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**THE EFFECTS OF MENSTRUAL
CYCLE PHASE, ORAL
CONTRACEPTIVE USE, AND THE
ASSOCIATED SYMPTOMS ON
PERFORMANCE & RECOVERY IN
FEMALES.**

Kelly Lee McNulty

PhD

2022



**Northumbria
University**
NEWCASTLE

NORTHUMBRIA UNIVERSITY

“The effects of menstrual cycle phase, oral contraceptive use, and the associated symptoms on performance and recovery in females”.

A thesis submitted in partial fulfilment of the requirements of Northumbria University for the degree of Doctor of Philosophy

By

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September 2022

ABSTRACT

As the number of women participating in sport and exercise has increased, there is a need for sport and exercise science research that considers the influence of woman-specific physiology on exercise performance outcomes and responses to exercise. As such, the purpose of this thesis was to investigate the effect of the menstrual cycle (MC), oral contraceptive pill (OCP) use, and related symptoms, on exercise performance and recovery outcomes in recreationally active sportswomen. In *Chapters 3 and 4*, the effects of MC phase and OCP use on exercise performance were investigated, respectively, by conducting a systematic review and meta-analysis on the literature to date. Together, these Chapters showed that exercise performance might be trivially reduced during the early follicular phase of the MC, compared to all other phases, and that OCP use might result in slightly inferior exercise performance, on average, when compared to naturally menstruating women. However, as the effects tended to be trivial and variable across studies, and study quality was judged as poor, general guidelines on exercise performance across the MC, and with OCP use, could not be formed. Whilst *Chapters 3 and 4* amalgamated studies that assessed exercise performance across the MC, and with OCP use, they did not consider the impact of cycle related symptoms and perceived effects on exercise outcomes. Therefore, *Chapter 5* examined the type, frequency, and severity of cycle related symptoms experienced by naturally menstruating women and combined, monophasic, oral contraceptive pill (_mOCP) users, and their perceived effects on exercise performance and recovery time post exercise. This Chapter showed that symptoms are commonly reported in sportswomen, with no difference in symptomology between naturally menstruating women and _mOCP users. Importantly, the magnitude of symptoms experienced was greater whilst bleeding, which was associated with a perceived reduction in exercise performance and a longer recovery time post exercise. *Chapter 6* extended the findings in previous Chapters by investigating the effect of the MC and _mOCP use, alongside related symptoms, on physical and perceptual measures of exercise performance and recovery time post an exercise session. The results revealed that performance was reduced when participants were bleeding compared to all other *phases*. Moreover, whilst recovery time post exercise was not directly affected by *phase* or group, perceptions of recovery differed. It is possible that the reduced performance whilst bleeding and perceptions of recovery were influenced by the experience of cycle related symptoms. Collectively, the work in this thesis provides a novel insight into the importance of considering not only reproductive hormonal milieus, but also the individual lived experiences of the MC and _mOCP use on exercise performance and recovery outcomes in sportswomen.

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LIST OF ABBREVIATIONS

BBT	Basal body temperature
CI	Confidence interval
CK	Creatine kinase
CMJ	Countermovement jump
CrIs	Confidence intervals
DOMS	Delayed onset of muscle soreness
EIMD	Exercise induced muscle damage
EPRQ	Elite performance readiness questionnaire
ER	Oestrogen receptor
FSH	Follicle stimulating hormone
GnRH	Gonadotropin-releasing hormone
GRADE	Grading of recommendations, assessment, development, and evaluations
HC	Hormonal contraceptive
HPO	Hypothalamic-pituitary-ovarian
HR	Heart rate
IL-6	Interleukin-6
IQR	Interquartile range
LH	Luteinizing hormone
LPD	Luteal phase defect
MC	Menstrual cycle
Mdn	Median
MSi	Menstrual symptom index
MVC	Maximum voluntary contraction
OCP	Oral contraceptive pill
^m OCP	Combined, monophasic, oral contraceptive pill
PICOS	Population, intervention, comparison, outcome, and study design
PRISMA	Preferred reporting items for systematic reviews and meta-analyses
PR	Progesterone receptor
RPE	Rating of perceived exertion
SD	Standard deviation
SI	Symptom index
SUCRA	Surface under the cumulative ranking score
VE	Ventilatory rate
$\dot{V}O_{2\text{max}}$	Maximal oxygen consumption
$\dot{V}O_{2\text{peak}}$	Peak oxygen consumption

PUBLICATIONS

Peer-reviewed publications arising from this thesis:

*Chapters 5: McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K. J., Howatson, G., & Hicks, K. M. (2021). The symptoms experienced by naturally menstruating women and oral contraceptive pill users and their perceived effects on exercise performance and recovery time post exercise. *British Journal of Sports Medicine* (in review).*

Chapters 3 and 4: Elliott-Sale, K. J. McNulty, K.L*, Goodall, S., Ansdell, P., Thomas, K., Swinton, P. A., Dolan, E., & Hicks, K. M. (2021). Reply to: Comment on: “The Effects of Menstrual Cycle Phase on Exercise Performance in Eumenorrheic Women: A Systematic Review and Meta-Analysis” and “The Effects of Oral Contraceptives on Exercise Performance in Women: A Systematic Review and Meta-analysis”. *Sports Medicine*, 51(5), 1111-1113.*

Chapter 3: McNulty, K.L, Elliott-Sale, K.J*, Dolan, E., Swinton, P.A., Ansdell, P., Goodall, S., Thomas, K., & Hicks, K.M. (2020). The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. *Sports Medicine*, 1-15.*

Chapter 4: Elliott-Sale, K.J, McNulty, K.L*, Ansdell, P., Goodall, S., Hicks, K.M., Thomas, K., Swinton, P.A., & Dolan, E. (2020). The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. *Sports Medicine*, 1-28.*

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Chapter 6: McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). Are performance and recovery time influenced by the menstrual cycle, oral contraceptives, and associated symptoms. 8-minute oral presentation at: Women in Sport Congress; 17th – 19th August; Melbourne, Australia.

Chapters 5 & 6: McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). The menstrual cycle, oral contraceptive pill use, and associated symptoms on exercise performance and recovery. Symposium at: The Physiological Society Physiology Symposium 2022; 11th May; Derby, United Kingdom.

Chapter 3: McNulty, K.L., Elliott-Sale, K.J., Dolan, E., Swinton, P.A., Ansdell, P., Goodall, S., Thomas, K., & Hicks, K.M. (2020). The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. Poster presentation at: Female Athlete Conference; 10th – 12th June 2021; Virtual event.

Chapter 4: Elliott-Sale, K.J., **McNulty, K.L.**, Ansdell, P., Goodall, S., Hicks, K.M., Thomas, K., Swinton, P.A., & Dolan, E. (2020). The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. 15-minute oral presentation at: Future Physiology Conference; 19th – 22nd April 2021; Virtual event.

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McNulty, K. L., Hicks, K. M., & Ansdell, P. (2021). Variation in physiological function within and between menstrual cycles: uncovering the contributing factors. *Experimental Physiology*, 106(7), 1405-1406.

DECLARATION

I declare that the work contained in this thesis has not been submitted for any other award and that it is all my own work. I also confirm that this work fully acknowledges opinions, ideas, and contributions from the work of others.

Any ethical clearance for the research presented in this thesis has been approved. Approval has been sought and gained by the Faculty of Health and Life Sciences Ethics committee for each study.

I declare that the Word Count of this Thesis is 53,291 words.

Name: Miss Kelly Lee McNulty

Date: 23/09/2022

CHAPTER 1 – INTRODUCTION

1.1 Introduction

The number of women participating in both sport and exercise has increased considerably in recent decades (Fink, 2015). However, this decreasing sex gap in sport and exercise participation does not translate into a balanced ratio of scientific research between men and women (Bruinvels *et al.*, 2017; Costello *et al.*, 2014). Specifically, a recent study by Cowley *et al.* (2021) highlights the current asymmetry in sport and exercise science research, with results showing a male bias in both the total number of participants and the number of single-sex publications. Given the reported sex differences in exercise performance, and the responses to exercise (Ans dell *et al.*, 2020), it precludes the application of findings from studies conducted on men-only to women. Despite this, at present, most sport and exercise guidelines are derived from studies with men as participants and generalised to women, which can result in a missed opportunity for sportswomen to fulfil their health and performance potential (Emmonds *et al.*, 2019). As such, there is a need for more women to be included in research, and for more woman-only research which looks at the effects of sex-specific factors on sport and exercise outcomes. Indeed, one unique consideration for sportswomen is the potential influence of the menstrual cycle (MC), and hormonal contraceptives (HCs), on exercise performance outcomes and responses to exercise.

