of menstrual cycles, especially in women with obesity and PCOS (Al-Eisa et al., 2017). Both moderate intensity aerobic activity, as well as high intensity interval training (HITT) have led to improvements in reproductive outcomes (Al-Eisa et al., 2017; Almenning et al., 2015). After 12 weeks of moderate aerobic exercise, significant improvement in follicle-stimulating hormone, luteinising hormone, androstenedione, oestrogen levels, and insulin sensitivity were found in women in with obesity, and with or without PCOS between 20 and 35 years old (Al-Eisa et al., 2017). In addition, a significant improvement of waist circumference was recorded. This exercise intervention included treadmill walking for 45-minutes three times a week for 12 weeks (Al-Eisa et al., 2017). It would have been beneficial to know if these improvements in reproductive related hormones translated to increased pregnancy or birth rates, however, no information for these outcomes were included.

On the other hand, a significant improvement in insulin resistance as well as a tendency towards lower visceral fat without a change in body weight was found after a HIIT intervention for women with PCOS (age 27.2 ± 5.5 years; BMI 26.7 ± 6.0 kg/m^2) three times a week for 10 weeks (Almenning et al., 2015). This randomized controlled trial included a HIIT, strength training, and control group with the main outcome being a change in insulin resistance. These findings suggest that aerobic exercise may improve ovulation by reducing the visceral fat, and insulin resistance with PCOS (Al-Eisa et al., 2017). Overweight and obese women with PCOS (age 18-40; BMI >27 kg/m^2) who took part in either a dietary management or exercise intervention (or both) had improved menstrual pattern and resumption of ovulation (Nybacka et al., 2011). The intervention in this study was individually adapted for participants (Nybacka et al., 2011). This could prove beneficial; however, the intervention was not thoroughly described (Nybacka et al., 2011). Therefore, it is challenging to have a good appreciation of what the exercise intervention entailed. Despite this critique, the findings are believed to be related to improved insulin sensitivity despite minor weight loss (Nybacka et al., 2011). Improvements in fertility outcomes such as menstrual pattern and resumption of ovulation from increased exercise participation and not necessarily weight loss, is an interesting finding that requires further investigation.

Although it seems the majority of exercise interventions for women with obesity and experiencing infertility involve aerobic exercise, some include resistance training in combination with aerobic exercise. For example, Miller combined aerobic and strength exercise in their three, one-hour group exercise sessions per week (2005). Unfortunately, no additional information was given on the specifics of the strength-training portion of the program as this study is published as a conference proceeding (Miller, 2005). They report only that participants took part in a 12-week group exercise and diet program. However, the intervention resulted in favourable metabolic and endocrine changes which have been found to impact fertility such as a decrease in cholesterol and a downward trend for both fasting leptin ($p = 0.06$) and two-hour glucose ($p = 0.07$) (Miller, 2005). Additionally, a study involving women with obesity and PCOS implemented an exercise intervention which consisted of endurance and resistance exercise (Bruner et al., 2006). The specifics of their resistance portion of the exercise intervention include beginning with 12 exercises targeting major muscle groups and completing first, two sets of 10 with a comfortable weight progressing to three sets of 15 and increasing the weight by 5% or 2.2 kg (whichever is greater) once comfortable (Bruner et al., 2006).

2.7 Barriers to Exercise Participation

Exercise is beneficial for improving fertility outcomes for women with obesity and experiencing infertility (Al-Eisa et al., 2017; Hakimi & Cameron, 2017). However, women with obesity and experiencing infertility may face multiple barriers to activity. Firstly, there are general barriers to participating in exercise that are likely to be experienced by many regardless of gender, age, or population. A cross-sectional survey study examining approximately 2000 adult men and women asked questions related to sociodemographic variables and perceived barriers to exercise (Herazo-Beltrán et al., 2017). Lack of motivation and time were the two most reported barriers to exercise participation. They also reported that lack of knowledge about exercise may lead people to overlook common spaces such as their home or neighborhood as places where they can be active (Herazo-Beltrán et al., 2017).

2.7.1 Exercise Barriers Experienced by People Defined as Obese

One study investigated barriers specific to those with class III obesity, defined as having a BMI greater than $35kg/m^2$ with at least one comorbidity or a BMI greater than $40kg/m^2$ (Joseph et al., 2019). Similarly, this was a cross-sectional study which administered questionnaires relating to exercise barriers and benefits, and sedentary and exercise behaviors (Joseph et al., 2019). Participants reported that physical exertion, pain, and musculoskeletal comorbidities were the top three barriers to their exercise participation (Joseph et al., 2019). In fact, approximately 70-80% of these participants agreed that physical exertion was an exercise barrier (Joseph et al., 2019). A qualitative study reported slightly different results, however, this is not unexpected given a qualitative study allows participants to put information into their own words, rather than picking from pre-existing answers. Specifically, the qualitative study used semi-structured interviews to guide discussions in both focus group and individual interview settings (McVay et al., 2018). This study examined adults defined as obese and reported various themes relating to exercise participation barriers such as anticipated effectiveness of the intervention (i.e., how effective the intervention would be at helping the participant lose weight), anticipated pleasantness of the intervention, and practical factors (e.g., cost) (McVay et al., 2018).

2.7.2 Exercise Barriers Experienced by Women with Obesity

Similar to those defined as having class III obesity, amongst a population of women with PCOS defined as overweight or obese, the most commonly reported barrier was that *"exercise tires me"* (Thomson et al., 2016, p. 6). Both *"exercise is hard work for me"* and *"I am fatigued by exercise"* were also highly reported (Thomson et al., 2016, p. 6). These barriers are directly related to the amount of perceived physical exertion. As mentioned, weight stigma may increase anxiety in women with obesity and experiencing infertility, and consequently is a barrier to exercise participation as it reduces adherence to exercise (Phelan et al., 2015; Ward & McPhail, 2019). One study identified barriers faced by women with PCOS such as lack of support during an intervention targeted at improving fertility, as well as non-standardized delivery of such programs (Ko et al., 2016).

Women with obesity and diagnosed with PCOS reported the following barriers significantly more than women in the control group, without PCOS: *"not confident can maintain"* the exercise intervention, *"fear of injury"* and *"physical limitations"* (Banting et al., 2014, p. 5). To note, in this population of women with PCOS only 37% were diagnosed with infertility (Banting et al., 2014). To my knowledge, there are no studies directly examining barriers to exercise participation for women with obesity and experiencing infertility. However, the effects of infertility-related anxiety combined with barriers reported by women with obesity further increases the complexities of the barriers to exercise participation (Ogawa et al., 2011). From an adherence perspective, women with obesity and experiencing infertility may face multiple barriers to activity which may impact adherence to exercise participation. A study conducted on an overweight and obese population demonstrated that symptoms of depression, low levels of mental health, and of social functioning predicted lower exercise adherence (Mazzeschi et al., 2012). Weight stigma also plays a role in poor exercise adherence as weight stigma can increase anxiety, and reduce health promoting behaviors, such as adherence to exercise interventions (Phelan et al., 2015; Ward & McPhail, 2019).

2.8 Facilitators to Exercise Participation

Just as there are barriers to exercise participation there are also general facilitators to participating in exercise regardless of gender, age, or population. Facilitators can be defined as factors, which aid in participation such as perceived benefits to exercise (Mazzola et al., 2017). Facilitators may also include practical factors such as reasonable costs and compatibility with one's schedule (McVay et al., 2018). Commonly reported facilitators to exercise participation, specifically, at a fitness facility include a comfortable atmosphere, diversity in instructors and staff and feelings of being part of a community to name a few (Nikolajsen et al., 2021).

2.8.1 Exercise Barriers Experienced by Women with Obesity

A mixed methodology study was used to investigate benefits and barriers to exercise including focus groups followed by an online survey (Leone & Ward, 2013). Participants included white women with obesity (average age 55; average BMI 36 kg/m^2) (Leone & Ward, 2013). They reported that improved quality of life, improved mental health, weight management, and disease prevention as main perceived benefits to exercise participation for this population (Leone & Ward, 2013). It is important to recognize these women are not of childbearing age nor express fertility issues, however understanding barriers for women with obesity alone can further our understanding of the population of interest. A population of overweight or obese women (age 25-35, BMI>25), reported facilitators such as social support and positive experiences (e.g., fun), as motivation to continue being active (Alvardo et al., 2015). Women with PCOS defined as overweight or obese reported perceived benefits to exercise before participating in an intervention (Thomson et al., 2016). These women ranked *"exercise improves the functioning of my cardiovascular system"*, *"exercise improves the way my body looks*", and *"exercise increases my level of physical fitness"* as the highest perceived benefits of exercise (Thomson et al., 2016, p. 6). One study investigated the barriers and facilitators to weight loss for women of childbearing age (Holley et al., 2016). Asking respondents about both exercise and diet, almost one quarter of women reported that to *"improve health"* and *"feel better in myself/lift mood"* as motivation to lose weight (Holley et al., 2016, p. 279). Though losing weight and exercise participation are not necessarily one and the same, motivation to do either from the perspective of women who are overweight or obese and defined as inactive is likely similar.

2.9 Exercise and Diet Interventions

Interventions incorporating diet and exercise may prove beneficial for women experiencing anovulation associated with obesity as these components can have a benefit on fertility (Hakimi & Cameron, 2017; Mutsaerts et al., 2016). However, emphasis on the broad concept of weight loss in exercise interventions has detracted from research on effective exercise prescription protocols for women with fertility issues (Hakimi & Cameron, 2017). For example, after a 10-week exercise intervention consisting of HIIT and strength training, there were reported improvements to fertility outcomes such as insulin resistance and reproduction-related hormonal outcomes without any change in body weight (Almenning et al., 2015). A systematic review and meta-analysis on the effect of exercise on reproductive health in young women stated that due to mixed results across studies, they could not conclude if improvements in reproductive health are related to weight loss (Mena et al., 2019). Therefore, though it may be assumed weight loss is the key to improvements in reproductive health for women with obesity, this is not supported by the current literature.

Improving fertility through exercise could be a cost-effective way to reduce the demand on medical and pharmaceutical interventions. Additionally, exercise and diet could help improve the likelihood that such surgical or pharmacological interventions succeed. During infertility treatment, it is recommended that patients defined as obese adhere to a proper diet and regular exercise. Unfortunately, this is challenging advice to follow without receiving concrete guidance on how to do so (e.g., exercise prescription) (National Institute for Health and Care Excellence, 2010). The increasing need for healthcare providers to play an active role in diet and exercise education is warranted (Rooney & Domar, 2014). However, limited resources (e.g., funding, mental resources to name a few) are available to offer specific diet and exercise interventions for this population (Boivin et al., 2017). Perhaps, greater recognition of exercise professionals as healthcare providers may better support efforts to implement exercise programming.

Systematic reviews on exercise and ovulation irrespective of a woman's BMI note that moderate quantities of vigorous exercise may be best for improving fertility, however further investigation is warranted (Hakimi & Cameron, 2017). Unfortunately, the definition of vigorous exercise varied throughout studies reported in this systematic review which, is not beneficial for comparison or replication (Hakimi & Cameron, 2017). Investigating specific populations of infertile women could prove beneficial for affordable and accessible alternatives to fertility treatments (Hakimi & Cameron, 2017). Despite the literature presented there is a lack of consensus on the type, duration, and intensity of exercise most beneficial at improving fertility outcomes (e.g., resumption of ovulation, pregnancy) for women with obesity and experiencing infertility (McLean & Wellons, 2012). Therefore, a critical narrative review would contribute to filling this gap by synthesising the current knowledge in the literature around the impact of exercise interventions on fertility outcomes for women with obesity and experiencing infertility. A review would contribute not only to the literature but, more importantly, to improving the understanding and implication of proper exercise prescription for this population, which in turn could maximize the benefits to fertility outcomes. Currently, there is not enough literature on exercise interventions for women with obesity and experiencing infertility to understand the dose-response for this population. The goal of a narrative review is to describe and synthesize the current literature to better inform future development of exercise interventions for this population (Kong et al., 2014). Given this, such information will have potential to not only improve existing interventions but guide practitioners in the field on which types of exercise interventions are being used to manage obesity and infertility. Lastly, by identifying gaps that need further investigation this narrative review aims to improve the quality of obesity and infertility research.

2.10 Rationale and Significance

Exercise can have many benefits on mechanisms related to infertility by improving overall health, increasing social support, and providing a sense of control (Conn, 2010). Despite these benefits, there is a lack of consensus on the type of exercise, frequency, intensity, and setting to prescribe to improve reproductive outcomes (McLean & Wellons, 2012). In sum, there are no evidence-based guidelines on how women with obesity and experiencing infertility can improve their fertility through exercise (Lundgren et al., 2016). Given this, the primary purpose of this study was to provide a description and analysis of the current exercise interventions used in obesity and infertility literature, with a secondary purpose to identify the primary fertility outcomes examined. We must broaden our understanding of the exercise protocols used, and the primary outcomes assessed to evaluate the impact of exercise interventions aimed at improving fertility for this population. To do so, the collective evidence on the components of the exercise interventions, and their subsequent impact on specific fertility outcomes have been closely examined. A systematic narrative review, rather than a systematic review was conducted. This is because, preliminary searches revealed that the interventions themselves varied so greatly that it would be very challenging it to compare and make assumptions about specific, quantitative aspects of the interventions. Therefore, a systematic narrative review was determined to be more appropriate. It does not allow for quantitative review or analysis of the treatment outcomes rather involves describing to better understanding what is being done in the field of obesity and infertility which, is more beneficial at this time.

2.11 Objectives

There are two main objectives of this study:

1. To determine what exercise interventions are currently being used for improving fertility outcomes for women with obesity.
2. To determine what specific fertility outcomes are being used in current obesity and infertility literature.

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Chapter Three Co-Authorship Statement

Along with my supervisors Dr. Daniel Fuller and Dr. Erin McGowan, direction for the methods of this thesis was determined. I conducted comprehensive literature reviews for the introduction in this chapter both during the time of writing this thesis and prior for graduate course assignments in HKR 6000 and HKR 6001 under the supervision of Dr. Daniel Fuller and Dr. Pamela Ward, respectively. I developed strict inclusion and exclusion criteria for this study in consultation with Erin Alcock, the science research liaison librarian at the Queen Elizabeth (II) Library, Memorial University. The appropriate information sources, search strategy, and search strings was determined with assistant from Erin Alcock. The literature search including importing documents into Covidence was carried out by Erin Alcock. I completed the study selection and data extraction. The exercise intervention categorization system was completed with assistance from Dr. Fabien Basset from Memorial University. Feedback on all parts of the manuscript was given by both supervisors throughout the development of the methods, results and discussion section and, at the time of submission.

Chapter Three: Manuscript

3.0 Abstract

Introduction: Obesity negatively impacts fertility. Women with obesity and experiencing infertility may improve fertility outcomes through exercise, however there is limited evidence on exercise prescription for this population. Specifically, there is limited information on: (1) exercise interventions that are effective for women with obesity and experiencing infertility, and (2) fertility outcomes impacted by exercise interventions. **Purpose:** This narrative review will provide an analysis of current exercise interventions and the fertility outcomes reported in the literature. **Methods:** A systematic search was completed in PubMed, Embase, Cochrane, and CINAHL. Inclusion criteria for this review included quantitative studies published between 2005-2021 reporting on exercise interventions for women (aged 18-40 years), experiencing obesity (defined as BMI >28kg/m^2), and infertility (lasting >1 year). Data were extracted on exercise technique, intensity, duration, and fertility outcomes. **Results:** Out of 574 articles, 16 publications met review criteria and were included. Ten of the 16 studies demonstrated improvements in the reported primary outcome, and all studies reported benefits in at least one fertility outcome. Cyclic exercise (i.e., walking, cycling) is the technique most incorporated into the exercise intervention, though a combination of cyclic, acyclic (i.e., circuit training, bootcamp), or individualized is often used. Several fertility outcomes are reported; however, rate of conception, pregnancy, and live birth rates are the most common. **Conclusion:** There are large variations in the specific exercise prescriptions recommended to improve fertility. Most studies examined reported statistically significant positive changes in fertility outcomes after an exercise.

Keywords: Obesity, Exercise, Infertility, Review

3.1 Introduction

Fertility relates to one's ability to reproduce, whereas infertility is experiencing difficulty reproducing or the inability to do so. Infertility can be defined in multiple ways, one being, the inability to conceive after 12 or more months of natural fertilization (Habbema et al., 2004). Infertility cannot be confirmed by pathological symptoms rather it is the absence of a desired state (Greil et al., 2010). Obesity negatively impacts fertility outcomes and often results in women with obesity experiencing greater time to conceive, and/or infertility (Silvestris et al., 2018). Obesity is defined as body mass index (BMI) of greater than 30kg/m^2 (World Health Organization, 2020). Women with obesity are three times more likely to experience infertility in comparison to women with a normal BMI (18.5-24.9 kg/m^2) (Brewer & Balen, 2010). Biochemically, obesity has the potential to negatively impact and alter one's endocrine environment, resulting in impaired development of an ovarian follicule, the basic unit of a women's reproductive biology (Talmor & Dunphy, 2015). Obesity often weakens the quality of a woman's oocyte and negatively impacts the ability to support and develop an embryo (Purcell & Moley, 2011; Song et al., 2020; Talmor & Dunphy, 2015). Polycystic ovarian syndrome (PCOS) is a complex reproductive disorder often resulting in primary or secondary infertility which, is exacerbated by obesity (Kirchengast & Huber, 2001; Rekha et al., 2019; Sam, 2007). Women with obesity and experiencing infertility may experience significant psychological distress including anxiety, weight stigma, and the inability to achieve a desired role in society (Chen et al., 2004; Cousineau & Domar, 2007; Davis et al., 2005; Greil et al., 2010; Mulherin et al., 2013).

Given the negative effect of obesity on fertility outcomes, intervention is often needed to improve chances of conception and/or reduce the time to conceive for women with obesity and experiencing infertility (Silvestris et al., 2018). Interventions range from behavioral (i.e., diet and exercise programs) to pharmacological and medical interventions such as ovulation induction drugs, artificial reproductive technologies (ART), and bariatric surgeries. Adhering to a program consisting of diet and exercise prescription is often emphasized for this population given interventions consisting of exercise participation and healthy eating can have a positive impact on fertility outcomes for women with obesity and experiencing infertility (Hakimi & Cameron, 2017; Kennedy et al., 2006). Exercise has been shown to positively impact fertility outcomes through improving ovulation rate and restoration of menstrual cycles (Al-Eisa et al., 2017; Conn, 2010; Duval et al., 2015a). Compared to diet-focused interventions, exercise interventions have been shown to have a higher compliance rate and a more enduring effect on mechanisms that affect fertility, such as resumption of ovulation (Palomba et al., 2008). Specifically, group and/or community-based exercise programs that provide aspects of social support are known to have greater success than individual treatment in achieving long-term behavioural changes (de La Cruz et al., 2016; Foreyt & Goodrick, 1994; Fraser & Spink, 2002). A community-based exercise program for women with obesity and experiencing infertility can have many benefits on mechanisms related to infertility by improving overall health, increasing social support, and providing a sense of control (Conn, 2010).

Despite the known benefits of exercise participation for this population, there are no evidence-based guidelines on how women with obesity and experiencing infertility can improve their fertility through exercise (Lundgren et al., 2016). In sum, there is a lack of consensus on the type, frequency, intensity, and setting to prescribe to improve fertility outcomes for women with obesity and experiencing infertility. Additionally, exercise interventions for this population often focus on weight loss, which has undermined the importance of developing effective exercise prescription protocols for women with obesity and experiencing infertility (Hakimi & Cameron, 2017). Therefore, the purpose of this study was to describe and analyze exercise interventions used and primary outcomes examined in current obesity and infertility literature. This review contributes to improving the quality of obesity and infertility literature, and more importantly, to improving the understanding and implication of proper exercise prescription for this population, which in turn could maximize the benefits of fertility outcomes.

3.2 Methods

This narrative review focused on examining current exercise intervention studies for women with obesity and experiencing infertility. The aims of a narrative review are to find what has already been accomplished in the literature to summarise, identify gaps, and to continue to build on previous work, to only name a few (Grant & Booth, 2009). The preferred reporting items for systematic reviews and meta-analysis (PRISMA) 2009 checklist was used as an underlying structure for this review. Based on the clearly articulated inclusion and exclusion criteria and search strategy to be followed while this review was conducted, it is more appropriate to title this a systematic approach to a narrative review. Despite generally following the PRISMA guidelines as a structure for this narrative review, risk of bias in and between studies was not assessed through quality appraisal and/or research quality, as this was not a systematic review.

3.2.1 Inclusion and Exclusion Criteria

Below are the detailed inclusion and exclusion criteria with their supporting explanations. A condensed version of the inclusion criteria can be found in Table 1. To be considered for this review, participants in the study must have been women aged 18-40 years of age, with an average BMI >28kg/m^2, and experiencing infertility lasting >1 year. The World Health Organization (WHO) defines obesity as BMI >30kg/m^2, consistent with the literature an average BMI>28kg/m^2 was used as the cut-off to ensure not excluding many studies fitting all other criteria. To clarify this justification, exclusion criteria for a particular study may very well be BMI >25 kg/m^2, however the average BMI reported for participants is often still >28 kg/m^2. To be included, the definition of infertility must have had been relating to no pregnancy despite regular intercourse. An example of a definition that would have met such criteria is defining infertility as: not achieving a pregnancy while exposed to the risk of conception (Gurunath et al., 2011). Additionally, if participants were referred to the particular study from a fertility clinic or physician such as those undergoing ART may also be included. This is because for patients to be eligible for such services they must meet basic infertility criteria. According to WHO, infertility is "failure to achieve a clinical pregnancy after 12 months or more of regular unprotected intercourse" (World Health Organization, 2020, p. 1). Therefore, without directly mentioning the definition of infertility, studies in which participants are recruited from such facilities would still meet the definition of infertility. Given this definition of infertility, same sex couples or single women undergoing ART who are single were not included in this review. Studies focusing on clearly defined outcome measures related directly to fertility as primary outcomes were selected.

Only English, peer-reviewed studies published between 2005 to present, which included an exercise intervention, were considered. During the preliminary stages of the review in early 2021, the 2005 criteria was chosen to ensure studies included were current – spanning the last approximately 15 years. With regards to an exercise intervention as inclusion criteria, this included an exercise intervention and control, or comparison group in addition to an exercise intervention alone. For example, comparing the exercise intervention to another exercise, diet, or counselling intervention, pharmacological treatment, or a combination of either was sufficient. This allowed for contrasting and comparing various methodologies in current infertility literature. Therefore, it was expected that the design of the study would vary, including randomized controlled trials (RCT), cohort studies, observational and quasi-experimental to name a few. Study design alone did not result in exclusion (except for reviews and case studies), since an exercise intervention can be implemented in a variety of research settings. The exercise intervention length must have been a minimum of 10 weeks, which is consistent with most current interventions for this population (Espinós et al., 2017; Kiel et al., 2018; Mahoney, 2014). Studies which do not meet the 10-week criteria but came close, and meet all other criteria, may be included based on researcher discretion. If this is the case, it will be directly mentioned in the results section. Any type (e.g., frequency, intensity) of exercise intervention was included. Any exercise intervention, which incorporated a pharmacological treatment, was not included unless it was a comparison group as previously outlined.

It was inevitable that several studies, which fit the inclusion and exclusion criteria, included diet components in combination with the exercise intervention. Therefore, studies which included diet recommendations, plans or a weekly, monthly, or one-time diet seminar were included in this review. However, if the information given on diet was strict, extensive, and given more than once weekly, the study was excluded to mitigate the effect that diet may have on changes in fertility outcomes in comparison to the exercise intervention alone. To summarize when diet was emphasized over exercise in the intervention it was excluded. For example, Miller (2008) conducted a study where participants took part in a 12-week program consisting of group strength training and aerobic exercise for one hour three times a week, one educational session per week on diet and exercise, and instructed to a 1200-1500 kcal/day diet (carbohydrates 40%, protein 28%, fat 32%). In this case, the focus on diet is not emphasized over exercise, as per the inclusion and exclusion criteria, and therefore this study was included in the review. On the other hand, a study by Van Elteni et al., (2018) was excluded as it used a web-based food diary. The diary alone was not grounds for exclusion; however, participants could receive feedback on their food diary daily (Van Elteni et al., 2018). Therefore, it could be argued that diet was emphasized and there is potential for information regarding diet to be given more than once weekly. Motivational interviewing or counselling given in conjunction with an exercise intervention is not considered grounds for exclusion of an article as motivational interviewing can be used to empower participants and effectively promote changes in diet and exercise behaviors through improving program adherence (Burke et al., 2003; Mahoney, 2014; O'Halloran et al., 2014; Smith West et al., 2007).

Table 1

Inclusion Criteria Table.

Criteria
Women aged 18-40
BMI >28kg/m^2
Experiencing infertility > 1 year* AND/OR referred by a physician for infertility
English articles
Peer reviewed
Articles published between 2005-2021
Includes PA/exercise intervention
PA/exercise intervention length must be 10 weeks minimum
No pharmacological treatment included in PA/exercise intervention
Diet can be included in the intervention as long as it is not emphasized over PA/exercise**
Can have comparison intervention or control group
Can include MI in conjunction with PA intervention

*As stated in the methods section, the definition of infertility must be related to no pregnancy despite regular intercourse.

**If information on diet is given more than once weekly, the study was excluded.

3.2.2 Information Sources and Search Strategy

In January 2021, a systematic electronic search was conducted with the help of a Science Research Liaison Librarian from the QEII Library at Memorial University. The following databases were searched: CINAHL, Cochrane, Embase, and PubMed. To identify relevant studies, a search strategy was built using key MeSH terms. MeSH is a controlled vocabulary developed by the National Library of Medicine, it is used on PubMed and can aid in selecting specific terms as the major focus of a search (Linke et al., 2011). The key concepts included: (i) fertility, using the terms “fertility” OR “infertility”; (ii) obesity, using terms “obesity” OR “overweight”; (iii) exercise, using terms “exercise” OR “physical activity” OR “lifestyle intervention” OR “healthy lifestyle”. These three search strings were combined to achieve the final result. The search strategies can be found in Table 2 for the databases CINAHL, Embase, and Pubmed. The search string for Cochrane database is not included, as it is a database for reviews, and though articles included in a review may be applicable, the reviews itself are not. Both CINAHL and Embase databases use the same subject heading search terms except for the concept of exercise, it does not include the term “healthy lifestyle”. Instead, the terms “lifestyle changes” and “lifestyle medications” are used in CINAHL and Embase respectively. In addition to the systematic search, relevant reference lists and systematic reviews were screened for potential additional studies.

Table 2

Search Strategy from Librarian.

Database	Search String	Results
PubMed	(“fertility”[MeSH Terms] OR fertil*[Text Word]) OR ("infertility"[MeSH Terms] OR infertility[Text Word]) AND ("obesity"[MeSH Terms] OR obes*[Text Word]) OR	346 (Using a PubMed limiter for Female = 255)

	("overweight"[MeSH Terms] OR overweight[Text Word]) AND ("exercise"[MeSH Terms] OR exercise[Text Word] OR physical activity[Text Word] OR lifestyle intervention[Text Word])	
CINAHL	(MH "Fertility") OR (MH "Infertility") OR fertil* OR infertil* AND (MH “obesity”) OR obes* OR overweight AND (MH "exercise") OR exercise OR (MH "Physical Activity") OR physical activity OR (MH "Life Style Changes") OR Lifestyle intervention	185 (Using CINAHL Limiter for Female = 122)
Embase	(‘fertility’/exp OR ‘infertility’/exp) OR fertil* OR infertil* AND ‘obesity’/exp OR obes* OR overweight AND 'exercise'/exp OR 'physical activity'/exp OR 'lifestyle modification'/exp OR ‘lifestyle intervention’	742 (Applying Embase limiter for Articles and Reviews = 461)

3.2.3 Study Selection

Retrieved records were imported into Mendeley and Covidence. After removing duplicates, study titles and abstracts were screened for eligibility. If it was unclear whether a study was eligible (i.e., abstract not present and/or vague title) the study was included in the full text review. Once titles and abstracts were screened, full texts were examined. Each text was assessed based on the clear inclusion and exclusion criteria previously described.

3.2.4 Data Extraction

Data extraction was completed in accordance with an article characteristic table. A condensed version of the data extraction chart can be found in Table 3. This sample table includes a few key sections with their description as well as an example article. The official table was completed in Microsoft Excel and is included in Appendix B with the data extraction chart outline/key following in Appendix C. The article characteristic table includes columns of information such as first author, year of publication, country, study design, type of publication to only name a few. The table also includes information about the population such as standard deviations of both age and BMI for future quantitative analysis. The characteristic table was essential for data extraction and was used to ensure key information from each article can be easily located and compared. This table is not to limit the amount of information synthesized from each article, rather to allow for easier, more straightforward comparisons between key pieces in the literature.

Table 3

Sample Data Extraction Chart and Outline.