The MC is a biological rhythm characterised by cyclical fluctuations in endogenous sex hormone concentrations, namely oestrogen and progesterone (Owen Jr, 1975). Often, the concentrations and/or ratio of these sex hormones are used to separate the MC into predefined cycle phases: 1) the early follicular phase, characterised by the lowest concentrations of oestrogen and progesterone; 2) the late follicular/ovulatory phase, characterised by the highest/moderate concentrations of oestrogen, respectively, and low progesterone; and 3) the mid-luteal phase, characterised by high oestrogen and the highest progesterone concentration (Thompson & Han, 2019). Whilst the primary role of the MC is to support reproductive function, it is well-established that the cyclical changes in oestrogen and progesterone across the MC can also affect biological tissues and systems containing the respective hormone receptor(s) (Wierman, 2007). For instance, these sex hormones have been shown to affect physiological processes within the cardiopulmonary (Behan & Wenninger, 2008; Knowlton & Lee, 2012), metabolic (Boisseau & Isacco, 2022; Hackney, 2021), musculoskeletal (Alexander *et al.*, 2021; Chidi-Ogbolu & Baar, 2019), and nervous (Del Río *et al.*, 2018) systems; the integration of which determines many outcomes in sport and exercise. As such, the changes in endogenous sex hormones across the MC have the potential to affect exercise performance

(Carmichael *et al.*, 2021; Constantini *et al.*, 2005; de Jonge, 2003; Frankovich & Lebrun, 2000; Lebrun, 1993; Lebrun *et al.*, 2013), as well as the responses to exercise (Knowles *et al.*, 2019; Nakamura & Aizawa, 2017; Thompson *et al.*, 2020).

To date, the effects of fluctuations in oestrogen and progesterone across the MC on exercise performance are conflicting, with a substantial divide between research that supports (Bambaeichi *et al.*, 2004; Campbell *et al.*, 2001; Ekenros *et al.*, 2013; Oosthuysse *et al.*, 2005; Pallavi *et al.*, 2017; Tenan *et al.*, 2016) and refutes (Casazza *et al.*, 2002; de Jonge *et al.*, 2001; Elliott *et al.*, 2003; McLay *et al.*, 2007; Thompson *et al.*, 2012; Vaiksaar *et al.*, 2011a) an effect. Thus, it is evident that a consensus is yet to be reached regarding the effects of sex hormone concentrations across the MC on exercise performance in sportswomen. Similarly, whilst longitudinal studies support a possible effect (both enhanced and impaired) of fluctuations in sex hormones across the MC on end-point training outcomes in women (Kissow *et al.*, 2022; Nakamura & Aizawa, 2017; Thompson *et al.*, 2020), few studies have investigated the responses to, and recovery process following exercise across the MC (Hackney *et al.*, 2019; Romero-Parra, Cupeiro, *et al.*, 2021). This is despite a potential sex hormone effect on mechanisms pertaining to recovery (Enns & Tiidus, 2010; Tiidus, 2005; Tiidus, 2003), and the importance of these timepoints in the adaptation process (Bishop *et al.*, 2008; Kellmann *et al.*, 2018). As such, further research providing a consensus on the effect of the MC on exercise performance, as well as investigating the responses to, and recovery from exercise, in sportswomen, is warranted.

The MC is susceptible to internal (*e.g.*, amenorrhea, oligomenorrhea, and menorrhagia) and external (*e.g.*, HC) perturbations, highlighting the diversity in sex hormone profiles between women (Elliott-Sale & Hicks, 2018). Around 50% of sportswomen use some form of HC, with the oral contraceptive pill (OCP) the most prevalent type (Heather *et al.*, 2021; Martin *et al.*, 2018). Whilst there are various types of OCPs, each with different compositions, potencies, and androgenic activity, most OCPs are combined, monophasic, OCPs (_mOCP) that contain ethinyl oestradiol and a type of progestin which are delivered in a fixed amount every day for 21 pill-taking days, followed by seven pill-free days (Elliott-Sale & Hicks, 2018). Consequently, OCP use results in a different sex hormone environment when compared with the natural MC, which might have different implications for exercise performance (Burrows & Peters, 2007; Rechichi *et al.*, 2009), as well as the responses to, and recovery from exercise (Castro *et al.*, 2022; Hayward *et al.*, 1998; Hicks *et al.*, 2017; Mackay *et al.*, 2019; Minahan *et*

al., 2015; Romero-Parra, Rael, *et al.*, 2021; Savage & Clarkson, 2002). Likewise, given the changing sex hormone profile across the OCP cycle it could be theorised that exercise performance (Elliott-Sale & Hicks, 2018), and the recovery response to exercise, might differ between pill-taking and pill-free days (Romero-Parra, Rael, *et al.*, 2021). However, at present, research has shown conflicting findings on the magnitude and directional effects of OCP use on exercise performance (Bryner *et al.*, 1996; Casazza *et al.*, 2002; Lebrun *et al.*, 2003; Rechichi & Dawson, 2009; Sarwar *et al.*, 1996), and the literature investigating the recovery response to exercise with OCP use is lacking (Castro *et al.*, 2022; Hayward *et al.*, 1998; Hicks *et al.*, 2017; Mackay *et al.*, 2019; Minahan *et al.*, 2015; Romero-Parra, Rael, *et al.*, 2021; Savage & Clarkson, 2002). As such, further research is needed to elucidate the implications of OCP use on exercise performance, and to examine recovery outcomes post exercise in OCP users.

Whilst exercise performance and the recovery process post exercise might be altered via hormonally mediated changes, another plausible reason for any effects could be the influence of cycle related symptoms and perceived outcomes of the MC and OCP use. Specifically, the cyclic fluctuations in endogenous sex hormones across the MC have been associated with a variety of physical (*e.g.*, period pain, breast pain, and bloating) and psychological (*e.g.*, mood changes, anxiety, and irritability) symptoms (Dickerson *et al.*, 2003; Ferries-Rowe *et al.*, 2020; Yonkers *et al.*, 2008), which are likely incompatible with optimal exercise performance and training in sportswomen. Indeed, cycle related symptoms are commonly reported in sportswomen and these symptoms are perceived to impact an individual's ability to perform and train (Bruinvels *et al.*, 2021; Martin *et al.*, 2018). Interestingly, the OCP is often prescribed to women to reduce negative cycle related symptoms within general and athletic populations (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). Thus, it is possible that OCP use might reduce any negative impact of cycle related symptoms on exercise performance and training in sportswomen (Martin *et al.*, 2018). Furthermore, an individual's beliefs surrounding their performance and training are important considerations (Kellmann *et al.*, 2018), and it has been reported that many women perceive that their MC or HC use influences their performance and training (Armour *et al.*, 2020; Bruinvels *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Read *et al.*, 2021; Solli *et al.*, 2020). Whilst most studies within this area have focused on the effect of a particular sex hormone milieu on physiology, and subsequent performance and training outcomes, the potential indirect effects of sex hormone fluctuations (*i.e.*, related symptoms and perceived outcomes),

have been relatively overlooked (Bruinvels *et al.*, 2022). Thus, there is minimal guidance for sportswomen, and those working with them, in relation to managing the individual lived experiences of the MC or OCP use. As such, there is a need for studies to adopt a multifaceted approach when investigating the effects of the MC and OCP use on exercise performance and recovery outcomes to better understand the full extent of these respective cycles in sportswomen.