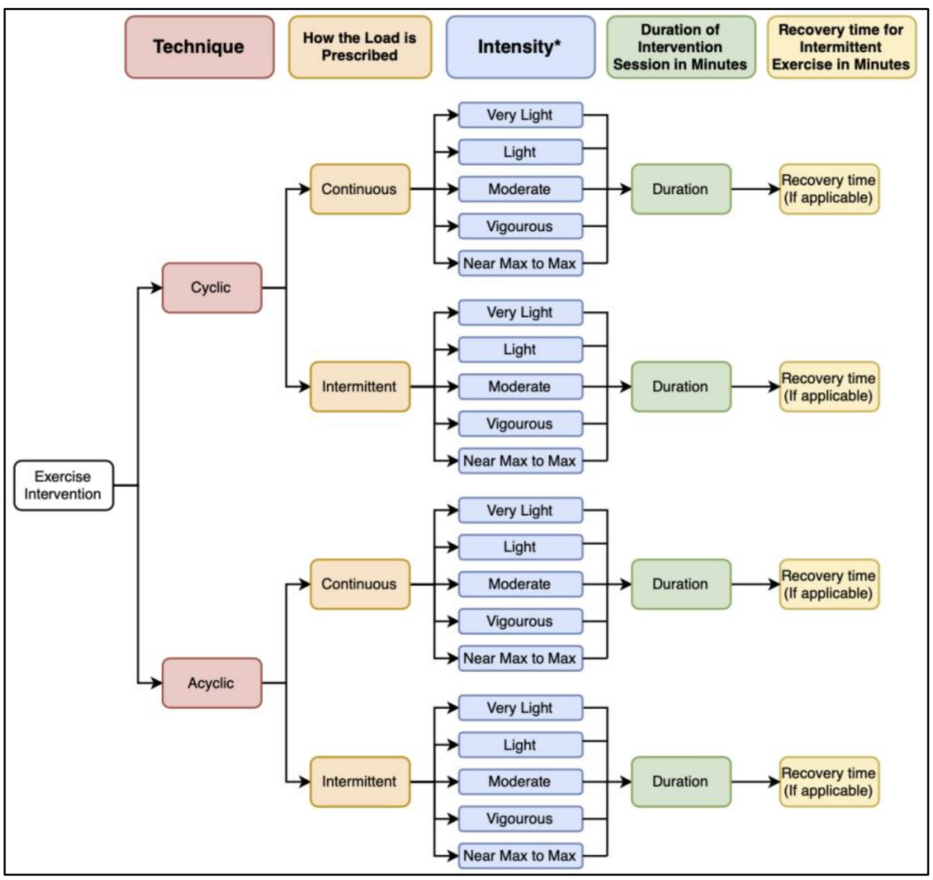
Example of Columns in Data Extraction Chart	**Explanation of Column**	**Sample Article**
First Author	Study's First author	Palomba
CR or CP	Control group or comparison group included in study?	CP
Population	Number of participants	40
SG Age	Study group age	26.8
Infertility Criteria 1	Infertility criteria to be met for inclusion in study	regular intercourse >1year
Intervention Technique	Type of exercise intervention technique or modality	Cyclic
Intervention Load Prescribed	How the load is prescribed	Sustained
Intervention Duration	Duration of exercise intervention	30
Intervention Length Mins/Week	Amount of intervention per week in minutes	90
Primary Fertility Outcome	Primary outcome of fertility measured in study	Pregnancy

3.2.5 Exercise Intervention Categories

Based on the preliminary search, it was identified that the exercise interventions used in obesity and infertility literature vary. To better understand and compare each intervention, an aim was to classify each intervention into groups of exercise based on five categories. Furthermore, classifying the exercise interventions gives exercise specialists the material they need to better replicate an intervention for such population. There are interventions that do not fit this classification system, and that was to be expected. The purpose of this classification system was not to force each intervention to fit into a specific category, rather to help with the description and analysis of the exercise interventions included. The classification is represented in Figure 1 followed by definitions and further explanation.

Figure 1

Exercise Intervention Classification.



*Intensity is classified by the American College of Sports Medicine (ACSM) Guidelines (Appendix A)

First, the exercise interventions were classified based on technique or modality into either cyclic or acyclic exercise. Cyclic and acyclic exercise means a consistent and repetitive, or inconsistent and sequential motor pattern, respectively (Mascherini et al., 2012). For example, running, walking, and cycling are classified as cyclic exercise, whereas bootcamp, tennis, climbing or circuits training is classified as acyclic exercise (Sibilia et al., 2004). Secondly, the interventions were classified based on how the load is prescribed with the possibility of being either intermittent or continuous exercise. Intermittent means with recovery time between bouts of exercise; recovering being either by stoppage of exercise or the lowering of intensity. For example, you can run 10km in a row or split it into 10 x 1000 meters with recovery in between bouts. Therefore, these exercise interventions would be considered cyclic continuous or cyclic intermittent, respectively. Thirdly, the exercise interventions were classified with respect to intensity according to the exercise-intensity continuum, which is divided into zones of effort. There are several approaches to classifying intensity, such as the ACSM, which was used for this review (Pescatello et al., 2014).

By using the ACSM guidelines for Exercise Testing and Prescription as a tool, either %HRmax, %VO_2max, rate of perceived exertion (RPE), or %1RM could have been used to categorize the intensity of the exercise (Appendix A). This was beneficial given that the reporting scheme for exercise interventions in the literature on obesity and infertility vary widely. Additionally, intensity is often an objective measure, such as %HRmax, %HR reserve and %VO2max, which allows for a more accurate classification of the exercise-intensity domain (Karvonen et al., 1957). On the other hand, some studies may report results using the RPE, which is a psychometric tool measuring subjective feelings and takes into account situational factors (Eston, 2012). After classifying based on intensity, the interventions were then categorized based on duration, the length of the intervention and lastly, recovery time. Recovery time is important for intermittent exercise, however there is evidently no recovery time incorporated into continuous exercise interventions. Days off in between the exercise sessions is not considered recovery time in the same sense as intermittent exercise, however, they are recovery days and this should be reported if available and when applicable.

Specifically, continuous exercise is defined as exercise lasting for at least 20-minutes at an intensity < 75% of VO2max or < %HRR or RPE < 14; an intensity that could be maintain for one hour (Linke et al., 2011). In comparison, intermittent is defined as periods of exercise lasting between five seconds to 20-minutes at an intensity > 75% of VO2max or > %HRR or RPE > 14. This was key, as an example, two separate running interventions may both be classified as a cyclic exercise, however one could entail being near or above 96% HRmax for short bursts of time, classifying it as cyclic, intermittent, near maximal-to-maximal exercise. On the other hand, a different running intervention could include sustained running for a period of over 20-minutes time ranging between 46-64%VO2 max. If this is the case, such an intervention would be classified as cyclic, continuous, and at a moderate-to-vigorous intensity. Though both may initially appear to be a running intervention, upon further investigation they are quite different; metabolically and physiologically they induce very different chronic responses at the cellular as well as at the systemic levels.

In this way, the exercise is classified specifically to ensure proper exercise prescription can be carried out and the exercise intervention can be replicated in the future for women with obesity and experiencing infertility. Further, accurately quantifying the workload or the density of training has helped in understanding what chronic responses have been induced, and therefore ensures the objectives of the exercise program have targeted the right physiological system for a specific population. Having five tiers of intervention categorization in combination with the data extraction chart, has allowed for a more comprehensive understanding of the exercise interventions used. This is beneficial for both those in the research community and those prescribing exercise interventions for this population.

3.2.6 Fertility Outcome Categories

In a similar way, fertility outcomes were categorized in obesity and infertility literature. Measuring fertility is complex and therefore classifying fertility outcomes into broader categories is beneficial in the review of literature. Primary fertility outcomes used in the literature have fit into the following categories: regularity of menstrual and ovulation cycles, hormonal (e.g., insulin, androgen, etc.), and rate of conception, pregnancy, and live birth. More specifically, hormonal outcomes can be broken down into sex hormone and insulin levels, as both are very important but distinctive hormonal panels. Though many studies may investigate more than one of these measures of fertility, it is the primary outcome, as defined by the authors of the study examined, which was the main concern for the purpose of this narrative review. For example, the primary fertility outcome examined by Miller (2005), falls under the category of regularity of menstrual and ovulation cycles. However, Miller (2005) did report that two women became pregnant during the study (16.6% of the sample) which, is an important fertility outcome, though not the primary outcome of this particular study.

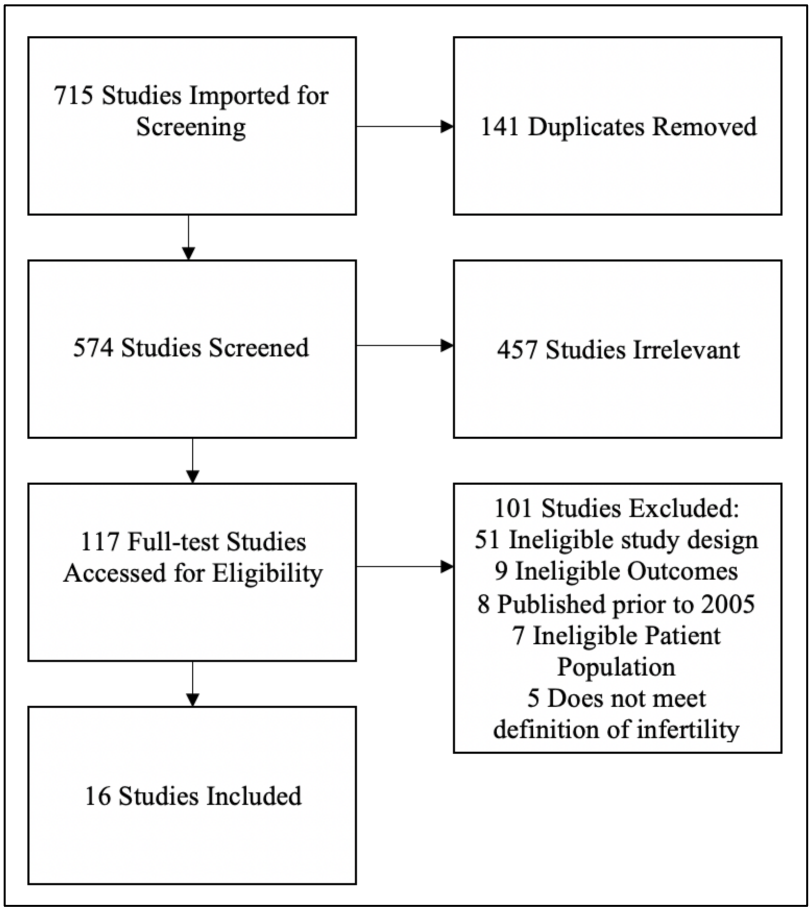
3.3 Results

3.3.1 Study Selection

After removing duplicates, 574 publications remained from the systematic search on CINAHL, Cochrane, Embase, and PubMed as well as relevant reference lists from reviewed studies and previous research. After screening the articles titles and abstracts, 457 studies were excluded. The basis of this exclusion was that the studies were deemed irrelevant to this review. For example, relating to diet rather than exercise, assessing male fertility, reviews assessing the effect of obesity on fertility, and not including human subjects to name a few. This exclusion resulted in 117 full-text studies assessed for eligibility. After close examination of the full text of the 117 studies, 101 studies were excluded. Main reasons for exclusion were ineligible study design, outcomes, patient population, or did not meet the definition of infertility. Examples of ineligible study design included studies with a qualitative design, literature reviews or overviews, and studies with no intervention. If there were articles of question to the reviewer, supervisors were contacted and the conflict was resolved through discussion. Ultimately, there were 16 publications (reporting on 15 studies) included in the analysis as represented in Figure 2 (Al-Eisa et al., 2017; Duval et al., 2015a; Espinós et al., 2017; Gorczyca et al., 2018; Khaskheli et al., 2013; Kiel et al., 2018; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Miller, 2005; Moran et al., 2011; Mutsaerts et al., 2016; Palomba et al., 2008, 2010; Sim et al., 2014; van Oers et al., 2016).

Figure 2

Selection of the 16 Included Articles (Reporting on 15 Studies)



3.3.2 Study Characteristics

Table 4 presents the characteristics of the included studies; the full summary can be found in the data extraction chart in Appendix B, followed by the data extraction outline/key in Appendix C. Of the 16 publications included, eight were RCT, six were prospective cohort, one was quasi-experimental, and one was an observational experimental design. Of the cohort studies, two were pilot cohort studies. Six studies were published between 2005-2011, and the remaining 10 were published between 2013-2018. The studies were conducted across a wide variety of countries, including Australia (*n*=2), Canada (*n*=1), Egypt (*n*=1), India (*n*=1), Italy (*n*=2), Norway (*n*=1), Pakistan (*n*=1), Spain (*n*=1), The Netherlands (*n*=3), and The United

States of America (*n*=3). Twelve of the publications were full-texts, three were published conference abstracts, and one was a preliminary report. Sample size of the studies range from a minimum of 12 to a maximum of 574 participants in a pilot cohort and RCT respectively.

Table 4

Study characteristics.

First Author	**Year**	**Study Design**	**Type of Publication**	**Participant Assignment**
Gorczyca	2018	Prospective Cohort	Conference Abstract	
Kiel	2018	RCT	Full-text	Random
Al-Eisa	2017	Quasi-Experimental	Full-text	Classified by BMI & PCOS Diagnosis
Espinos	2017	RCT	Full-text	Random
van Oers	2016	RCT (Secondary Analysis)	Full-text	Random
Mutsaerts	2016	RCT	Full-text	Random
Duval	2015a	RCT	Conference Abstract	Random
Mahoney	2014	Cohort	Full-text	
Sim	2014	RCT	Full-text	Random
Khaskheli	2013	Observational Experimental	Full-text	
Kuchenbecker	2011	Prospective Pilot Cohort	Full-text	
Moran	2011	RCT	Full-text	Random
Palomba	2010	RCT	Full-text	Random
Maiya	2008	Prospective Cohort	Preliminary Report	Choice & Classified
Palomba	2008	Pilot Cohort	Full-text	Choice
Miller	2005	Prospective Pilot Cohort	Conference Abstract	

Table 5 presents information relating to participants in the included interventions. The average age of the study groups in the publications range from 26.8-34.0 years of age. Out of the 16 studies, 14 reported on the average BMI prior to the intervention and the average ranged from 28.9-44.0 kg/m^2. Of the populations studied in the publications analyzed, seven included populations related directly to infertility treatment, for example, presenting for, undergoing, or accepted to undergo ART. Five of the publications included a population that were diagnosed with PCOS. In two of the cohort studies that included a comparison group, participants are given the choice to take part in either the intervention group or the comparison group.

Table 5

Sample, Group, & Participant characteristics.

First Author	Sample Size	Number of Groups	Intervention Group Size	Intervention Group Age	Intervention Group BMI
Gorczyca	14	1	14	33.4 ± 4.5	40
Kiel	18	2	8	33.1 ± 5.9	28.9
Al-Eisa	90	3	30	27.6 ± 5.7	38.4
Espinos	41	2	21	32 ± 3.2	34.6
van Oers	564	2	280	29.7 ± 4.5	36
Mutsaerts	574	2	289	29.7 ± 4.5	36
Duval	55	2	24	Unknown	Unknown
Mahoney	12	1	12	32 ± 5.3	44
Sim	49	2	27	32.9 ± 3.3	35.1
Khaskheli	85*	1	85	31.1 ± 2.5*	36.2*
Kuchenbecker	22	1	22	28.9 ± 4.1	37.8
Moran	38	2	18	33.8 ± 3.5	34
Palomba (2010)	96	3	32	27.5 ± 5.0	31.26
Maiya	42	2	21	34 ± 2.0	33.12
Palomba (2008)	40	2	20	26.8 ± 5.1	33.1
Miller	12	1	12	30 ± 4.7	>30

*Khaskheli et al., do not include the mean age and mean BMI for their intervention group specifically. Rather, they included information related to the 98 participants who signed up for the intervention, however, only 86 are considered to have had regular active participation in the intervention.

All publications examined meet the inclusion criteria for this review as outlined in Table 1. However, each study often specified its own inclusion criteria for participants that may have included additional required specifications. One study technically did not meet the minimum criteria of a 10-week intervention, as the average length of this intervention was five to nine weeks (Moran et al., 2011). This is because, the intervention was conducted during the period before the IVF cycle began (Moran et al., 2011). This study was included because it met all other criteria and did not deviate too far from the norm with respect to intervention length. Though the inclusion criteria specified a BMI of >28kg/m^2, one study reported an average BMI of 28kg/m^2 and therefore, there are women in the study with a lower BMI, however, given all other criteria were met, this study was included as well (Kiel, 2018). With regards to infertility criteria, six studies indicated that participants must be physician referred and diagnosed or enrolled in the study from a fertility clinic (Al-Eisa et al., 2017; Gorczyca et al., 2018; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Miller, 2005). On the other hand, five studies related their infertility criteria to ART, such as accepted for, undergoing, previously underwent, or intending to commence an ART such as IVF or intracytoplasmic sperm injection (Espinós et al., 2017; Khaskheli et al., 2013; Kiel et al., 2018; Moran et al., 2011; Sim et al., 2014). Other infertility criteria included chronic anovulation or ovulatory cycle but with no conception for 12 months (Mutsaerts et al., 2016; van Oers et al., 2016). Infertility criteria for two studies included regular intercourse for one year without conception, with history of irregular menstruation with normal follicule stimulating hormones and estradiol levels (Palomba et al., 2008, 2010).

Though some studies did not relate their definition of infertility to ART, they may still be associated with ART in that the intervention precedes ART. There were six studies in which the intervention precedes fertility treatment in comparison to prompt fertility treatment alone (Espinós et al., 2017; Kiel et al., 2018; Moran et al., 2011; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). There were seven studies in which it is clear that fertility treatment was ‘required’ to be delayed to participate in the intervention (Duval et al., 2015a; Espinós et al., 2017; Khaskheli et al., 2013; Kiel et al., 2018; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). Other studies in this review may have required treatment delay as well, however it is not clear or explicitly stated.

3.3.3 Intervention Components

The studies reported on 16 different interventions which were delivered in three different formats: alone or individual (*n*=10), in a group setting (*n*=1), individual and group setting combined (*n*=1), or the format of the intervention is unknown (*n*=4). Setting of the exercise interventions ranged from individual or home based (*n*=9), supervised exercise in a hospital or clinic setting (*n*=4), supervised but the exact setting is unknown (*n*=1), and unclear or unknown (*n*=2). Some studies included group education or counselling sessions, however, the exercise intervention itself was home based (Duval et al., 2015a; Mahoney, 2014; Moran et al., 2011; Mutsaerts et al., 2016; van Oers et al., 2016). The overall length of the interventions ranged from five to 26 weeks. An intervention lasting greater than 10 weeks was the most common (*n*=14). Though one study did report a minimum of a five-week intervention, as previously mentioned, on average it lasted approximately five to nine weeks as it took place during the period before an IVF cycle was to commence (i.e., the timing prior to oocyte pickup) (Moran et al., 2011). The frequency of the intervention in days per week ranged from once every two weeks (i.e., fortnightly, *n*=1), two (*n*=2), three (*n*=6), three to five (*n*=1), three to six (*n*=1), or unknown (*n*=5). Overall session time of the interventions ranged from 60 to 300 minutes per week. It is important to note these session times were the aim of the exercise protocol and does not guarantee that each participant met these targets weekly.

The 16 studies in this review reported on 15 different interventions as one of the publications is a secondary analysis of a RCT (van Oers et al., 2016). With respect to the technique of the exercise intervention, seven studies used an individualized approach to the exercise intervention either alone, or in combination with another technique (Duval et al., 2015a; Gorczyca et al., 2018; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Mutsaerts et al., 2016; van Oers et al., 2016). A cyclic technique is used in four of the interventions (Al-Eisa et al., 2017; Espinós et al., 2017; Palomba et al., 2008, 2010). An acyclic technique alone was only used in one study (Kiel et al., 2018). Combinations of individualized, cyclic, and acyclic techniques are used in four of the interventions (Duval et al., 2015b; Mahoney, 2014; Mutsaerts et al., 2016; van Oers et al., 2016). Cyclic and acyclic techniques combined are combined in two studies (Miller, 2005; Moran et al., 2011). There were two studies in which the technique of the exercise intervention could not be determined (Khaskheli et al., 2013; Sim et al., 2014). For example, participants were advised to increase daily step counts, however it is unclear through which technique they may do so (Sim et al., 2014).

Majority of studies did not report sufficient information on the prescribed load of the exercise intervention to determine how the load was prescribed. Therefore, 11 studies were classified as unknown (Duval et al., 2015a, 2015b; Espinós et al., 2017; Gorczyca et al., 2018; Khaskheli et al., 2013; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Miller, 2005; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). One intervention combined the use of sustained and intermittent loads during the exercise intervention (Moran et al., 2011). While one intervention prescribed an intermittent load alone (Kiel et al., 2018). In three of the studies, the load prescribed was sustained (Al-Eisa et al., 2017; Palomba et al., 2008, 2010). With regards to intensity of the exercise intervention, most were moderate (*n*=8), while few were vigorous (*n*=2), and the rest were unknown (*n*=6). Only five studies indicated there was a cooldown period after the exercise intervention lasting from five to 15 minutes (Al-Eisa et al., 2017; Kiel et al., 2018; Maiya et al., 2008; Palomba et al., 2008, 2010).

Diet was integrated into 12 of the 16 studies. Diet components included a wide range of suggestions and directions for participants that may be communicated through various platforms, such as apps, phone calls, in-person group or individual sessions. A diet component, for example, may have consisted of reduced calorie intake and a strict schedule of three main meals and two snacks (Espinós et al., 2017). Others may have included portion-controlled entrées, low calorie shakes, grocery shopping tips, and menu preparation, to name a few (Gorczyca et al., 2018; Mahoney, 2014). Participants may also have been given a calorie target in combination with a percentage of carbohydrates, proteins, and fats to aim for the duration of the study (Miller, 2005).

A counselling component was incorporated into six of the studies reviewed (Duval et al., 2015b; Kuchenbecker et al., 2011; Mahoney, 2014; Mutsaerts et al., 2016; Sim et al., et al., 2014; van Oers et al., 2016). A counselling component most often consisted of a form of motivational counselling or interviewing with the aim to promote awareness of healthy living, goal setting, and promote behavior change (Duval et al., 2015b; Kuchenbecker et al., 2011; Mahoney, 2014; Mutsaerts et al., 2016; van Oers et al., 2016). Other forms of counselling may have included sessions with a fertility counsellor (Sim et al., 2014).

3.3.3.1 Primary Fertility Outcome. The primary outcome of each study was categorized into three main categories: rate of conception, pregnancy, and live birth (*n*=11), hormonal (*n*=1), and regularity of menstrual or ovulation cycle (*n*=4). Rate of conception, pregnancy, and live birth rate may be defined in the study as clinical pregnancy rate after IVF, vaginal birth of a healthy singleton, or live birth rate at a certain number of months during or after the intervention (Duval et al., 2015a; Espinós et al., 2017; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). The one study which reported on hormones as the primary outcome, more specifically was categorized into sex hormone with anti-mullerian hormone as the primary outcome examined (Al-Eisa et al., 2017). Regularity of menstrual or ovulation cycle was a primary outcome in four studies and included menstrual cycle improvement, menstrual cyclicity, ovulation rate, and resumption of ovulation (Kuchenbecker et al., 2011; Mahoney, 2014; Miller, 2005; Palomba et al., 2010). There were seven interventions which reported on live birth rate (Duval et al., 2015a; Espinós et al., 2017; Khaskheli et al., 2013; Moran et al., 2011; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016).

3.3.4 Effects of the Intervention

Analysis on the effect of the intervention on the primary outcomes, which, could include an effect on the outcome categories of rate of conception, pregnancy, and live birth (*n*=11), hormonal (*n*=1), and regularity of menstrual or ovulation cycle (*n*=4), showed that overall, there were positive (*n*=10), negative (*n*=1), and no significant changes (*n*=5), when all categories are combined. Though not all studies report a positive effect on the primary fertility outcome as defined by the authors of a particular study, all interventions still had a positive effect on other fertility outcomes (*n*=16). For example, Espinos et al. (2017) did not find a significant change in their primary outcome, clinical pregnancy rate after a single IVF cycle which, is also categorized into the group of rate of conception, pregnancy, and live birth. However, the intervention group did have a higher cumulative live birth rate, a trend towards a higher implantation rate, and six anovulatory women (*n*=11) resumed regular menstrual cycles (Espinos et al., 2017). Likewise, one study reported a negative effect on their primary outcome, vaginal birth of a healthy singleton within 24 months after either the start of the intervention or prompt infertility treatment, which is also categorized as rate of conception, pregnancy, and live birth (Mutsaerts et al., 2016). However, after the 24-month period, the rate of birth of a healthy baby was significantly higher in the control group compared to those who took part in the intervention, therefore, resulting in a negative effect on the intervention group. After accounting for conception that occurred during the 24-month window but resulted in birth after that period, there were no significant differences. Of interest, significantly more women became pregnant due to natural conception in comparison to the control group in this study as well (Mutsaerts et al., 2016). Palomba (2008) did not have sufficient power to detect a difference in their primary fertility outcome (i.e., pregnancy), nevertheless, they did report significant improvements in menstrual cyclicity, which, is considered an important fertility outcome. Therefore, though the effect of an intervention on the primary fertility outcome of a study as defined by the authors is the focus of this review, overall effects on all fertility outcomes are important. Of the 16 interventions reporting a positive effect on fertility outcomes, the majority reported statistically significant positive effects (*n*=13). Some report positive effects, however, are not statistically significant for various reasons such as preliminary results or lack of statistical power to report fertility outcomes that may not have been the primary outcome (Khaskheli et al., 2013; Mahoney, 2014; Maiya et al., 2008).

When exploring fertility outcomes, for rate of conception, pregnancy, and live birth rates, five studies reported positive outcomes, one study reported negative outcomes, and no significant changes were reported for five studies. Four studies had the fertility outcome of regularity of menstrual or ovulation cycles, and all four studies reported positive effects (Kuchenbecker et al., 2011; Mahoney, 2014; Miller, 2005; Palomba et al., 2010). Some improvements in this category included a spontaneous menstrual cycle for women previously amenorrheic, or a significantly higher rate of ovulation (Mahoney, 2014; Palomba et al., 2010). Additionally, as mentioned, six out of 11 women resumed regular cycles during an intervention who were previously anovulatory (Espinós et al., 2017). Lastly, the one study examining hormonal panels as their primary outcome did find a positive change after the exercise intervention (Al-Eisa et al., 2017).

They reported significant positive changes in fasting blood glucose, insulin, and overall, 67% of women responded positively to the intervention (Al-Eisa et al., 2017).

In this review, 11 studies reported an improvement in rates of pregnancy (Duval et al., 2015a; Espinós et al., 2017; Gorczyca et al., 2018; Khaskheli et al., 2013; Kiel et al., 2018; Maiya et al., 2008; Miller, 2005; Mutsaerts et al., 2016; Palomba et al., 2008; Sim et al., 2014; van Oers et al., 2016). Four reported improvements in other fertility outcomes but did not examine pregnancy (Al-Eisa et al., 2017; Kuchenbecker et al., 2011; Mahoney, 2014; Palomba et al., 2010). One study did not result in a statistically significant difference in the rate of pregnancy in comparison to standard treatment (Moran et al., 2011). However, this study reported 12/18 live births for the intervention group in comparison so 5/20 for the control (Moran et al., 2011). Of interest, four out of 11 of the studies that reported an improvement in pregnancy, also reported a difference in natural or spontaneous conception (Duval et al., 2015a; Khaskheli et al., 2013; Kiel et al., 2018; Mutsaerts et al., 2016). Specifically, three reported a statistically significant difference in natural conception in comparison to the control group, and one study did not have a control group. Of the seven studies which reported on live birth rate specifically, three reported an improvement in or tendency to a higher live birth rate (Duval et al., 2015; Espinós et al., 2017; Sim, Dezarnaulds, et al., 2014). Duval et al. (2015a) reported a tendency, rather than a significant difference, to higher birth rate (62.5% intervention vs. 38.7% control, p=0.08). Overall, the most important findings regarding effect of the intervention are that exercise interventions for women with obesity and experiencing infertility led to improvements in live birth rates (n=3), pregnancy rates (n=11), and natural conception (n=4).

3.3.5 Adherence to the Intervention

Information pertaining to adherence of the exercise intervention in this review was scarce. Only five studies reported directly on adherence to the intervention (Espinós et al., 2017; Gorczyca et al., 2018; Kiel et al., 2018; Palomba et al., 2008, 2010). Espinós et al. (2017) reported that close supervision led to high adherence to the exercise intervention which resulted in weight loss. Higher rates of pregnancy were reported in participants who had greater adherence to the exercise intervention (Gorczyca et al., 2018). In this intervention, increased pregnancy rate was associated with higher step counts and greater adherence (i.e., longer length of participation in the exercise intervention) (Gorczyca et al., 2018). Kiel et al., (2018) stated that adherence to their exercise intervention (considered HIIT), was high. Palomba et al., (2010) reported high rates of adherence to their combined dietary and structured exercise program. Lastly, another study by Palomba et al., (2008) reported similar adherence to both diet and exercise interventions.

3.4 Discussion

3.4.1 Summary of Evidence

The purpose of completing this review was to explore what types of exercise interventions have been completed in the literature for women with obesity and experiencing infertility, and what fertility outcomes have been measured in these interventions. The focus was on the type of exercise, frequency, intensity, and setting of the intervention, and the effects the intervention had on the fertility outcomes being measured. To my knowledge, this is the first study to investigate and categorize the types of exercise interventions and fertility outcomes measured in these interventions for this population. This review reveals that exercise interventions for women with obesity and experiencing infertility generally have an overall positive effect on fertility outcomes and almost no negative effects. These findings are in line with a systematic review assessing exercise and ovulation in reproductive age women, which reported that exercise may improve fertility in women with anovulatory disorders (i.e., PCOS), however, researchers did not often explore the types of exercise interventions (Hakimi & Cameron, 2017). Similarly, a systematic review including young adult women demonstrated that exercise, most often as part of a diet and exercise intervention, may have beneficial effects on reproductive health outcomes (Mena et al., 2019). This narrative review reveals that cyclic, sustained, and moderate exercise are the most common types of exercise technique, load prescribed, and intensity used, respectively. Rates of conception, pregnancy, and live birth is the most common category of fertility outcomes explored.

3.4.2 Findings

3.4.2.1 Rates of conception, pregnancy, and live birth. In general, the exercise interventions examined in this review have consistently led to improvements in fertility outcomes. All publications included in this review reported statistically significant improvements to fertility outcomes except for two which, are either preliminary results or the statistical nature of the study seemed unclear or underpowered (Khaskheli et al., 2013; Maiya et al., 2008). Arguably, the most important and meaningful finding is that the exercise interventions most often led to improvements in rates of conception, pregnancy, and live birth rates for women with obesity and experiencing infertility (Mahoney, 2014). Of the 16 studies in this review, 11 reported an effect on either conception, pregnancy, or live birth rates, which is in line with recommendations for reporting outcomes for infertility trials (Duval et al., 2015a; Espinós et al., 2017; Gorczyca et al., 2018; Harbin Consensus Conference Workshop Group, 2014; Khaskheli et al., 2013; Kiel et al., 2018; Maiya et al., 2008; Moran et al., 2011; Mutsaerts et al., 2016; Palomba et al., 2008; Sim et al., 2014; van Oers et al., 2016). These recommendations highlight that the primary outcome in infertility trials should be live birth rate. If other fertility outcomes are explored, it is still important to also report the live birth rate (Harbin Consensus Conference Workshop Group, 2014). Four studies included in this review did not report the live birth rate (Al-Eisa et al., 2017; Kuchenbecker et al., 2011; Mahoney, 2014; Palomba et al., 2010). This is not in line with the current recommendations. However, it is important to note that the recommendations specific to infertility trials were published in 2014, and many of the studies that did not report live birth rate were completed before the recommendations were published.