Overall, understanding the effect of the MC and OCP use on exercise performance, as well as the responses to and recovery from exercise, is essential to optimise the support provided to sportswomen, and hence the primary aim of this thesis. Indeed, using a multifaceted approach that intertwines both the influence of endogenous and exogenous sex hormone profiles and individual lived experiences (*i.e.*, cycle related symptoms and perceived effects of the MC and OCP use), this thesis provides a comprehensive overview of the effects of the MC and OCP use on exercise performance and recovery outcomes in sportswomen. Specifically, *Chapter 2* of this thesis reviews the literature pertaining to the effects of the MC and OCP use on exercise performance, as well as the recovery process post exercise. *Chapter 3* investigates whether the changes in sex hormone concentrations across the MC affect exercise performance in naturally menstruating women by conducting a systematic review and meta-analysis on the literature to date. *Chapter 4* explores the effect of OCP use on exercise performance, comparing: 1) between OCP users and naturally menstruating women; and 2) within OCP users on pill-taking versus pill-free days, by conducting a systematic review and meta-analysis on the literature to date. *Chapter 5* examines the cycle related symptoms experienced by naturally menstruating women and _mOCP users and their perceived effects on exercise performance and recovery time post exercise. *Chapter 6*, the final experimental section in this thesis, investigates the effect of the MC and _mOCP cycle, alongside related symptoms, on physical and perceptual measures of exercise performance and recovery time post an exercise session. *Chapter 7* provides an overarching discussion of the thesis, including the principal findings and proposed mechanisms, within the context of existing literature, with practical implications and recommendations for future research closing this Chapter. Finally, *Chapter 8* provides the conclusions of the thesis.

CHAPTER 2 – LITERATURE REVIEW

2.1. Introduction to literature review

This Chapter provides a comprehensive synopsis of the literature pertaining to the effects of the MC and HC use (namely the OCP), on exercise performance, as well as the responses to and recovery from exercise. Specifically, *Section 2.2* introduces the ‘sportswoman’ and gives a summary of the trends in women’s participation in sport and exercise, along with a discussion pertaining to the current sex bias in sport and exercise science research. *Section 2.3* presents an overview of the models of reproductive function in women, providing information on the MC, as well as OCP use; the two most common reproductive hormone models experienced by sportswomen. How the fluctuations in endogenous sex hormones across the MC might affect exercise performance is covered in *Section 2.4*, along with a critical evaluation of the literature to date. Moreover, since many sportswomen use OCPs, the effects of exogenous sex hormones on exercise performance are debated in *Section 2.4*. Following this, *Section 2.5* discusses the effects of the MC and OCPs on the responses to and recovery from exercise. Moving beyond the reproductive hormonal milieu, *Section 2.6* highlights the potential effect of an individual’s lived experience (*i.e.*, cycle related symptoms and perceived effects) of the MC and HC use on exercise performance and training outcomes. Finally, the aims and hypotheses of the investigations in this thesis are presented in *Section 2.7*.

2.2 The ‘sportswoman’

2.2.1 Trends in women’s sport and exercise participation

Unless otherwise stated, the term ‘sportswomen’ is used throughout this thesis to encompass a wide range of women who exercise, from recreationally active women to elite woman athletes. Historically, inequalities have existed in the inclusion of women in sport and exercise at both recreational and elite levels (Patel *et al.*, 2010). Specifically, during the early 1800s scientists cautioned women against physical activity, with concerns that “*physical effort, like running and jumping, might damage female reproductive organs and make them unattractive to men*” (McCrone, 2014, p. 193). Whilst some medical practitioners at the time challenged this belief, up until the late 1800s it was thought that vigorous physical exercise was unsuitable for women, and as such women were limited to activities deemed suitable at the time, such as walking, dancing, horseback riding, and tennis (Rosser & Rosser, 2008). Additionally, the view that women should not participate in sport and exercise was echoed within the elite sport

environment (Chase, 1992). For example, the founder of the Olympic Games, Baron Pierre de Coubertin, claimed that the Games were created for “*the solemn and periodic exaltation of male athleticism*” (Fuller, 1987, pp. 4-10), further stating:

It is indecent that spectators should be exposed to the risk of seeing the body of a woman being smashed before their eyes. Besides, no matter how toughened a sportswoman may be, her organism is not cut out to sustain certain shocks. (Fuller, 1987, pp. 4-10).

Therefore, participation in the first modern-day Olympic Games, held in Athens in 1896, was limited to men only (Patel *et al.*, 2010). However, as the twentieth century progressed, sportswomen gradually became an accepted part of sport and exercise (Patel *et al.*, 2010), and since the early 1900s there has been a gradual rise in the number of women participating in sport and exercise (Fink, 2015).

Today, women are participating in sport and exercise in record numbers (International Working Group on Women and Sport, 2007), attributable to changing societal and cultural views, as well as the increasing development of, and investment in, women’s sport (Forsyth & Roberts, 2018). For instance, a range of strategies, organisations, charters, and laws have been introduced by Governments and sporting organisations worldwide, with the purpose of increasing the number of women participating in sport and exercise (Costello *et al.*, 2014; Cowley *et al.*, 2021). These types of initiatives have helped to increase the number of women involved in recreational sport and exercise and increase the number of women participating at an elite level. The number of women participating in the Summer Olympics can be taken as a representative example: in 1900, 22 women competed at the Paris Games (2% of total participants in five sports), whereas at the most recent Games in Tokyo, 5,457 women competed (49% of total participants in 33 sports), making it the most sex-balanced Games in history (International Olympic Committee, 2021). As such, tremendous progress has been made for women in sport and exercise over the past century, and further progress can be anticipated moving through the twenty-first century. Given that the number of women participating in sport and exercise continues to rise, understanding the specific needs of sportswomen has become increasingly essential (Costello *et al.*, 2014; Cowley *et al.*, 2021). Indeed, like their male counterparts, sportswomen are now training hard, achieving personal bests, and continuing to push the physical limits of human performance (Pitchers & Elliott-Sale, 2019). Therefore, there is a growing demand for researchers to improve scientific knowledge of woman-specific physiology and performance/training, as well as develop and

disseminate effective strategies to optimise the overall health and performance of sportswomen.

2.2.2 ‘Invisible sportswomen’: the gap(s) in sport and exercise science research

Research investigating the effects of woman-specific physiology dates to 1876, when Professor Mary Putnam-Jacobi studied the effect of menstruation on a range of variables including muscle strength, pulse pressures, and daily physical activity levels (Jacobi, 1877). The data demonstrated that menstruation did not hinder women’s performance and her essay ‘*The Question of Rest for Women during Menstruation*’ was awarded Harvard University’s esteemed Boylston Prize. Despite this pioneering work, as well as the decreasing sex gap in women’s sport and exercise participation (see *Section 2.2.1*), woman-specific research falls short of that carried out in men (Bruinvels *et al.*, 2017; Costello *et al.*, 2014; Cowley *et al.*, 2021). For example, the most recent study to examine the sex of participants in 5,261 original research articles published between 2014 and 2020, within six popular sport and exercise science journals, demonstrated that women participants continue to be underrepresented within sport and exercise science research, with the results showing a bias towards men (Cowley *et al.*, 2021). Specifically, when analysing the total number of participants, only 34% of study participants were women, and studies exclusively in women participants accounted for only 6% of participant groups in original research (Cowley *et al.*, 2021). Therefore, it is plausible that the underrepresentation of women in the current sport and exercise research landscape has created a gap in the knowledge base pertaining to sportswomen (Emmonds *et al.*, 2019; Mujika & Taipale, 2019; O’Halloran, 2020).

Historically, this lack of woman-specific research in sport and exercise can be attributed to past guidelines and perceptions of women (Bruinvels *et al.*, 2017). Indeed, the sex bias in research dates to before World War II, where medical trials were solely conducted on men (McGregor & Choo, 2012). At the time women were deemed as ‘protected subjects’, due to the overarching fear that any clinical testing could potentially harm unborn foetuses (McGregor & Choo, 2012). Additionally, despite observations that men and women were physiologically different, men were deemed adequate proxies for women at this time (McGregor *et al.*, 2013). Today, one frequently cited reason for the exclusion of women from sport and exercise science research is that women are perceived as being ‘too complex’, ‘time consuming’ and/ or ‘expensive’ to study, given that women are more physiologically variable than men (Cowley *et al.*, 2021; Emmonds *et al.*, 2019; Mujika & Taipale, 2019). Indeed, the complexities of the fluctuations

in endogenous sex hormones across the MC, and the introduction of exogenous sex hormones through HC use, are considered major barriers to the inclusion of women in research (Bruinvels *et al.*, 2017). Consequently, a large proportion of the current information from sport science research is generalised to women, often without researchers and practitioners questioning whether this direct transfer is valid (Sims & Heather, 2018). As such, it is likely that there are numerous unexploited opportunities to optimise performance and training in sportswomen that have not been considered (Elliott-Sale *et al.*, 2021; Emmonds *et al.*, 2019).