Sim et al. (2014) reported that pregnancy is not used as a primary outcome as often as it should be, specifically in weight loss and ART interventions. However, pregnancy is a common, and meaningful outcome in the literature examined in this review. Studies reported improvements in rates of pregnancy (*n*=11), improvements in other fertility outcomes without mentioning pregnancy (*n*=4), and no significant difference in rates of pregnancy in comparison to the control (*n*=1). Keeping in mind that these studies are not all specific to weight loss or ART interventions as Sim et al. discusses, however, many do incorporate aspects of both. Natural or spontaneous conception is another meaningful outcome that is not reported on in many studies in this review. It seems as if rates of natural conception are an afterthought, or something recognized once the intervention has ended and never a primary goal or outcome of the intervention itself. As previously mentioned, four out of 11 of the studies reported an improvement in pregnancy, also reported a difference in natural or spontaneous conception (Duval et al., 2015a; Khaskheli et al., 2013; Mutsaerts et al., 2016; van Oers et al., 2016). This is in line with a systematic review reporting that preconception diet and exercise interventions improve natural conception but not necessarily live birth rate when live birth rate is measured after the intervention and IVF, in comparison to prompt IVF (Lan et al., 2017). This systematic review included women with obesity and experiencing infertility, however they were not the focus and therefore included other women of child-bearing age undergoing ART (Lan et al., 2017). Improving rates of natural conception is incredibly meaningful as it has the potential to remove the financial burden associated with fertility treatment (van Oers et al., 2016).

3.4.2.2 Intervention components. A major goal of this review was to describe and better understand the exercise interventions used in obesity and infertility literature. However, this was challenging, as the main components of the interventions, such as technique, load, and, intensity, vary widely across the literature. Despite there being a wide variety of exercise interventions reported in this review, there are similarities in the interventions.

3.4.2.2.1 Intervention Technique. Almost half (*n*=7) of the studies examined implemented an individualized technique, either entirely or partially individualized (Duval et al., 2015a; Gorczyca et al., 2018; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Mutsaerts et al., 2016; van Oers et al., 2016). For example, an individualized intervention may be tailored to the participants specific abilities, needs, and personal and social circumstances (Kuchenbecker et al., 2011). This approach can be beneficial; however, it adds a layer of complexity. It is difficult to compare, draw conclusions, or make recommendations for future interventions when limited specific information is provided about the intervention.

A few studies (*n*=5) only implemented one technique in their exercise intervention (Al-Eisa et al., 2017; Espinós et al., 2017; Kiel et al., 2018; Palomba et al., 2008, 2010). Cyclic exercise either alone or in combination with another technique is most common in this review. A cyclic technique is incorporated into seven of the 16 studies (Al-Eisa et al., 2017; Espinós et al., 2017; Mahoney, 2014; Miller, 2005; Moran et al., 2011; Palomba et al., 2008, 2010). An acyclic technique is incorporated into four studies (Kiel et al., 2018; Mahoney, 2014; Miller, 2005;

Moran et al., 2011). Therefore, cyclic activities such as stationary bicycle or walking on a treadmill were more common than acyclic activities such as high intensity interval training (HIIT) or bootcamp sessions for this population. This is understandable, given the participants are women with obesity and are mostly untrained, therefore, low impact exercise such as walking or biking would be a better option to ease participants into exercise participation and limit barriers such as pain and perceived physical exertion, while maintaining motivation, and adherence (Joseph et al., 2019). Despite this finding, a small study (*n*=17) with a population of previously sedentary overweight and obese population of adults showed similar adherence and enjoyment for HIIT in comparison to more low-impact, moderate exercise intervention (Vella et al., 2017).

In the studies where the intervention is entirely individualized, it would be beneficial to have more information about the specific approach, as this could provide insight into important components for optimizing fertility outcomes. This would be in line with recommendations to ensure there is sufficient information provided about the intervention to allow for replication (Altman et al., 2001; Barbour et al., 2017; Harbin Consensus Conference Workshop Group, 2014). One example of an individualized approach to an intervention included advising participants to reach 10,000 steps per day and partake in two to three, 30-minute moderate-intensity exercise sessions per week (Mutsaerts et al., 2016). In this case, all participants had the same goal. However, they could work to attain those targets in any way they wish. A different approach to an individualized exercise program included being "tailored to the ability and personal and social circumstances of each participant" (Kuchenbecker, p.2507, 2011). Nevertheless, the value of an individualized approach cannot be undermined given it considers the uniqueness of each individual and likely improves adherence and outcomes in doing so.

Perhaps multi-component, interdisciplinary interventions that incorporate cyclic, acyclic, or both techniques into an individualized approach are more appropriate. It would be ideal for both replication and for the participant if the exercise component was clearly articulated while acknowledging how the program was tailored to participants needs. Based on these findings, for future implication and application purposes, this is the type of individualized approach that should be taken when possible.

3.4.2.2.2 Intervention Intensity. Several studies (*n*=6) did not report on the intensity of their intervention (Duval et al., 2015a; Khaskheli et al., 2013; Kuchenbecker et al., 2011; Mahoney, 2014; Miller, 2005; Sim, Dezarnaulds, et al., 2014). There is one study where a range of intensity was given for the intervention, from moderate-to-vigorous (Gorczyca et al., 2018). The lack of information on intensity is surprising, given how important intensity is in the delivery of an exercise intervention. Intensity does not require an extra amount of explanation or information, and there are already developed guidelines and measurements to use for reporting and prescribing the intensity of exercise (Pescatello et al., 2014). In fact, there are physical signs or symptoms that can be used to classify intensity (e.g., little sweat and breathing harder to describe moderate intensity activity) (Canadian Society for Exercise Physiology, 2021). Therefore, intensity should be a simple task to report, and it has potential to be consistent in the methods across all exercise intervention research. Very few studies (*n*=5) provide enough information to determine how the load was prescribed in the exercise intervention (Al-Eisa et al., 2017; Kiel et al., 2018; Moran et al., 2011; Palomba et al., 2008, 2010). Understanding how the load was prescribed in an intervention could be important for exercise specialists who may be delivering the intervention. It is unfortunate that there is limited information on how the load was prescribed, as this information is essential to understanding the exercise intervention.

3.4.2.2.3 Intervention Setting. It is surprising that only four of the studies included in this review utilized group exercise interventions (Duval et al., 2015a; Kiel et al., 2018; Miller, 2005; Sim et al., 2014). Group and/or community-based exercise programs are known to have greater success than individual treatment in achieving long-term behavioural changes as they incorporate aspects of social support (de La Cruz et al., 2016; Foreyt & Goodrick, 1994). A community-based exercise program for women with obesity and experiencing infertility can have a multifactorial effect on mechanisms related to infertility by improving overall health, increasing social support, and providing a sense of control (Conn, 2010). Adherence to group exercise has been maximized through age similarity among group members (Dunlop et al., 2012). Research in social psychology has identified that humans prefer to socialize and engage with others who are similar, such as having shared experiences (Byrne, 1971). Growing bodies of research indicate that adherence to structured exercise training programs is related to social support, and the perceived cohesiveness of the group (Fraser & Spink, 2002; Spink et al., 2014). Given this, it is inferred that an exercise program for women of childbearing age, with similar experiences such as obesity and infertility could improve adherence in these interventions. Therefore, exercise interventions for women with obesity and infertility should make use of the power of the group and develop controlled, structured, group-based exercise training programs. The merit of both group and individualized exercise interventions deserves further attention and should explore the integration of both aspects and its benefits. For example, a combination of an individualized exercise intervention performed in a group setting could prove to be beneficial for this population. Therefore, further investigation is needed to maximize potential for improving fertility outcomes.

The majority of studies provided varying degrees of information pertaining to the exercise interventions. There are two studies which provided little to no information about the intervention at all (Khaskheli et al., 2013; Sim et al., 2014). The exercise component of one intervention was to gradually increase step counts to a daily target of 10,000 steps (Sim et al., 2014). In this multi-component intervention, it is impossible to make inferences about the type, frequency, or session time of exercise participation with step counts alone. This intervention included a weekly group session where advice was given on diet, exercise, psychological and behavioral aspects (Sim et al., 2014). Advice was given by a team consisting of a fertility fellow, midwife with fertility experience, as well as a counsellor and dietitian experienced in obesity. The second study that included very limited information on the exercise intervention involved a 'program of lifestyle change' that took place once every two weeks, focusing on exercise and diet habits (Khaskheli et al., 2013). Unfortunately, no other information related to the intervention was provided. Both of these interventions reported positive results (i.e., improved fertility outcomes), therefore, it would have been beneficial to have more information about the exercise program or intervention for replication. Larger studies are needed to dissect the components of multi-component diet and exercise regimes, which, is the aim of this review (Sim et al., 2014). However, it is somewhat ironic that studies such as the one by Sim et al. (2014), recognized the need for such dissection yet provided very limited information about their exercise intervention. This study focused on the bigger picture of the multi-component programs and reported promising results on fertility outcomes which, is beneficial. However, it is not necessarily beneficial in the sense that practitioners could replicate and prescribe such an intervention to this population.

These findings are consistent with reports on interventions for this population in that although the results appear to be promising, more comprehensive interventions are warranted (Hakimi & Cameron, 2017; Kiel et al., 2018; Moran et al., 2011). A review on the impact of exercise on fertility outcomes concluded that there is lack of good quality RCTs for this population (Hakimi & Cameron, 2017). Therefore, it can be challenging to decipher what components of the intervention make it successful, and to incorporate these components into practice for the improvement of fertility outcomes in this population.

3.4.2.3 Fertility outcomes. Though systematic reviews report a benefit of exercise and diet on fertility, they note a fundamental problem of the inconsistent reporting of outcome measures (Hakimi & Cameron, 2017). Most studies do report on a wide range of fertility outcomes. However, once categorized for this review, the fertility outcomes are very similar. As previously mentioned, the primary fertility outcome of 11 of the 16 studies falls into the category of rate of conception, pregnancy, and live birth (Duval et al., 2015a; Espinós et al., 2017; Gorczyca et al., 2018; Khaskheli et al., 2013; Kiel et al., 2018; Maiya et al., 2008; Moran et al., 2011; Mutsaerts et al., 2016; Palomba et al., 2008; Sim et al., 2014; van Oers et al., 2016). Therefore, this highlights the importance of using consistent terminology when reporting outcomes. In keeping with recommendations given by "Improving the Reporting of Clinical Trials of Infertility Treatments" (IMPRINT), live births should be the primary outcome reported (Harbin Consensus Conference Workshop Group, 2014). Live births are reported in seven of the studies in this review (Duval et al., 2015a; Espinós et al., 2017; Khaskheli et al., 2013; Moran et al., 2011; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). In some instances, reporting on live birth rate as the only main outcome, may limit the findings if live birth rates have not been improved. When, in fact rates of other just as significant outcomes might be improved, such as the rates of natural conception. For example, in a study previously described, live births were not improved after an exercise intervention and IVF in comparison to prompt IVF, however, those in the intervention group had significantly higher rates of natural conception and so, did not need to avail of IVF services (Mutsaerts et al., 2016). Therefore, it is important to report on live birth rates as the primary outcome, however, depending on if the study involves an intervention prior to ART, it might be just as important to report on rates of natural conception. This is because, not having to use ART and conceiving naturally, could have an enormous financial and emotional incentive, and would be the preferred option for many if possible.

3.4.2.4 Emphasis on weight loss. A criticism of interventions for women with obesity and experiencing infertility is the emphasis on weight loss (Hakimi & Cameron, 2017; Kiel et al., 2018). This is because, focusing on weight loss has detracted from research on effective prescription protocols as this review has outlined (Hakimi & Cameron, 2017). Although, in this review, a significant difference in weight loss for women with obesity and infertility who have taken part in the exercise intervention is often reported (Al-Eisa et al., 2017; Espinós et al., 2017; Khaskheli et al., 2013; Kuchenbecker et al., 2011; Mahoney, 2014; Maiya et al., 2008; Miller, 2005; Moran et al., 2011; Mutsaerts et al., 2016; Sim et al., 2014). However, in some cases it is unclear whether the results were statistically significant (Khaskheli et al., 2013; Palomba et al., 2010; van Oers et al., 2016). Emphasis should be on the fact that though weight loss is often greater in women who become pregnant in the studies included in this review, however, the differences are not always statistically significant (Espinós et al., 2017; Gorczyca et al., 2018). Of interest, there are three studies in this review that do not report a statistically significant difference in weight loss in the intervention group in comparison to controls despite improvements in fertility outcomes for the intervention group (Duval et al., 2015; Gorczyca et al., 2018; Kiel et al., 2018). This is promising and further suggests that improvements in fertility outcomes may not be related directly to weight loss, but rather to engaging in exercise. Palomba et al., (2008) reported a significant reduction in weight loss in the diet group in comparison to the structured exercise training group. Both exercise and diet interventions resulted in significant improvements to fertility outcomes (e.g., menstrual cyclicity) (Palomba et al., 2008). However, despite more weight loss in the diet group, a trend towards higher pregnancy and cumulative pregnancy rates was reported in the exercise group (Palomba et al., 2008). Overall, positive changes to fertility outcomes can be achieved with reductions of 5-10% of BMI without reaching a normal weight, which, is promising for women with obesity and experiencing infertility (Espinós et al., 2017). It has been suggested that even a modest weight loss can have a significant impact on fertility outcomes, mainly spontaneous pregnancy (i.e., natural conception) (Duval et al., 2015a; Mahoney, 2014). Sim et al. (2014) hypothesized that it may not be the actual weight change that improved fertility outcomes, rather, the distribution of body fat. Therefore, weight loss should not be the only focus of obesity and infertility research, rather an intermediary factor that needs further investigation. Weight and weight management is one of the many factors that play a role in obesity and infertility.

3.4.2.5 Nutrition and diet. All but four interventions include a nutritional or diet component in addition to the exercise intervention (Al-Eisa et al., 2017; Kiel et al., 2018; Maiya et al., 2008; Palomba et al., 2008). Exercise interventions themselves are multifactorial and complex (Kiel et al., 2018). Therefore, combining exercise and diet can make it challenging to decipher the effect of exercise on fertility outcomes alone. At the same time, incorporating both exercise and diet into interventions for women with obesity and experiencing infertility can prove beneficial, as this narrative review highlights. However, it seems that more complex interventions have higher rates of attrition than structured exercise training programs alone (Nybacka et al., 2011). Additionally, exercise interventions have a lower dropout rate than diet focused interventions (Hakimi & Cameron, 2017; Thomson et al., 2011). Women experiencing infertility seem to have higher levels of motivation than other populations taking part in exercise interventions (Palomba et al., 2010). Speculations on why motivation is so high in this population relate to the fact these women desire conception and pregnancy so immensely, and many have not responded to previous treatment (Palomba et al., 2010). To add to this motivation, exercise is a cheaper alternative to traditional infertility treatments such as pharmacological or medical options.

3.4.2.6 Artificial reproductive technology. There are six studies which were associated with ART (Espinós et al., 2017; Kiel et al., 2018; Moran et al., 2011; Mutsaerts et al., 2016; Sim et al., 2014; van Oers et al., 2016). The studies associated with ART resulted in no significant change (n=4), negative (n=1), and positive (n=1) effects on the primary fertility outcome. In these studies, ART, most commonly IVF, occured after the exercise intervention. Of the six interventions associated with IVF, only one study did not involve a treatment delay (Moran et al., 2011). This is because, the intervention took place prior to the IVF cycle, which, was 5-9 weeks before oocyte pickup (Moran et al., 2011). This is an interesting finding, as taking part in an exercise intervention prior to ART is considered a treatment delay, rather than treatment itself. Perhaps a controlled, prescribed, exercise intervention prior to ART should not be considered a treatment delay rather an additional treatment given the improvements in natural conception associated with exercise for this population. Given the wait time between first meeting with a healthcare provider, to receiving ART, an exercise intervention prescribed by an exercise specialist should be considered the first line of treatment.