It would be incorrect to suggest that there is currently no research available pertaining to sex hormones in women and sport and exercise. Indeed, many experimental studies (see *Section 2.4*), narrative and systematic reviews (Burrows & Peters, 2007; Carmichael *et al.*, 2021; Constantini *et al.*, 2005; de Jonge, 2003; Frankovich & Lebrun, 2000; Kissow *et al.*, 2022; Knowles *et al.*, 2019; Lebrun, 1993; Lebrun *et al.*, 2013; Rechichi *et al.*, 2009; Thompson *et al.*, 2020), books/book chapters (Forsyth & Roberts, 2018; Hackney, 2016), and meta-analyses (Blagrove *et al.*, 2020; Romero-Parra, Cupeiro, *et al.*, 2021) have addressed the effects of variations in hormonal milieus across the MC and with HC use on performance and training outcomes. However, the majority conclude that findings are weakened by inconsistencies in terminology (namely in the definition of reproductive status) and from poor methodological rigor (namely in the measurement of reproductive status), and thus studies of higher quality are needed before accurate conclusions can be made (see *Section 2.4.5*). As a result, this further compromises the ability to draw evidence-based conclusions and recommendations for sportswomen, and those working with them (Elliott-Sale *et al.*, 2021).

2.3 Models of reproductive function in women

It is well known that reproductive function changes across the lifespan in women (Hackney, 2016). Specifically, during puberty in girls, oestrogen and progesterone, the predominant sex hormones in women, begin to rise, and from menarche to post-menopause, women are exposed to a continuously changing profile of endogenous sex hormones, as they undergo circannual changes, commonly referred to as the MC (Reilly, 2000). In addition, reproductive function can be altered in women through exogenous hormones, such as HCs and hormonal replacement therapy, as well as environmental/lifestyle factors (*e.g.*, energy availability, exercise, and stress), disease (*e.g.*, polycystic ovary syndrome, endometriosis, and thyroid dysfunction), *in-vitro* fertilisation treatment, and pregnancy, highlighting the diversity in sex hormone profiles

within and between women (Elliott-Sale *et al.*, 2021), as well as further emphasising the need for sex-specific consideration within sport and exercise science. Given that the MC and HC use are most pertinent models of reproductive function to sportswomen, they will be the focus of the subsequent section and thesis herein.

2.3.1 The reproductive system in women

The changes in reproductive function across a woman's lifespan are primarily controlled by the reproductive system, which is essential not only for reproduction, but for overall health (Hackney, 2016). It is known that this system consists of multiple hormonal and regulatory components (Hackney, 2016). Specifically, to ensure proper functioning, the reproductive system is regulated by the complex interplay of endocrine feedback loops between three neuroendocrine glands: 1) the hypothalamus, located in the brain; 2) the pituitary gland, a protrusion off the bottom of the hypothalamus; and 3) the ovaries, located on either side of the uterus (Sam & Frohman, 2008). This controlling regulatory axis in women is commonly referred to as the hypothalamic-pituitary-ovarian (HPO) axis (Figure 2.1; [Popat *et al.*, 2008]). The signalling process for this axis begins in the hypothalamus, which is responsible for the production of gonadotropin-releasing hormone (GnRH; [Sam & Frohman, 2008]). The release of GnRH stimulates the glandular cells of the anterior pituitary gland to synthesise and release follicle stimulating hormone (FSH) and luteinizing hormone (LH; [Davis & Hackney, 2017]). Follicle stimulating hormone and LH are responsible for stimulating follicle maturation and triggering ovulation (Davis & Hackney, 2017). These hormones travel in the blood stream to the ovaries, where they bind to their specific ovarian receptors, resulting in the production and secretion of the two predominate sex hormones in women: 1) oestrogen; and 2) progesterone (Davis & Hackney, 2017). Indeed, LH binds to LH receptor sites on thecal cells, within the ovaries, which convert available cholesterol into androgens that are then transported to the granulosa cells (McNatty *et al.*, 1979). Here, FSH binds to FSH receptor sites stimulating the conversion of androgens, via aromatase enzymes, into oestrogen and progesterone (Filicori, 1999). In naturally menstruating women, the release of GnRH follows a cyclic pattern, consequently LH and FSH are released in a similar manner, which in turn results in the cyclic release of oestrogen and progesterone (Speroff & Fritz, 2005).

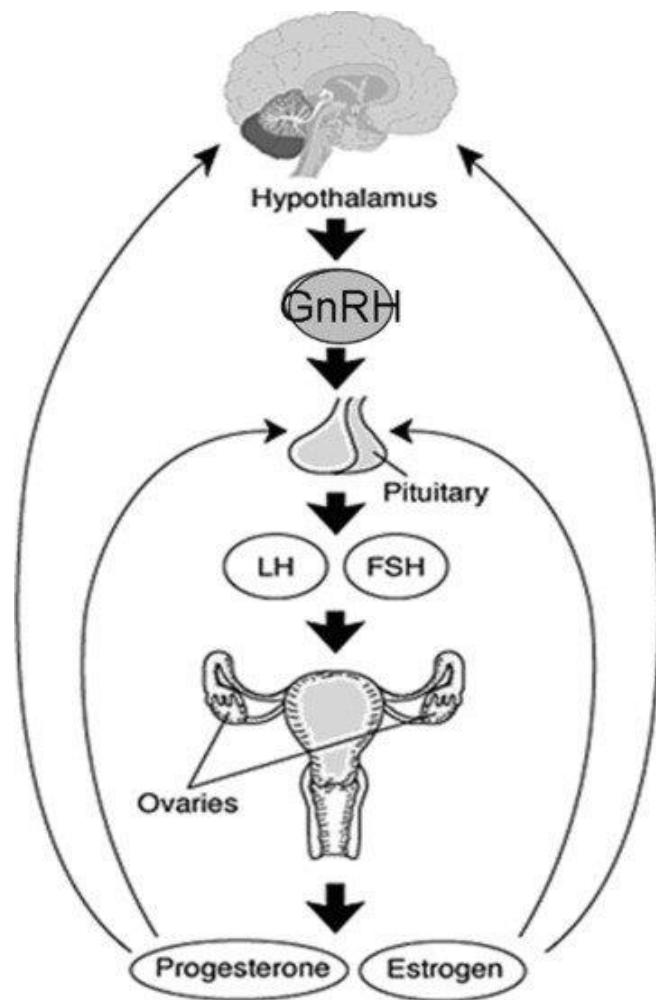


Figure 2-1 The hypothalamic-pituitary-ovarian axis as represented in Popat *et al.* (2008). FSH, follicle stimulating hormone; GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone.

2.3.2 Reproductive hormones in women

As highlighted above in *Section 2.3.1*, whilst there are many hormones involved in controlling the reproductive system of women, oestrogen and progesterone are the two main sex hormones (Hackney, 2016). Before the cyclical fluctuations in these sex hormones are discussed (see *Section 2.3.3*), it is important to understand their structure and function. Indeed, oestrogen and progesterone belong to a group of structurally related steroid hormones, that are synthesized from cholesterol (Davis & Hackney, 2017). Specifically, oestrogen refers to a group of similarly structured 18-carbon steroid hormones consisting of oestrone, oestriol, and oestradiol (also known as 17- β -oestradiol), which are primarily produced in the ovaries and to a lesser extent by the adrenals (Wierman, 2007). Whilst all oestrogen types are structurally similar, oestradiol is the most important in terms of reproductive function, given it is the most

biologically active (Bennink, 2004; Heldring *et al.*, 2007). Specifically, when compared with oestrone, oestradiol is approximately three times more biologically active, and 16 times more biologically active than oestriol (Bennink, 2004). As such, oestradiol concentrations are typically the primary focus of investigations studying the effects of oestrogen. As a steroid hormone, oestrogen can freely pass through the plasma membrane and move into the nucleus, where it can bind to its nuclear receptors (Chidi-Ogbolu & Baar, 2019). Oestrogens exert their effects via oestrogen receptors (ERs); ER- α and ER- β (Eyster, 2016). Oestrogen receptors are present in most human tissues (Jia *et al.*, 2015) and, in addition to the reproductive system, oestrogen is considered integral to the physiological function of the nervous (Ansdel *et al.*, 2019), musculoskeletal (Alexander *et al.*, 2021; Almeida *et al.*, 2017; Chidi-Ogbolu & Baar, 2019; Elliott-Sale, 2014; Enns & Tiidus, 2010; Wiik *et al.*, 2009), metabolic (Boisseau & Isacco, 2022; Hackney, 2021), and cardiorespiratory (Behan & Wenninger, 2008; Knowlton & Lee, 2012) systems. The expression of these receptors is important as they are located on tissues, and within systems which are integral to exercise performance and training (Lebrun *et al.*, 2013). In addition to the classic nuclear steroid hormone receptor actions, oestrogens can also act in a non-genomic manner, which can exert rapid effects on cellular signalling pathways (Dent *et al.*, 2012; Simoncini & Genazzani, 2003). Therefore, it is evident that oestrogen can affect a multitude of physiological and psychological systems, and thus subsequently affect aspects of exercise performance and training in sportswomen (see *Sections 2.4, 2.5, and 2.6*) but where, and how, oestrogen can exert its influence is likely to be highly multifaceted.

Progesterone is predominantly produced in the ovaries (by the corpus luteum; [Davis & Hackney, 2017]). Progesterone mainly exerts its effects on the nuclear progesterone receptors (PR); PR-A and PR-B (Kaya *et al.*, 2015), which often produce either enhancing or opposing effects to that of oestrogen (Vegeto *et al.*, 1993). For example, oestrogen primes target tissues to respond to progesterone, whereas when progesterone concentrations are high, it can inhibit the binding of oestrogen to ERs, by blocking the binding site, which results in the conversion of oestradiol- β -17 to oestrone, a less active oestrogen type (Sims & Heather, 2018). As such, progesterone is thought to have anti-oestrogenic actions (Frankovich & Lebrun, 2000). Like oestrogen, progesterone can also exert non-nuclear, rapid effects on cells through progesterone membrane receptors (Gellersen *et al.*, 2009; Moussatche & Lyons, 2012; Singh *et al.*, 2013). Whilst progesterone is not considered to influence physiological function to the extent of oestrogens, progesterone can exert numerous effects on the body, which are most apparent in the reproductive system (*i.e.*, it is responsible for the stabilisation of the endometrial lining in

preparation for fertilisation and pregnancy; [Davis & Hackney, 2017]). Additionally, progesterone has also been shown to increase resting heart rate (HR; [Sedlak *et al.*, 2012]), basal body temperature (BBT; [Charkoudian *et al.*, 1999]), as well as influence the nervous system (Ans dell *et al.*, 2019), and the brain (Mani & Oyola, 2012). Overall, it is evident that together endogenous oestrogen and progesterone have a multitude of roles, in addition to their roles in reproductive function, which could have pivotal influences on multiple physiological functions which underpin exercise performance and training. However, the cyclical fluctuations in endogenous oestrogen and progesterone across the MC (see *Section 2.3.3*) and the influence of exogenous sex hormones through HC use (see *Section 2.3.4*) likely complicate these individual and coupled effects.

2.3.3 The menstrual cycle

The MC lasts on average 28 days, with cycles varying in length between 21 to 35 days (Davis & Hackney, 2017). Day one of the cycle begins on the first day of menstruation (commonly referred to as the period), which is the result of the shedding of the endometrial lining of the uterus, and typically lasts between two to eight days (Davis & Hackney, 2017). At the beginning of the MC follicles within the ovaries are grown slowly under the influence of small concentrations of FSH, primary follicles then develop into secondary and then tertiary follicles over the next \approx 14 days (Ferin *et al.*, 1993). These cells produce the steroid hormone androstenedione, which is converted into oestrogen and results in a gradual rise in oestrogen concentrations (Ferin *et al.*, 1993). Increasing oestrogen concentrations inhibit FSH and LH production, preventing additional follicular development, and stimulate further oestrogen synthesis in granulosa cells (Davis & Hackney, 2017). This is followed by a rapid increase in oestrogen which results in an increase in LH production, commonly known as the ‘LH surge’, after which oestrogen concentrations fall for several days (Davis & Hackney, 2017). This ‘LH surge’ is essential for ovulation and stimulates the release of the secondary oocyte (*i.e.*, egg[s]) from the follicle where it(they) travel(s) to the fallopian tubes for implantation (Davis & Hackney, 2017; Ferin *et al.*, 1993). The empty follicle collapses and undergoes a process termed ‘luteinisation’, which produces an endocrine structure known as the corpus luteum (Davis & Hackney, 2017). Lipids within the corpus luteum are used to synthesise steroid hormones and result in a large increase in progesterone concentrations and increased oestrogen concentrations (Ferin *et al.*, 1993; Stricker *et al.*, 2006). The lifespan of the corpus luteum is \approx 12 days, and if pregnancy does not occur, the corpus luteum becomes an inactive structure and progesterone and oestrogen production is reduced (Davis & Hackney, 2017). Declining

progesterone concentrations cause blood vessels in the endometrium to contract, resulting in the death of surface cells, which are eventually sloughed, resulting in menstruation (Davis & Hackney, 2017). The declining oestrogen and progesterone concentrations halt negative feedback to the anterior pituitary, resulting in increased FSH production, and thus begins the hormonal regulation of the consecutive MC (Ferin *et al.*, 1993)

The above cyclical fluctuations in oestrogen and progesterone across the MC create significantly different transient sex hormone profiles, which are often used to differentiate between MC phases (Elliott-Sale *et al.*, 2021). For instance, in its simplest form the MC can be divided into two phases: 1) the follicular phase; and 2) the luteal phase, separated by ovulation. Specifically, the follicular phase is defined from the first day of menses to the day of ovulation, and the luteal phase from the day after ovulation until the following onset of menses (Elliott-Sale *et al.*, 2021). However, this classification can be an oversimplification as it does not capture all timepoints whereby circulating concentrations of oestrogen and progesterone, and the ratios between the two, vary substantially. As such, these two phases are often further subdivided into the early, mid-, and late follicular, as well as the early, mid-, and late luteal, with or without, the inclusion of ovulation (Elliott-Sale *et al.*, 2021). Although, it is important to acknowledge that this type of classification can often be an exaggeration as it again does not allow for capture of the timepoints whereby circulating concentrations of oestrogen and progesterone and their ratios differ. Indeed, the concentration of total oestradiol during the MC remains low during the early follicular phase ($\approx 150 \text{ pmol}\cdot\text{L}^{-1}$), before rapidly increasing and reaching its primary peak ($\approx 650 \text{ pmol}\cdot\text{L}^{-1}$) prior to ovulation, oestradiol then rapidly declines post ovulation before rising to a secondary peak in the mid-luteal phase ($\approx 500 \text{ pmol}\cdot\text{L}^{-1}$; [Allen *et al.*, 2016; Baird & Fraser, 1974; Reed & Carr, 2015; Stricker *et al.*, 2006]). In contrast, progesterone concentrations remain low ($< 5 \text{ nmol}\cdot\text{L}^{-1}$) throughout the follicular phase of the MC, which is followed by a significant elevation in the luteal phase to around $35 \text{ nmol}\cdot\text{L}^{-1}$ (Stricker *et al.*, 2006). On the basis of these fluctuations, recent research proposes that there are four distinctly different sex hormone profiles across the MC which represent the significant changes in both oestrogen and progesterone concentrations (Elliott-Sale *et al.*, 2021): 1) phase one, indicated by the onset of bleeding until \approx day 5 of the cycle, categorised by the lowest oestrogen and progesterone concentrations; 2) phase two, occurring in the ≈ 14 to 16 h prior to ovulation, classified by peaking oestrogen and low progesterone concentrations; 3) phase three, indicated by a positive urinary ovulation test and lasts ≈ 24 to 36 h , categorised by medium oestrogen concentration and low progesterone concentrations; and 4) phase four,

occurring \approx 7 days after ovulation has been confirmed, classified by high oestrogen and the highest progesterone concentrations. Importantly these timepoints allow for three main sex hormone ratios (low: low, phase one; high: low, phases two and three; and high: high, phase four) of oestrogen and progesterone to be investigated. Given that oestrogen and progesterone have pivotal influences on multiple physiological functions (see *Section 2.3.2*) which could influence performance and training, the changes in oestrogen and progesterone ratios across the MC might result in optimal windows for exercise performance and recovery post exercise in sportswomen (see *Section 2.4*).