Of interest were the comparisons made between the methodology of studies associated with ART such as Espinos et al. (2017) and Mutsaerts et al. (2016). With respect to their primary fertility outcome, Espinos et al. (2017) resulted in no significant change and Mutsaerts et al. (2016) resulted in having a negative effect. However, the intervention group in these studies had a significantly higher cumulative live birth rate and natural conception rate. In the discussion by Espinos et al. (2017) they make note of perhaps why Mutsaerts et al. (2016) did not find a significant difference in cumulative live birth rates such as being a large, multicentered study with a much lower intensity of monitoring. Additionally, they note that the intervention was tailored to the participants, and therefore can vary quite differently between centers (Espinós et al., 2017; Mutsaerts et al., 2016). Here lies an issue with studies in the field of obesity and infertility. It is challenging to detect a significant difference in live birth rates without having a large sample, however, having a large sample makes the delivery of such interventions more complex. Therefore, as is suggested by findings in this review, reporting on rates of natural conception in conjunction with live birth rates as the primary fertility outcome is needed to better reflect the results of exercise interventions for this population.

3.4.2.7 Intervention setting. An important, but seemingly understudied or underreported area of intervention research in this population was the impact of the intervention setting. In fact, extracting any information about the setting such as if the intervention was supervised, and where it took place was challenging, and in many instances, required inferences as the information was unclear. The setting of the exercise intervention (i.e., supervised, individual, hospital-setting, home-based, etc.) can play a role in adherence. Therefore, it was surprising that many studies in this review did not discuss more about their setting. Only one intervention truly made use of a supervised group exercise program, though the setting of the intervention is still unclear (Miller, 2005). Additionally, no intervention specified that it took place in a fitness facility. A recent pilot exercise intervention for women with obesity and experiencing infertility in NL, though delivered online due to the pandemic, was originally hosted out of a private woman's fitness facility to build community in a body-positive, motivational, non-judgemental space. Setting is also relevant when thinking about what is feasible in terms of implementing an exercise intervention in the real world. For example, a hospital supervised exercise intervention may be necessary from a research point of view, however, is likely not feasible long term on a larger scale. Therefore, having trained exercise professionals in the community setting is important for this population to exercise safely. Not only setting, but for example, the presence of other stimuli in the intervention setting such as music can impact adherence. Integrating preference-based music into a structured exercise program has been shown to significantly increase adherence to the exercise regime (Alter et al., 2015). Music has also been shown to reduce perceived exertion which, is a barrier to exercise participation (Fritz et al., 2013; Joseph et al., 2019). There did not seem to be any information or emphasis placed on setting or external stimuli in the setting such as music in the studies in this review. Going forward, attention should be given to the intervention setting and the importance it may have in creating a supportive and motivational environment.

3.4.2.8 Intervention Adherence. As reported in the results section, there are five studies that discuss adherence to the intervention (Espinós et al., 2017; Gorczyca et al., 2018; Kiel et al., 2018; Palomba et al., 2008, 2010). High adherence to an exercise regime was considered an indication that it could be a feasible exercise intervention for women with obesity and experiencing infertility (Kiel et al., 2018). Therefore, information pertaining to adherence could be helpful in determining the exercise prescription (i.e., technique, frequency, etc) that may be optimal for this population. Given this, it is unfortunate that few publications report on rates of adherence. One study hypothesized that the high rates of adherence observed was likely due to the design of the study as well as the participant population (Palomba et al., 2010).

3.4.3 Strengths and Limitations

In general, the exercise interventions in the studies examined have consistently led to improvements in fertility outcomes. This is an interesting finding and raises questions about the possibility of a limitation of publication bias in the field of obesity and infertility. Publication bias is when negative results are withheld from publication (Joober et al., 2012). This has the potential to negatively impact the 'integrity of knowledge' surrounding the field of interest (Joober et al., 2012). Though the results warrant confidence that exercise does improve fertility outcomes, publication bias is something that should be kept in mind when critically examining any literature. This review included articles published in English only, which can add to the limitation of publication bias. The interventions themselves vary so greatly that it is difficult to compare and make assumptions about specific, quantitative aspects of the interventions. As a result, a systematic narrative review, rather than a systematic review was conducted. A systematic narrative review does not allow for quantitative review or analysis of the treatment outcomes as describing to better understanding what is being done in the field of obesity and infertility is more beneficial at this time. Lastly, with regards to the exercise intervention classification system, researchers and exercise professionals may wish to know whether an intervention is a cardiorespiratory exercise intervention, a resistance training intervention, or a combination of both. The distinction of cyclic versus acyclic exercise may not necessarily provide that information clearly. However, though it may require interpretation, a 'combined' intervention which includes cardiorespiratory and resistance exercise is, cyclic and acyclic.

In this systematic narrative review, a systematic searching strategy was used. This was to ensure transparency and give a clear account of how relevant evidence was compiled. However, a narrative review allows a more interpretive and creative synthesis of the results which has potential to decrease transparency. A strength of this review, and obesity and infertility literature in general, is the motivation women experiencing infertility have to conceive. Financial motivations could play an additional role in increased adherence, given that in many countries couples have to contribute either partly, or entirely for fertility treatment such as ART (van Oers et al., 2016). Therefore, adherence to exercise interventions are quite high in comparison to similar interventions for other populations (Kiel et al., 2018; Palomba et al., 2008). Exercise interventions have shown to have a lower dropout rate in comparison to diet alone (Kiel et al., 2018). In a study by Palomba et al. (2008), they compared exercise to diet intervention for women with obesity and experiencing infertility. The dropout for the interventions were 3 and 7 participants out of twenty for the exercise and diet interventions, respectively.

3.4.4 Implications for Practise and Research

This review shows that multidisciplinary interventions with a focus on exercise for women with obesity and experiencing infertility should be implemented to improve fertility outcomes, mainly rates of live birth and natural conception. To identify and make recommendations about which components of the exercise interventions or combinations of components are most effective, further robust research is warranted. In order to facilitate this reporting, as part of the review, the Reporting Sheet for Obesity, Infertility, and Exercise Intervention Research (Appendix D) was created. This form provides researchers with an easy to complete method of reporting components of an exercise intervention. To be clear, the recommendation is to complete the reporting sheet and include it as supplemental material, as well as to be provide clear and concise information about the exercise intervention in the methodology section. Including the reporting sheet in the supplementary information will mitigate word limit considerations. Reporting in this way can facilitate replication and comparison of the exercise intervention components between different interventions and allow for better understanding of which components of an exercise intervention might be beneficial for improving fertility outcomes among women with obesity and experiencing infertility.

3.5 Conclusion

The results of this review suggest that further investigation of exercise interventions as a first line therapeutic modality, rather than a last resort option, for women with obesity and experiencing infertility is warranted. Exercise, if taught and delivered correctly by skilled exercise professionals, is an inexpensive, accessible treatment strategy for this population. An important finding of this review is the positive effect of an exercise intervention on rates of natural conception. This is meaningful because, being able to conceive naturally significantly decreases the cost (i.e., financial, physical, psychological) associated with traditional fertility treatment. Future research should focus on creating effective exercise prescription protocols for women with obesity and experiencing infertility with the outcome of improving rates of natural conception and subsequently, live births.

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Chapter Four: Summary

4.1 Summary

The idea for this review came to light during the COVID-19 pandemic when initial plans to run an exercise intervention for women with obesity and experiencing infertility trial in Newfoundland (NL) became unfeasible because of lockdowns and restrictions. Based on the preliminary literature searches completed for the initial project, it was clear that there was limited literature on exercise interventions for women with obesity and experiencing infertility to understand a dose-response for this population. Therefore, before offering an exercise intervention for women with obesity and experiencing infertility targeting fertility outcomes, it was essential to understand what had been currently done in the field.

To gain a better understanding of the literature, this thesis first examined the literature around trends of obesity and infertility, common fertility outcomes, the effect of obesity on fertility outcomes, and interventions to improve fertility outcomes for women with obesity and experiencing infertility. Then, exercise as treatment for improving fertility outcomes was explored, including barriers and facilitators to exercise participation. Through the literature review, it was determined there is no consensus on the exercise prescription that would be most beneficial at improving fertility outcomes for women with obesity and experiencing infertility (McLean & Wellons, 2012). Specifically, it is not yet clear what type of exercise, frequency, intensity, and setting might result in the greatest improvements to fertility outcomes for this population (Lundgren et al., 2016). These initial findings shaped the objectives of this research which included determining what exercise interventions are currently being used to improve fertility outcomes for women with obesity, and secondly, what fertility outcomes are being explored. The overall aim of these objectives was to describe and analyze, and in doing so, evaluate the impact of exercise interventions aimed at improved fertility outcomes for this population. To achieve these objectives, a systematic narrative review of obesity and infertility literature was conducted.

This systematic narrative review was completed with well-defined inclusion and exclusion criteria, and search strategy in order to categorize both the exercise interventions and, fertility outcomes explored in current obesity and infertility literature. There were 16 studies included in this review. Arguably, the most important findings, are that exercise interventions for women with obesity and experiencing infertility led to improvements in live birth rates (*n*=3), pregnancy rates (*n*=11), and natural conception (*n*=4). Though not all of the studies reported on rates of conception, pregnancy, and live birth rates (*n*=5), reporting on live birth rate is recommended and should be presented in infertility trials regardless of the primary fertility outcome (Harbin Consensus Conference Workshop Group, 2014). Several other important findings were noted about the exercise interventions for women with obesity and experiencing infertility included in this review. First, all interventions examined have consistently led to improvements in fertility outcomes. However, these interventions vary widely and often do not include sufficient information for exercise prescription, making it challenging to decipher what piece of the intervention made it successful. Additionally, the lack of information related to exercise prescription makes it challenging to replicate many of the exercise interventions to improve fertility outcomes for women with obesity and experiencing infertility. Secondly, the fertility outcomes used in the literature may appear to vary greatly, however once categorized for this review, most often fell into the category of rates of conception, pregnancy, and live births. Overall, the results demonstrated that even though the relationship between obesity and infertility is very complex, fertility outcomes can be improved by exercise participation for women with obesity and experiencing infertility, although we do not know which exercise type, intensity, and load and other exercise characteristics are most effective.

More information is needed regarding technique, load prescribed, intensity, and duration of the exercise intervention, to replicate the exercise interventions. Many of the interventions were individualized and home-based programs. This is beneficial in that the exercise intervention is tailored to the specific needs of the participant; however, it significantly limits the ability to make conclusions about the intervention or if participants closely followed and met intervention protocols. Additionally, individualized home-based programs makes it challenging to understand how programs were tailored, and how those principles can be incorporated into future research. Diet, including meal planning and education sessions, were incorporated into many interventions, making it challenging to pinpoint what may have significantly impacted the fertility outcomes. Another challenge of exercise intervention research for women with obesity and experiencing infertility is that many women must delay fertility treatment to take part in the intervention. Lastly, limited studies made use of group exercise or give information relating to the intervention setting, factors known to impact exercise adherence.

4.2 Conclusion

It is well documented that obesity negatively impacts fertility outcomes. Interventions, such as exercise, are recommended for women with obesity and experiencing infertility as they have been found to improve fertility outcomes. However, there are large discrepancies in the specific exercise prescription recommended as well as inconsistent use of outcomes to define fertility across the literature. Overall, cyclic, sustained, and moderate are the most common types of exercise technique, load prescribed, and intensity used, respectively. Rates of conception, pregnancy, and live birth was the most common category of fertility outcomes explored. Despite the inconsistencies in both methodologies and reporting outcomes in obesity and infertility literature, the results are consistent. All studies examined in this review reported improvements to fertility outcomes after an exercise intervention.

4.3 Future Directions

As recommended, live birth should be the primary outcome of clinical trials of infertility treatment (Harbin Consensus Conference Workshop Group, 2014). Recommendations from this review highlight that the gold standard for primary fertility outcomes in exercise intervention studies should be live birth rates and rates of natural conception when an intervention is associated with artificial reproductive technology. For studies where menstrual and ovulation cycles, or hormonal panels, are the main outcome of interest, rates of live birth and natural conception should still be reported. This is because, menstrual and ovulatory cycles, as well as hormonal panels, should not be considered a true measure of fertility, rather an intermediary factor between exercise and stronger predictors of fertility, such as rates of live birth and natural conception. Reporting live birth rates and natural conception which, is consistent with recommendations by the Harbin Consensus Group should be followed (Harbin Consensus Conference Workshop Group, 2014). In conjunction, the reporting sheet for obesity, infertility, and exercise intervention research (Appendix D) is necessary to ensure proper exercise prescription can be reproduced. Together, this should guarantee that an intervention that has a positive effect on primary fertility outcomes (i.e., live birth and natural conception) can be replicated in future research.

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Appendices

Appendix A

Exercise Intensity Zones.

Aerobic Exercise				Resistance Exercise
Relative Intensity				
Intensity	**%HRmax**	**%VO2max**	**Perceived Exertion**	**%1RM**
Very Light	<57	<37	Very light	30
Light	57-<64	37-<45	Very light to fairly light	30-<50
Moderate	64-<76	46-<64	Fairly light to somewhat hard	50-<70
Vigorous	76-<96	64-<91	Somewhat hard to very hard	70-<85
Near Maximal to Maximal	>=96	>-91	>=Very hard	>=85

*Adapted from ACSM 2014 (Pescatello et al., 2014)

Appendix B

Data Extraction Chart.