2.3.4 Changes to the natural menstrual cycle

It is important to consider that not all women have a natural MC (Elliott-Sale & Hicks, 2018). The cyclical fluctuations in sex hormones across the MC described in *Section 2.3.3*, might be altered by internal factors (*e.g.*, amenorrhea, oligomenorrhea, anovulation, and luteal phase defect [LPD]; [Elliott-Sale *et al.*, 2021]). Whilst an understanding of these internal dysfunctions is necessary for setting the inclusion criteria for participants in the experimental Chapters of this thesis, and for individuals working with sportswomen, how these internal disturbances affect health and performance in sportswomen is beyond the scope of this thesis (the interested reader is directed to Elliott-Sale *et al.* [2021]). The MC can also be manipulated through external ways, namely HC use (Elliott-Sale & Hicks, 2018). Indeed, HCs work by altering the natural MC by changing a woman's internal reproductive hormonal milieu (Davis & Hackney, 2017). Hormonal contraceptives are primarily designed to reduce the chances of an unplanned pregnancy, but are commonly used by sportswomen for secondary reasons, such as: 1) alleviating the symptoms of dysmenorrhea and menorrhagia; 2) reducing the occurrence of cycle related symptoms; 3) treating androgenisation symptoms (*i.e.*, acne); 4) helping with various clinical conditions (*i.e.*, symptomatic fibroids, functional ovarian cysts, benign breast disease, endometriosis and adenomyosis); and 5) decreasing the risk of ovarian and endometrial cancer and pelvic inflammatory disease (Elliott-Sale & Hicks, 2018). Additionally, many sportswomen use HCs to predict, alter (or omit entirely), and control bleeding, particularly around important sporting events and competitions (Schaumberg *et al.*, 2018). Thus, reliable, and reversible contraception, along with the means to alleviate cycle related symptoms associated with the natural MC and the ability to eliminate unpredictable menstruation, make HCs a desirable option for many sportswomen.

2.3.5 The prevalence and type of hormonal contraceptive use in sportswomen

In 1960, the ‘Food and Drug Administration’ in the United States of America legalized the first HC (Enovid®; [Elliott-Sale & Hicks, 2018]). At the time this HC contained 150 µg of the synthetic oestrogen, mestranol, and 10 mg of the progestin, norethynodrel (Elliott-Sale & Hicks, 2018). Following this, the first HC (Anovlar®) was legalized in Europe in 1961 (Elliott-Sale & Hicks, 2018). Since the legal introduction of these first birth control pills, the term ‘HCs’ has come to define a wide range of preparation types (*i.e.*, combined, progestin-only, and mono-bi-tri-phasic), delivery methods (*i.e.*, OCPs, injections, implants, and patches) and brands (*i.e.*, Microgynon®, Mirena®, and Depo-Provera®; [Elliott-Sale & Hicks, 2018]). For a comprehensive overview of the different types of HCs please see Elliott-Sale and Hicks (2018). Despite the expansion in preparation types and delivery methods, OCPs remain the most prevalent form of HCs used by sportswomen today (Heather *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022; Oxfeldt, Dalgaard, Jørgensen, & Hansen, 2020; Parker *et al.*, 2022). As a result, this makes the OCP the second most common reproductive hormonal profile in sportswomen after naturally menstruating women, and thus the type of HC focused on within this thesis.

2.3.6 The physiology of the combined, monophasic, oral contraceptive pill

Most OCPs are _mOCPs, which contain low to standard doses of ethinyl oestradiol (a synthetic oestrogen), and either levonorgestrel, norethisterone, desogestrel, norgestimate, norgesterol, or gestodene (synthetic progesterone’s), delivered in a fixed amount every day for 21 pill-taking days (*i.e.*, consumption or active phase), followed by seven pill-free days (*i.e.*, withdrawal/ nonactive/ placebo pill phase; [Elliott-Sale & Hicks, 2018]). These exogenous hormones in _mOCPs act via negative feedback on the gonadotropin-releasing hormone (GnRH) receptors, preventing pituitary secretion of FSH and LH, and ultimately resulting in a downregulation of endogenous sex hormone concentrations (Davis & Hackney, 2017). Although, it should be noted that endogenous sex hormones are not completely suppressed by _mOCPs. Indeed, during the pill-free days of _mOCP use the levels of endogenous oestrogen rise slightly to a level similar to the early follicular phase of the MC, before being inhibited again during the pill-taking days (Hirschberg, 2022). It is also theorised that early in the pill-free days exogenous sex hormones might still be present in small concentrations, whilst endogenous sex hormones are still downregulated, whereas late in the pill-free days endogenous sex hormones are higher as exogenous sex hormones have been cleared from the system (Rechichi *et al.*, 2009). Ultimately, _mOCP use, results in four

distinct hormonal environments: 1) a downregulated endogenous oestradiol profile of $\approx 60 \text{ pmol}\cdot\text{L}^{-1}$ for 21 days that rises during the seven pill-free days to $\approx 140 \text{ pmol}\cdot\text{L}^{-1}$; 2) a chronically downregulated endogenous progesterone profile of $\approx 5 \text{ nmol}\cdot\text{L}^{-1}$; 3) a daily surge of exogenous oestrogen and progestin which peak within one hour after ingestion [from $\approx 2 \text{ pg}\cdot\text{ml}^{-1}$ to $\approx 6 \text{ pg}\cdot\text{ml}^{-1}$], with baseline values accumulating slightly from $\approx 2 \text{ pg}\cdot\text{ml}^{-1}$ to $\approx 3 \text{ pg}\cdot\text{ml}^{-1}$ over the 21 pill-taking days; and 4) seven exogenous sex hormone free days (Elliott-Sale *et al.*, 2021; Rechichi *et al.*, 2009). These profiles, reflecting pill-taking and pill-free days, are referred to as pseudo phases, as they are ‘artificial’ phases in comparison with the phases of the natural MC. Moreover, it is important to consider that various _mOCPs differ regarding androgenic activity (*i.e.*, progestins with androgenic properties to those with anti-androgenic properties). It is theorised that changes in endogenous sex hormones, and the presence of exogenous sex hormones, from _mOCP use might further influence exercise performance and training outcomes (see *Section 2.4*). Moreover, given the relatively stable reproductive hormonal environment experienced by _mOCP users they can form as a control and/or comparator group within research studies between naturally menstruating women (Elliott-Sale *et al.*, 2013).

2.4 The effects of the menstrual cycle and oral contraceptive pill use on exercise performance

Time dependent variations (*i.e.*, chronobiology) in exercise performance have received much attention within the field of sport and exercise science research (Atkinson & Reilly, 1996). As such, it is acknowledged that there might be potential time-windows for individuals during which optimum exercise performance might be achieved (Atkinson & Reilly, 1996). Indeed, physical performance is known to fluctuate around diurnal, circadian, and/or seasonal rhythms (Atkinson & Reilly, 1996). However, as highlighted in *Section 2.2*, it is also important to consider the cyclical changes in concentrations of oestrogen and progesterone across the MC, and their implications for exercise performance in sportswomen (Constantini *et al.*, 2005; de Jonge, 2003; Frankovich & Lebrun, 2000; Lebrun, 1993; Lebrun *et al.*, 2013). Furthermore, many sportswomen use _mOCPs (see *Section 2.2.6*) which can provide a relatively stable and controllable sex hormone state for exercise performance, as well as having the potential to eliminate the negative side-effects of the MC (Elliott-Sale & Hicks, 2018). Although, it is important to consider that this downregulation of endogenous oestrogen and progesterone, and

the presence of exogenous hormones, because of _mOCP use, introduce other potential modifying factors which could affect exercise performance (Burrows & Peters, 2007; Rechichi *et al.*, 2009). The following section will discuss the proposed influence of the MC and OCP use on key physiological systems and evaluate, from the current literature, whether these influences translate into changes in exercise performance (*i.e.*, namely strength and endurance) in sportswomen. Exercise performance can be quantified in various ways, however for the purposes of this Chapter, exercise performance was defined as total work done, time to completion, time to exhaustion, mean, peak, and ratio outputs, rate of force production and decline, and indices of fatigue. Additionally, maximum oxygen uptake (maximal oxygen uptake [$\dot{V}O_{2\text{max}}$] or peak oxygen uptake [$\dot{V}O_{2\text{peak}}$]) is included as a physiology-based outcome that has a relatively strong relationship with performance and has been commonly reported.