First Author	Year	Location	Study Design	Type of Publication	CR or CP	Assignment	Population Characteristics 1	Population Characteristics 2	Population Characteristics 3	Sample Size	Number of Groups	Intervention Population	CR Population	CP Population	Sample Age	Population Age SD
Gorczyca	2018	USA	Prospective Cohort	Conference Abstract	No					14	1	14				
Kiel	2018	Norway	Randomized Controlled Trial	Full-text	CR	Random	Accepted for ART			18	2	8	10			
Al-Eisa	2017	Egypt	Quasi- Experimental	Full-text	CR & CP	Classified by BMI & PCOS Diagnosis	Study group without PCOS	CP with PCOS		90	3	30	30	30		
Espinos	2017	Spain	Randomized Controlled Trial	Full-text	CR	Random	Presenting for first IVF cycle			41	2	21	20			
van Oers	2016	The Netherlands	Randomized Controlled Trial (Secondary Analysis)	Full-text	CR	Random	Exercise intervention prior to fertility treatment			564	2	280	284			
Mutsaerts	2016	The Netherlands	Randomized Controlled Trial	Full-text	CR	Random	Exercise intervention prior to fertility treatment			574	2	289	285			
Duval	2015	Canada	Randomized Controlled Trial	Conference Abstract	CR	Random	67% had PCOS			55	2	24	31		30.3	4.7
Mahoney	2014	USA	Cohort	Full-text	No		PCOS			12	1	12				
Sim	2014	Australia	Randomized Controlled Trial	Full-text	CR	Random	Undergoing IVF, ICSI or cyrostored embryo transfer			49	2	27	22			
Khaskheli	2013	Pakistan	Observational Experimental	Full-text	No		Undergoing fertility treatment for 2-5 years			98	1	85			31.06	2.48
Kuchenbecker	2011	The Netherlands	Prospective Pilot Cohort	Full-text	No					22	1	22				
Moran	2011	Australia	Randomized Controlled Trial	Full-text	CR	Random	Undergoing IVF	Previously underwent 1 ART cycle		38	2	18	20			
Palomba	2010	Italy	Randomized Controlled Trial	Full-text	CR & CP	Random	PCOS	Clomiphene citrate resistant		96	3	32	32	32		
Maiya	2008	India	Prospective Cohort	Preliminary Report	CR	Choice	PCOS			42	2	21	21			
Palomba	2008	Italy	Pilot Cohort	Full-text	CP	Choice	Anovulatory	PCOS		40	2	20		20		
Miller	2005	USA	Prospective Pilot Cohort	Conference Abstract	No		Hx of oligomenorrhea (cycle interval >35days; n=1)	Hx irregular menses (cycle intervals discrepant by >5days; n=3)	Hx amenorrhea (more than 90 days without menses; n=8)	12	1	12				

First Author	Intervention Age	Intervention Age SD	CR Age	CR Age SD	CP Age	CP Age SD	Sample BMI	Sample BMI SD	Intervention BMI	Intervention BMI SD	CR BMI	CR BMI SD	CP BMI	CP BMI SD	Infertility Criteria 1	Infertility Criteria 2	Infertility Criteria 3
Gorczyca	33.4	4.5							40	5.9					Physician referred & diagnosed		
Kiel	33.1	5.9	31.7	4.3					28.9	2.4	31.2	1.3			Accepted for ART		
Al-Eisa	27.6	5.7	28.7	3.84	27.9	4.1			38.4	4.1	32.44	4.22	35.4	3.9	Physician referred & diagnosed		
Espinos	32	3.2	32.9	3.9					34.6	3	34	4.1			primary infertility	indication for IVF/ICSI	absence of hormonal treatment during <3 months
van Oers	29.7	4.5	29.8	4.6					36	Unknown	36	Unknown			Chronic anovulation	ovulatory cycle but no coneption >12 months	
Mutsaerts	29.7	4.5	29.8	4.6					36	Unknown	36	Unknown			Chronic anovulation (class I and II anovulation (WHO))	ovulatory cycle but no coneption >12 months	
Duval	Unknown	Unknown	Unknown	Unknown			40.1	7.5	Unknown	Unknown	Unknown	Unknown			regular intercourse >1year with regular menstrual cycles (age <35)	women without regular menstrual cycles or >35 years without conception after regular intercourse >6 months	Known cause of fertility
Mahoney	32	5.33							44	5.75					Enrolled from Fertility Clinic		
Sim	32.9	3.3	32.8	3.1					35.1	3.8	38				Intending to commense ART at fertiling clinic		
Khaskheli							36.21	1.35							Undergoing fertility treatment for 2-5 years		
Kuchenbecker	28.9	4.1							37.8	5.2					infertility >1 year	Partner total motile sperm concentration >=10 million	Enrolled from Fertility Clinic
Moran	33.8	3.5	32.5	3.3					34	4.5	33.9	4.4			Previously underwent IVF	Undergoing IVF	
Palomba	27.5	4.95	26.5	4.26	28.43	8.31			31.26	2.66	32.32	3.73	31.05	2.98	regular intercourse >1year	Hx Irregular periods	Normal FSH & Estradiol
Maiya	34	2	33	2					33.12	1.72	30.63	1.09			Physician referred & diagnosed		
Palomba	26.8	5.1			25.8	4.5			33.1	1.3	N/A	N/A	33.2	1.4	regular intercourse >1year	Hx Irregular periods	Normal FSH & Estradiol
Miller	30	4.7							>30	Unknown					Enrolled from Fertility Clinic		

First Author	ART Association	ART Prior Post	Treatment Delay	Intervention Technique	Intervention Load Prescribed	Intervention Intensity 1	Intervention Intensity 2	Intervention Group	Intervention Duration	Intervention Recovery Time	Intervention Cool Down	Intervention Setting	Diet Component	Counselling Component
Gorczyca	No		Unknown	Individualized	Unknown	moderate	vigorous	Individual	17		N/A	Individual exercise, outcomes assessed in clinic	Yes	No
Kiel	Yes	Post	Yes	Acylic	Intermittent	vigorous		Individual & Group	10	1 or 3	5	Initially supervised exercise, then individual, undertaken at university and hospital setting	No	No
Al-Eisa	No		Unknown	Cyclic	Sustained	moderate		Unknown	25		15	Supervised exercise, clinic	No	No
Espinos	Yes	Post	Yes	Cyclic	Unknown	moderate		Individual	12			Supervised exercise, hospital	Yes	No
van Oers	Yes and No	Post	Yes	Individualized	Unknown	moderate		Individual	24			Individual exercise, Hospital (outpatient) visits, telephone calls	Yes	Yes (Motivational)
Mutsaerts	Yes and No	Post	Yes	Individualized	Unknown	moderate		Individual	24			Individual exercise, Hospital (outpatient) visits, telephone calls	Yes	Yes (Motivational)
Duval	No		Yes	Individualized	Unknown	Unknown		Individual	26			Individual and fertility clinic, meetings with dietition and kinesiologist, follow up phone calls, 12 individual group workshops conducted by dietition or psychologist	Yes	Yes (Motivational)
Mahoney	No		Unknown	Individualized, Cyclic, & Acylic	Unknown	Unknown		Individual	12			Individual exercise, counselling session every two weeks (setting not clear)	Yes	Yes (Motivational)
Sim	Yes	Post	Yes	Unknown	Unknown	Unknown		Individual	12			Individual exercise, feedback based on self-report diaries, supervised group advice sessions	Yes	Yes
Khaskheli	No		Yes	Unknown	Unknown	Unknown		Unknown	26			Unclear, private clinics (unclear but seems to be supervised)	Yes	No
Kuchenbecker	No		Unknown	Individualized	Unknown	Unknown		Individual	26			Unknown, fertility clinic	Yes	Yes (Motivational)
Moran	Yes	Post	No	Cyclic & Acylic	Sustained & Intermittent	moderate		Individual	5 to 9			Individual, one intial education visit, one face-to-face follow up, and one follow up phone call	Yes	No
Palomba	No		Unknown	Cyclic	Sustained	moderate		Unknown	6		5	Supervised exercise (by cardiologist & EEG)	Yes	No
Maiya	No		Unknown	Individualized	Unknown	moderate		Individual	13		Yes (No time given)	Individual (Home) exercise	No	No
Palomba	No		Unknown	Cyclic	Sustained	vigorous		Unknown	30		5	Supervised exercise (by cardiologist & EEG)	No	No
Miller	No		Unknown	Cyclic & Acylic	Unknown	Unknown		Group	12			Supervised exercise, setting unknown	Yes	No

First Author	Total Intervention Length (Weeks)	Intervention Frequency (Days)	Intervention Session Time (Mins/Week)	Primary Fertility Outcome	Primary Fertility Outcome Category	Additional Info	Results Primary	Results General
Gorczyca	17	Unknown	300	Pregnancy	Rate of conception, pregnancy, and live birth	Average of 17 weeks completed of moderate to Vigorous physical activity (MVPA) targeting 300min/week & Reduced energy intake & Provided with lifestyle strategies	Positive	Positive
Kiel	10	3	115	Pregnancy	Rate of conception, pregnancy, and live birth	10 weeks ~ 3x week HIT (2 sessions a week 4x4min at 85-95%HRmax and 1 session at 10x1min max intensity) VS. standard preconception care prior to assisted reproduction	No significant change	Positive
Al-Eisa	12	3	135	Anti-mullerian Hormone	Hormonal (sex hormone)		Positive	Positive
Espinos	12	3	180	Clinical Pregnancy rate after single IVF cycle	Rate of conception, pregnancy, and live birth	Comparison between women who resumed ovulation (RO+) or not (RO-) after the intervention. Of infertile women whom took part in the intervention, 4 and 3 women conceived in the first 3 and last 3 months respectively.	No significant change	Positive
van Oers	24	2 to 3	60-90	Vaginal birth of a healthy singleton	Rate of conception, pregnancy, and live birth	Target of 10,000 steps per day with at least 30 minutes of moderate-intensity exercise 2-3 times a week	No significant change	Positive
Mutsaerts	24	2 to 3	60-90	Vaginal birth of a healthy singleton	Rate of conception, pregnancy, and live birth	Target of 10,000 steps per day with at least 30 minutes of moderate-intensity exercise 2-3 times a week. Associated with ART yes and no as the intervention is prior to fertility treatment, and if no conception treatment could consist of ART eventually if pharmacological treatments do not work.	Negative	Positive
Duval	26	Unknown	Unknown	Live birth rates (at 18 months)	Rate of conception, pregnancy, and live birth		Positive	Positive
Mahoney	12	3 to 5	90-300	Menstrual cyclicity	Regularity of menstrual or ovulation cycles		Positive	Positive
Sim	12	Unknown	Unknown	Clinical Pregnancy Rate after in 12 months after 12 week intervention	Rate of conception, pregnancy, and live birth		Positive	Positive
Khaskheli	26	0.5	Unknown	Pregnancy outcomes; miscarriages, preterm labour, full pregnancy	Rate of conception, pregnancy, and live birth	Metaoblic and endocrine pre and post testing for various hormones completed.	Positive	Positive
Kuchenbecker	26	Unknown	Unknown	Resumption of Ovulation	Regularity of menstrual or ovulation cycles	Only preliminary results	Positive	Positive
Moran	5 to 9	3 to 6	60-90	Pregnancy and live birth outcomes	Rate of conception, pregnancy, and live birth		No significant change	Positive
Palomba	6	3	90	Ovulation rate	Regularity of menstrual or ovulation cycles	Exercise + Diet group A, Observation + Clomiphene Citrate (week 3) treatment group B, Execise & Diet + Clomiphene Citrate (week 3) treatment Group C	Positive	Positive
Maiya	13	Unknown	Unknown	Ovulation rate, pregnancy rate, and reduced ovarian cyst size	Rate of conception, pregnancy, and live birth	3 months of home based graded aerobic exercise – intensity prescribed between 50-80 $\%HR_{max}$	Positive	Positive
Palomba	24	3	90	Pregnancy	Rate of conception, pregnancy, and live birth		No significant change	Positive
Miller	12	3	180	Menstrual cycle improvement	Regularity of menstrual or ovulation cycles	Low impact PA 3-5xweek for 30-60min & RT 2-3xweek & counselling sessions every 2 weeks on diet	Positive	Positive

First Author	Results Statistically Significant	Results Main Outcome	Results Main Effects
Gorczyca	Yes (PA assessed by pedometer signifcantly higher in those who became pregnant, $p=0.02$; women who became pregnant participated in the exercise program 11 weeks longer than those who did not $p=0.016$)	Rate of conception, pregnancy, and live birth	Eight women (57%) became pregnant
Kiel	Yes (Insulin sensitivity, fasting glucose, visceral fat, waist circumference and VO2peak significantly improved in exercise intervention group)	Rate of conception, pregnancy, and live birth	four women became pregnant in both PA (50%) and control (44%) group after ART; two women in intervention and one in control became pregnant prior to ART; insulin sensitivity significantly improved in exercise group; fasting glucose visceral fat, waist circumference and VO2 peak significantly improved in PA group; no significant changes between groups in body composition
Al-Eisa	Yes (Weight loss, fertility hormones, follicle-stimulating hormone, prolactin,oestrogen, antral follicle count, baseline anti-Mullerian hormone, and adiponectin were significantly correlated to the improvement in reproductive function ($p<0.05$ each))	Hormonal	significantly lowered fasting blood glucose, fasting insulin, prolactin and anti-mullerian hormone; significantly higher follicule stimulating hormone, adiponectin, oestrogen and fasting glucose to insulin ratio; 20 (67%) women from the obese group responded positively to the intervention i.e., significant improvements in reproductive functions such as increase in ovulation rates and improve in menstrual cyclicity
Espinos	Yes (Significantly higher live birth rate in the exercise intervention group $p=0.045$, non-significant trend towards a higher clinical pregnancy rate after fresh embryo transfer which was the primary outcome)	Rate of conception, pregnancy, and live birth	Non-significant trend towards a higher clinical pregnancy rate after fresh embryo transfer; intervention group had a significantly higher cumulative live birth rate; data suggest that weight loss resulted in a significantly increased cumulative live birth rate; Six of 11 anovulatory women resumed regular menstrual cycles during the intervention; trend towards a higher implantation rate
van Oers	Yes (Statistically significantly higher rates of natural conception in the intervention group)	Rate of conception, pregnancy, and live birth	Lifestyle intervention increased the natural conception rate in anovulatory, but not in ovulatory, obese infertile women; Wasit-to-hip ratio had no interaction regarding overall live birth rate or natural conception rate
Mutsaerts	Yes (Statistically significantly higher rates of natural conception in the intervention group, statistically significnatly higher live birth rate after 24 months for the control group who received prompt fertility treatment)	Rate of conception, pregnancy, and live birth	Within 24 months after randomization, the frequency of vaginal births of healthy singletons at term was significantly lower in the intervention group than in the control group; After the inclusion of data from pregnancies that were conceived within 24 months after randomization but ended following that period, there were no significant between-group differences in the rates of vaginal births of healthy singletons at term or in the rates of live births; significantly more women in the intervention group than in the control group had ongoing pregnancies that resulted from natural conception;
Duval	Yes (women in the interventiongroup had significantly higher pregnancy rate ($p = 0.003$)and spontaneous pregnancy rate ($p = 0.003$).	Rate of conception, pregnancy, and live birth	As compared with the control group, women in the intervention group had significantly higher pregnancy rate and spontaneous pregnancy rate; There was no significant difference between groups for pregnancy following assisted reproductive technology; a tendency to a higher rate of live birth was observed in the intervention group;
Mahoney	Unknown (Frequency in brisk walking exercise significantly increased ($p=.024$). Frequencyin home or gym exercise increased ($p=.050$).) Unknown if changes in menstrual cyclicity were statistically significant)	Regularity of menstrual of ovulation cycles	The mean daily caloric intake decreased from 2430 (±1151) kcal preintervention to 1078 (±453) kcal postintervention. This represents asignificant ($p=.005$) reduction of 1352 kcal; significant mean weight reduction of of 7(±5) pounds post lifestyle modification intervention, which represented an overall mean loss of 2.6%; significant ($p=.050$) mean increase in frequency of exercising at a gym or at home from "rarely" to "a few times per month" participation after the lifestyle intervention (but no significant change in duration); mean participation in brisk walking increased significantly ($p=.024$) to "three to four times per week." (no significant change in duration of brisk walk-ing activity); There were no reported improvements in menstrual regularity among subjects with a prior history of irregular cycles; Fifty percent ($n=2$) of the four amenorrheic participantsreported having two spontaneous menstrual cycles
Sim	Yes (The intervention group achieved a pregnancy rate of 48% compared with 14%($P=0.007$), took a mean two fertility treatment cycles to achieve each pregnancy compared with four in the control group ($P=0.002$), and had a marked increasein the number of live births ($P=0.02$)	Rate of conception, pregnancy, and live birth	The intervention group achieved a pregnancy rate of 48% compared with 14% ($P=0.007$); intervention group took a mean two fertility treatment cycles to achieve each pregnancy compared with four in the control group ($P=0.002$); intervention group had a marked increase in the number of live births (44% vs. 14%;$P=0.02$); intervention group had greater anthropometric changes; mean loss at 12 weeks was greater for participants in the intervention group; Participants in the intervention group had significantly improved fertility treatment outcomes in terms of mean number of treatment cycles required to achieve a pregnancy (2.4) compared with those assigned to standard care (3.7;$P=0.002$);
Khaskheli	Unknown (does not seem to be statistically significant)	Rate of conception, pregnancy, and live birth	35 (41.17%) women had spontaneous conception ($p = 0.569$); 19 (22.35%) women conceived with ovulation induction therapy and 31 (36.47%) women failed to conceive at all; Pregnancy outcome was full term live birth in 32 (59.25%) women, preterm birth in 13 (24.07%) women and miscarriage in 9 (16.66%) women;
Kuchenbecker	Yes (Those who resumed ovulation had statistically significant differences in weight loss and abdominal fat)	Regularity of menstrual of ovulation cycles	Resumed ovulation women lose more body weight and abdominal fat on DEXA than women who remained anovulatory; early and consistent loss of intra-abdominal fat is associated with resumption of ovulation;
Moran	No significant difference in pregnancy and live birth rate but - A reduction in waist circumference was associated with an increased odds of pregnancy and women who achieved pregnancy had greater reductions in waist circumference on ITT analysis.	Rate of conception, pregnancy, and live birth	There were no differences in pregnancies or live births between the active intervention and controls; There was a significant effect of treatment on change in weight and BMI ($P< 0.001$) such that active intervention showed weight or BMI reductions ($P< 0.001$) whilst the control group showed no weight ($P= 0.092$) or BMI ($P= 0.097$) changes; For waist circumference, there was a trend for a greater reduction for women who became pregnant compared with those that did not and greater reductions for the baseline value carried forward or last visit carried forward
Palomba	Yes (Ovulation rate significantly higher in goup with CC adminstration after execise/diet compared to either CC or exericse/diet alone)	Regularity of menstrual of ovulation cycles	After 6 weeks of structured exercise training plus hypocaloric diet, the ovulation rate was significantly higher in Group C (Structured exercise training plus hypocaloric diet for 6 weeks, with one cycle of clomiphene citrate after the first 2 weeks) [12/32 (37.5%)] than in Groups A (Structured exercise training plus hypocaloric diet for 6 weeks) [4/32 (12.5%)] and B (2 weeks of observation followed by one cycle of clomiphene citrate therapy) [3/32 (9.4%)];
Maiya	Unknown (preliminary results and doesn't specifiy if statistically significant)	Rate of conception, pregnancy, and live birth	Study group showed significant decrease in mean body mass index as compared to control group; the study group also showed increase in ovulation and pregnancy rate, and decrease n ovarian cyst size as compared to control group;
Palomba	No significant difference in menstrual cycles and fertility between groups - But statistically significantly higher frequency of menses and ovulation in exercise group compared to diet	Rate of conception, pregnancy, and live birth	After intervention, a significant improvement in menstrual cycles and fertility was noted in both groups, with no differences between groups; The frequency of menses and the ovulation rate were significantly ($P<0.05$) higher in the structured exercise training group than in diet group but the increased cumulative pregnancy rate was not significant; At 12-week follow-up, long term physical activity level was significantly improved versus baseline in SET group, whereas it remained unchanged in diet group; After 24 weeks, the ovulation rate was significantly higher in structured exercise training group than in diet group. The cumulative ovulation rate was also significantly higher in structured exercise training group than in diet group; A trend towards higher pregnancy and cumulative pregnancy rates in the structured exercise training group versus the diet group was observed at 24 weeks
Miller	Yes (Significant reduction in BMI and cholesterol, 83% improved menstrual cyclicity)	Regularity of menstrual of ovulation cycles	Ten of the twelve subjects (83%) showed menstrual improvement with eight overall becoming eumenorrheic; Two women who began the study amenorrheic conceived within the 12-week follow-up period; favorable metabolic and endocrine changes are possible in obese, infertile women after 12 weeks of diet and exercise; BMI and total cholesterol significantly decreased over the 12-week study period;

First Author	Results Live Birth	Results Pregnancy	Results Weight Loss	Results Adherence	Results Dropout
Gorczyca	No	Yes	Weight loss was greater in those who became pregnant but not statistically significnat (p=0.17)	Greater adherence to the exercise intervention resulted in higher rates of pregnancy. Length of treatment and reported step counts were associated with increased pregnancy rate.	N/A
Kiel	No	A trend to Yes, but underpowered	No statistically significant changes in body composition between groups	Adherence to the HIT programme was high, indicating that this could be a feasible exercise regime for this population.	1 participant
Al-Eisa	No	Unknown	Weight loss significantly correlated with improvements in reproductive function	N/A	N/A
Espinos	Yes	Yes	Significant reduction in weight and visceral adiposity	Close supervision of the intervention lead to high adherence and weight loss	None
van Oers	Yes	Yes	Effect of the intervention on the rate of the healthy live births was not altered by BMI, N/A with respect to if increase in weight loss resulted in increase in healthy live birth rate	N/A	63 participants from intervention
Mutsaerts	Yes	Yes (natural conception)	Weight loss statistically significant in intervention compared to control	N/A	63 participants from intervention
Duval	Yes	Yes (natural conception)	No significant difference in changes in body weight or waist circumference (modest weight loss following an interdisciplinary lifestyle intervention in obese infertile women could improve significantly their pregnancy rate, mainly the occur-rence of a spontaneous pregnancy)	N/A	N/A
Mahoney	No	Unknown	Significant mean weight reduction	N/A	2 participants
Sim	Yes	Yes	Statistically significant difference in weight, BMI, and waist circumference for those in the intervention group	N/A	10 participants
Khaskheli	Yes	Yes (& natural conception)	Mean change in BMI 9.6 +/- 1.23 kg/m^2 which is a significant reduction (No control group)	N/A	13 participants
Kuchenbecker	No	Unknown	Women who resumed ovulation lost statistically significantly more weight and had a higher loss of abdominal fat than those who did not resume ovulation	N/A	10 participants (considered high/normal)
Moran	Yes	No	Signifcant difference in weight loss for intervention group but no significant difference in waist circumference	N/A	8 Participants
Palomba	No	Unknown	Not clear	high rate of adherence to the dietary and SET programmes,with no dropouts, was probably due to sample characteristics and theprotocol design. The infertile patients had a high level of motivation because they were all overweight or obese and had not been responsive previously to CC administration	None
Maiya	No	Yes	Significant difference in BMI in comparion to control group	N/A	
Palomba	No	A trend to Yes, but underpowered	BMI was reduced significantly more in the diet group in comparison to the exericse group	Similar adherence to diet and exercise interventions	3/20 exercise group, 7/20 diet group
Miller	No	Yes (but no control)	Significant difference in BMI	N/A	N/A

Appendix C

Data Extraction Chart Outline/Key.

Column	Explanation	Possible Entries
First Author	study's first author	
Year	study year	year
Location	country where study was conducted	country
Study Design	type of experimental design	randomized controlled trial, cohort
Type of Publication	type of publication	full-text, report, letter, conference abstract
CR or CP	control group or comparison group included in study?	CR, CP
Assignment	how participants were assigned into groups	randomized, given choice, classified
Population Characteristics 1	additional related defined characteristics of the population	PCOS, anovulatory, infertility clinic patients, preceeding infertility treatment
Population Characteristics 2	additional related defined characteristics of the population	
Population Characteristics 3	additional related defined characteristics of the population	
Sample Size	number of participants in study	# participants
Number of Groups	number of groups in the study (i.e. comparison, control, intervention, etc.)	# groups
Intervention Population	number of intervention group participants	# participants
CR Population	number of control group participants	# participants
CP Population	number of comparison group participants	# participants
Population Age	age of participant population (only if ages are not given seperately according to grouping)	age in years
Population Age SD	age of participant population standard deviation (only if ages are not given seperately accoding to grouping)	
Intervention Age	Intervention group age	age in years
Intervention Age SD	Intervention group age standard deviation	age in years
CR Age	control group age	age in years
CR Age SD	control group age standard deviation	age in years
CP Age	comparison group age	age in years
CP Age SD	comparison group age standard deviation	age in years
Population BMI	participant population BMI (only if BMI is not given seperatly according to grouping)	
Population BMI SD	participant population BMI standard deviation (only if BMI is not given seperatly according to grouping)	
Intervention BMI	Intervention group BMI	BMI in kg/m2
Intervention BMI SD	Intervention group BMI standard deviation	BMI in kg/m2
CR BMI	control group BMI	BMI in kg/m2
CR BMI SD	control group BMI standard deviation	BMI in kg/m2
CP BMI	comparison group BMI	BMI in kg/m2
CP BMI SD	comparsion group BMI standard deviation	BMI in kg/m2
Infertility Criteria 1	infertility criteria to be met for inclusion in study	infertility >1year, irregular periods, hormonal criteria, anovulation, physician referred
Infertility Criteria 2	continued infertility criteria to be met for inclusion in study	
Infertility Criteria 3	continued infertility criteria to be met for inclusion in study	
ART Association	is the intervention associated with assisted reproductive technology (ART)	Yes, No
ART Prior Post	If yes, did participants undergo art prior the intervention (pre) or will they undergo art after the intervention (post)	Pre, Post
Treatment Delay	If participants have to delay fertility treatment to take part in the intervention	Yes, No
Intervention Technique	technique of the exercise intervention	Cyclic, Acyclic, Individualized, Unknown
Intervention Load Prescribed	how the exercise load is prescribed in the intervention	Sustained, Intermittent, Unknown
Intervention Intensity 1	intensity of exercise intervention (minimum if a range is reported)	very light, light, moderate, vigorous, near maximal to maximal
Intervention Intensity 2	intensity of exercise intervention (maximum if a range is reported)	very light, light, moderate, vigorous, near maximal to maximal
Intervention Group	if exercise portion of intervention took part in group fitness or individual setting	group, individual
Intervention Duration	duration of exercise intervention	time in minutes
Intervention Recovery Time	duration of exercise intervention recovery time (applicable for intermittent exercise)	time in minutes
Intervention Cool Down	duration of exercise intervention cool down	time in minutes
Intervention Setting	setting and details of where the exercise intervention took place	hospital, at home, at a gym, unknown, etc.
Diet Component	if a diet component is included in the intervention	Yes, No
Counselling Component	if a counselling component is included in the intervention	Yes, No
Total Intervention Length (Weeks)	length of intervention in weeks	# weeks
Intervention Frequency (Days)	amount of intervention per week in days	# days
Intervention Session Time (Mins/Week)	amount of intervention per week in minutes	# mins
Primary Fertility Outcome	primary outcome of fertility measured in study	pregnancy, ovulation rate, mensutral cyclicity
Primary Fertility Outcome Category	category to which the primary ferility outcome fits into	choice of 3 categories, 1 sub cateogry, or N/A
Additional Info	additional information relating to methods	
Results Primary	result of intervention on primary fertility outcome	positive, negative, no significant change, unknown
Results General	result of intervention on other fertility outcomes (If applicable)	positive, negative, no significant change, unknown
Results Statistically Significant	if the result of the intervention (realting to fertility outcomes) is statistically significant	Yes, No, Unknown (explanation if needed)
Results Main Outcome	the outcome that appears to be most affected by the intervention	hormones, menstrual cycle, pregnancy rate, etc.
Results Main Effects	the effects of the intervention on fertility outcomes	
Results Live Birth	did the intervention improve rates of live birth?	Yes, No, Unknown
Results Pregnancy	did the intervention improve rates of conception, pregnancy, and live birth rates?	Yes, No, Unknown
Results Weight Loss	Was a statistically significant weight loss achieved?	Yes, No, Unknown
Results Adherence	information relating to adherence of the exercise intervention	
Results Dropout	participants lost due to dropout	# participants

Appendix D

Reporting Sheet for Obesity, Infertility, and Exercise Intervention Research.

This form is intended to be attached to an appendix, supplemental information, or integrated into the methodological section of an exercise intervention study specifically for obesity, infertility, and exercise research to ensure replication of the exercise intervention can be completed.
* Required

1. Classification of the exercise intervention based on technique or modality. *
Check all that apply.
   - o Cyclic Exercise (Cyclic exercise is a consistent, and repetitive motor pattern i.e., walking, running, and cycling)
   - o Acyclic Exercise (Acyclic exercise is an inconsistent, and sequential motor pattern i.e., bootcamp, tennis, and circuit training.)
   - o Individualized Exercise Program
   - o Combination of Techniques

2. Classification of the exercise intervention based on how the load is prescribed. *
Check all that apply.
   - o Intermittent Exercise (Intermittent exercise has recovery time between bouts of exercise; recovering being either by stoppage of exercise or the lowering of intensity.)
   - o Sustained or Continuous Exercise
   - o Combination

3. If applicable, duration of recovery time for intermittent exercise (recovery time in minutes).

   ____

4. Classification of the exercise intervention based on intensity. If your exercise intervention has a range of intensities (i.e., moderate to vigorous) or is a progressive exercise select all that apply. *
Check all that apply.
   - o Very Light (%HRmax <57, %VO2max <37, Perceived Exertion = Very light, %1RM =30)
   - o Light (%HRmax =57 to <64, %VO2max =37 to <45, Perceived Exertion = Very light to fairly light, %1RM =30 to <50)
   - o Moderate (%HRmax =64 to <76, %VO2max =46 to <64, Perceived Exertion = Fairly light to somewhat hard, %1RM =50 to <70)
   - o Vigorous (%HRmax =76 to <96, %VO2max =64 to <91, Perceived Exertion = Somewhat hard to very hard, %1RM =70 to <85)
   - o Near Maximal to Maximal (%HRmax <=96, %VO2max >91, Perceived Exertion =Very hard, %1RM <=85)

5. Session time of the exercise sessions (Time in minutes/session). *

____

6. Frequency of the exercise sessions (Number of sessions/week). *

____

7. Total length of the exercise intervention (In weeks). *

____

8. Check the days of the week the exercise intervention is intended to be completed on. *
Check all that apply.

- Monday
- Tuesday
- Wednesday
- Thursday
- Friday
- Saturday
- Sunday

9. If the exercise intervention is not specific to the days of the week, please describe the between days i.e., the number of days off between the exercise intervention participation.

____

____

10. Intervention Location (Setting of the exercise intervention). *
Check all that apply.

- Home-based exercise intervention
- Clinic/Hospital based exercise intervention
- Community-based exercise intervention
- Research lab-based exercise intervention
- Other:

11. If other, please explain.

____

____

____

12. Intervention Environment *
Check all that apply.

- Group-based exercise intervention
- Individual-based exercise intervention
- Other

13. If other, please explain.

____
____
____

14. Did your exercise intervention include any of the following? *
Check all that apply.

- Warm-up
- Cool-Down
- Stretching

15. Please describe other information related to the setting of the exercise intervention (i.e., music, presence of mirrors, etc.). *

____
____

16. Is there any additional information about the exercise intervention that may be beneficial for replication of your exercise program? I.e., use of motivational counselling, diet education, combination of exercise with another intervention, etc.

____
____
____

17. Please confirm you have reported on live birth rates as an outcome in your intervention study in accordance with reporting guidelines. *Please note, reporting live birth rates even if not the primary outcome of the exercise intervention is strongly advised.*

- Yes
- No

Please find the link to the google form where you can use a PDF, printable version of the form: https://forms.gle/KGy1pnmARGgxEnRQ7