2.4.1 Potential mechanisms of endogenous and exogenous sex hormones on strength performance

Force generation is ultimately responsible for human movement (Dulhunty, 2006) and the ability to generate high levels of force (commonly referred to as “strength”) is a key determinant of performance in many sports. In addition to performance measures, changes in muscle strength can often be measured to determine the magnitude of fatigue, muscle damage, and acute and long-term adaptations to training (Dulhunty, 2006). The ability to produce force comes from a sequence of both chemical and protein interactions (*i.e.*, starting from the propagation of the motor-pathway to the interaction of contractile proteins within the skeletal muscle; [Dulhunty, 2006]). It is well-documented that oestrogen and progesterone can exert their influence at several points throughout this process (Eyster, 2016; Wiik *et al.*, 2009), within the motor-pathway and contractile apparatus. As such, fluctuations in these sex hormones across the MC and with OCP use could ostensibly influence force production, and consequently strength performance.

Oestrogen and progesterone are known to influence central nervous system function (Stoffel-Wagner, 2001) and thus might influence the neural control, and the expression of, force. Specifically, oestrogen and progesterone might affect muscle strength through actions on cortical tract excitability, which is regulated through γ -aminobutyric acid (GABA-ergic) transmissions. Indeed, these sex hormones are among a larger group of hormones referred to as ‘neurosteroids’ or ‘neuroactive’ steroids, which can exert their action at the level of the brain and are often synthesised within the central nervous system itself (Melcangi *et al.*, 2008; Paul

& Purdy, 1992; Rupprecht & Holsboer, 1999). Additionally, because of their high lipid solubility, sex hormones in the plasma can traverse the blood-brain barrier (Stoffel-Wagner, 2001). Oestrogens are known to have a net excitatory effect on the nervous system (*i.e.*, oestradiol binds to ER- α sites on GABA-ergic mediated neurons, causing an attenuation in GABA synthesis [Schultz *et al.*, 2009; Wallis & Luttge, 1980]), whereas progesterone, and its metabolites, have a net inhibitory effect on the nervous system (*i.e.*, the activity and effects of GABA are potentiated, leading to decreased neuronal discharge rate (Smith, 1989) and increased inhibition of pyramidal neurons [Hsu & Smith, 2003]). Recently, Ansdell *et al.* (2019) demonstrated the link between sex hormone-induced changes in excitability and voluntary activation of the knee extensors in women. The authors showed that around the ovulatory phase of the MC the neuroexcitatory effects of high oestrogen concentrations were observed alongside an increased voluntary activation of the knee extensors. In contrast, during the mid-luteal phase (when progesterone concentrations are high), cortical inhibition was increased, alongside a concomitant decrease in voluntary activation, highlighting the neuroinhibitory effect of progesterone. Thus, the sex hormone influence on central nervous system function might influence muscle function and subsequently strength performance. At the other end of the motor pathway, previous work has demonstrated a positive influence of oestrogen on motor unit firing rates which could underpin changes in maximal strength (Tenan *et al.*, 2016). For example, Tenan *et al.* (2013) showed that in the second half of the MC motor unit discharge rates at recruitment were greater in women.

Skeletal muscle also expresses functional oestrogen receptors (both ER α and ER β ; [Lemoine *et al.*, 2003; Nakamura & Aizawa, 2017; Wiik *et al.*, 2009; Wiik *et al.*, 2003]). As such, beyond its role as a sex hormone, oestrogen has been shown to influence muscle hypertrophy and cross-sectional area (Alexander *et al.*, 2021; Lowe *et al.*, 2010b). Indeed, oestrogen is associated with the growth of myoblast cells *in-vitro* (Kahlert *et al.*, 1997), and with *in-vivo* development of muscle size in female mice (Sciote *et al.*, 2001). In humans, however, this association between oestrogen and muscle growth is less understood. For example, whilst some studies have demonstrated that oestrogen, through hormonal replacement therapy, might attenuate and even reverse the age-related decline in lean muscle mass and size observed in postmenopausal women (Ronkainen *et al.*, 2009; Sipila *et al.*, 2001; Sørensen *et al.*, 2001; Taaffe, Newman, *et al.*, 2005; Taaffe, Sipilä, *et al.*, 2005; Teixeira *et al.*, 2003), other studies have shown no effects of oestrogen on muscle mass, size, or cross-sectional area (Bassey *et al.*, 1996; Bemben & Langdon, 2002; Brown *et al.*, 1997; Maddalozzo *et al.*, 2004; Skelton *et al.*, 1999; Taaffe *et al.*,

al., 1995). Moreover, research demonstrates that oestrogen rapidly increases intracellular calcium concentrations via its actions on membrane ERs in several tissues (Morley *et al.*, 1992; Younglai *et al.*, 2005). Whilst this body of evidence is predominantly within animal studies or *in vitro* settings, it could be speculated that oestrogen could exert its actions in skeletal muscle through an increased calcium mobilisation, which enhances actin and myosin binding (Collins *et al.*, 2019).

In terms of exogenous sex hormones in OCPs, historically it was hypothesised that the androgenic component of OCPs might be ergogenic and as a result promote greater improvements in strength performance (Elliott-Sale & Hicks, 2018). Indeed, in 1987, the International Olympic Committee banned the use of OCPs containing norethindrone, a synthetic progestin with possible anabolic, oestrogenic, and androgenic properties (Duda, 1988). At that time, some laboratories were unable to distinguish between the metabolites of norethindrone and nandrolone, a common anabolic androgenic steroid (Duda, 1988). Although, the ban on the use of OCPs containing norethindrone was overturned within five months. In contrast, today, it is often thought that OCPs might potentially exert a negative effect on strength performance because of the downregulation of endogenous oestrogen.

2.4.2 Studies investigating the effects of the menstrual cycle and oral contraceptive pill use on measures of strength performance

Early research by Sarwar *et al.* (1996) investigated the effect of different phases of the MC on skeletal muscle strength in 10 young, healthy women. The women were tested weekly for quadricep and handgrip strength across two MCs, with phases estimated back from the first day of bleeding (day 1), and ovulation (14 days prior to menstruation). The authors reported that quadriceps and handgrip strength was 11% greater mid-cycle (days 12 to 18) compared with the early follicular (days 1 to 7), mid-follicular (days 7 to 12), mid-luteal (days 18 to 21), and late luteal (days 21 to 32) phases. In agreement with the findings by Sarwar *et al.* (1996), Bambaeichi *et al.* (2004) observed greater peak torque of knee extensors and flexors, and maximum voluntary contraction (MVC) at ovulation, compared to the early and late follicular and mid- to late luteal phases of the MC. Interestingly, while both Bambaeichi *et al.* (2004) and Sarwar *et al.* (1996) attributed these phase differences in strength measures to the rise in oestrogen prior to ovulation in conjunction with low progesterone levels, neither study measured endogenous sex hormone concentrations. In a similar study by Phillips *et al.* (1996) that identified MC phase via BBT, as well as urinary ovulation tests, and verified MC phase

using serum sex hormone analysis (in some, but not all, participants), the authors demonstrated greater voluntary force during the late follicular phase, compared to the early follicular phase of the cycle. Additionally, immediately post-ovulation there was a systematic and rapid decrease in voluntary force, followed by a recovery of force in the luteal phase. These results suggest a potential association between rising/high oestrogen concentrations and improved strength performance. More recent work also supports an effect of changes in endogenous oestrogen across the MC on measures of strength performance. Indeed, Gordon *et al.* (2013) evaluated the effects of MC phase (verified using serum sex hormone analysis) on the development of peak torque in the knee flexors and extensors in 11 well-trained women. The authors showed reductions in peak torque of the knee extensors and flexors during menses (days 1 to 3) when oestrogen concentrations were at their lowest, in comparison to the mid-luteal (days 19 to 20) phase when oestrogen concentrations were high.

In contrast with the above studies, which have implicated the fluctuations in oestrogen and progesterone across the MC in strength performance, numerous studies have reported no effect. For example, de Jonge *et al.* (2001) demonstrated no changes in any muscle function parameters (*i.e.*, maximal isometric quadricep strength, isokinetic knee flexion and extension strength, as well as handgrip strength) across MC phases (menstruation, late follicular, and luteal phases, identified using serum sex hormone analysis) in 19 eumenorrheic women. In agreement with these findings, Elliott *et al.* (2003) indicated that the cyclic variation in endogenous sex hormones between the early follicular and mid-luteal phases of the MC (as determined using the gold standard ‘three-step’ method of calendar-based counting, urinary ovulation detection kits, and serum sex hormone analysis) did not affect muscle strength (*i.e.*, maximum voluntary isometric strength of the first dorsal interosseous muscle), in seven eumenorrheic women. Similarly, using this recommended ‘three-step’ method both Fridén *et al.* (2003) and Ekenros *et al.* (2013) reported no difference in handgrip strength between the early follicular, ovulatory, and mid-luteal phases of the MC. Collectively, these results suggest that the fluctuations in women’s reproductive hormone concentrations across the MC do not affect measures of strength performance. The conflicting findings between studies that have supported and refuted any effect of the MC on strength performance could be attributed to the heterogeneity in research design and quality. Indeed, studies have used a variety of measures of strength performance (*e.g.*, dynamic, and isometric contractions in the upper and lower limbs), participants of differing training status (*e.g.*, recreational to well-trained), and most are

further limited by not addressing pertinent methodological considerations for MC research in sport and exercise (see *Section 2.2.5* for a thorough explanation of these considerations).

In addition to the effects of the MC on measures of strength performance, several studies have compared OCP users with naturally menstruating women to investigate any potential differences between these groups. Indeed, an early study by Wirth and Lohman (1982) reported that handgrip endurance times and force output measurements at 50% of MVC were greater in naturally menstruating women compared to OCP users, despite reporting no change in MVC between the groups. In contrast with the findings from Wirth and Lohman (1982), Bell *et al.* (2011) reported no differences in measures of strength (*i.e.*, hamstring neuro-mechanics, and lower extremity stiffness) between the 15 naturally menstruating women and 15 OCP users. Similarly, Gordon *et al.* (2013) studied the effects of the MC and OCP use on the development of peak torque across a range of isokinetic speeds, in 17 well-trained women (11 naturally menstruating and 6 OCP users). The data revealed that there was no difference in peak torque of either the knee flexors or extensors, at any speeds, between naturally menstruating women and OCP users. Further, using a higher-quality design (*e.g.*, randomised controlled trial) when compared to the studies by Bell *et al.* (2011) and Gordon *et al.* (2013), both Ekenros *et al.* (2013) and Lebrun *et al.* (2003) also showed no changes in strength performance with OCP use. Specifically, Ekenros *et al.* (2013) employed a cross-over design, such that participants taking an OCP upon recruitment were tested on day 2, 3 or 4 during the pill-free days and on days 7 or 8 and 14 or 15 during the pill-taking days, after which they stopped taking the OCP and were tested on day 2, 3 or 4, 48 h after ovulation, and 7 or 8 days after ovulation. Despite using a robust research design, the authors reported no differences in muscle strength between groups. Likewise, Lebrun *et al.* (2003) employed a randomised, double-blind, placebo-controlled trial in naturally menstruating women. Testing was performed across two phases of the MC, after which participants were randomly assigned to either an OCP ($n = 7$) or placebo ($n = 7$) group and were tested between days 14 and 17 of the second cycle of OCP (*i.e.*, the same triphasic OCP) use or placebo administration. The authors reported that isokinetic strength was unchanged with OCP use in highly trained sportswomen participating in running, cycling, triathlon, rowing, and cross-country skiing. Collectively, these studies highlight that any potential differences in strength measures between naturally menstruating women and OCP users remain relatively inconclusive.

Finally, to explore the within effect of OCP use (*i.e.*, across the OCP cycle), studies have also assessed strength performance between pill-taking and pill-free days. For example, Rechichi

and Dawson (2009) examined whether jumping performance (countermovement jump [CMJ] and drop jump) was affected between _mOCP consumption, and _mOCP early and late withdrawal, as verified using serum sex hormone analysis. The findings showed a reduction in 30 cm drop jump height during the _mOCP late withdrawal phase when compared to the _mOCP consumption and early withdrawal phases, whereas 45 cm drop jump height was higher during the pill-taking days compared to the pill-free days. The authors concluded that drop jump performance varies between pill-taking and pill-free days, likely because of the presence of exogenous sex hormones and the downregulation of endogenous sex hormones on neuromuscular timing and the stretch-shortening cycle. Although, the data from this study appear conflicting with reactive strength from a 30 and 45 cm drop jump being greatest at different stages across the OCP *cycle*. In contrast with Rechichi and Dawson (2009), most studies investigating measures of strength performance between pill-taking and pill-free days have shown no differences (Elliott *et al.*, 2005; Peters & Burrows, 2006; Petrofsky *et al.*, 1976; Sarwar *et al.*, 1996). Like the research investigating the MC, discrepancies between studies investigating changes in measures of strength performance between naturally menstruating women and OCP users, and across the OCP *cycle*, could be due to the variation in research design, strength measures assessed, differences in participant training status, as well as poor methods specific to research in sportswomen (see *Section 2.2.5*).

2.4.3 Potential mechanisms of endogenous and exogenous sex hormones on endurance performance

Endurance performance requires an integrative response from an array of physiological systems (*i.e.*, musculoskeletal, cardiovascular, and respiratory systems) and functions (*i.e.*, thermoregulation, and substrate metabolism). It is well-documented that sex hormone receptors are present throughout these physiological systems (Wierman, 2007), and that endogenous and exogenous sex hormones can exert their influence on thermoregulation (Charkoudian & Stachenfeld, 2016), and substrate metabolism (Boisseau & Isacco, 2022). As such, there is ample opportunity for the fluctuations in endogenous sex hormones across the MC, and the presence of exogenous sex hormones in OCPs, to influence endurance performance.

Early in the oxygen transport pathway (*i.e.*, the circulatory system), hormone mediated effects are evident. Specifically, increases in pulmonary blood volume and pulmonary diffusion capacity have been reported during the mid-luteal phase compared with the early follicular phase of the MC, at rest and during exercise (Smith *et al.*, 2015). It has been hypothesised that

the improved diffusion capacity in the mid-luteal phase might ensure optimal arterial oxygenation, and therefore prevent exercise-induced arterial hypoxemia that results in the development of fatigue and compromises endurance performance. Although, it should be acknowledged that the study by Smith *et al.* (2015) included triphasic OCP users within their sample and reported no differences in the sex hormone concentrations between phases. Thus, it is difficult to attribute the findings from Smith *et al.* (2015) to the fluctuations in endogenous sex hormones alone. Moreover, several studies have shown that at rest (MacNutt *et al.*, 2012; Schoene *et al.*, 1981) and during exercise (Dombovy *et al.*, 1987a; Schoene *et al.*, 1981) ventilatory rate ($\dot{V}E$) is greater in the luteal phase, which could be attributable to the effects of progesterone on central respiratory drive, or indirectly through the increase in BBT (de Jonge, 2003). However, conflicting literature does exist demonstrating no effect of the MC on minute ventilation, particularly at high exercise intensities (Beidleman *et al.*, 1999; Bemben *et al.*, 1995; de Souza *et al.*, 1990). Alternatively, within the cardiovascular system, oestrogen is known to enhance vasodilation of the vascular smooth muscle of coronary, brachial, and the peripheral microvascular arteries as well as peripheral vascular beds, which could increase blood supply to the heart and muscles (Adkisson *et al.*, 2010; Limberg *et al.*, 2010). Theoretically, an increase in blood supply might help to enhance endurance performance via a greater oxygen delivery to the working muscle. Although, it should be noted that the ability to capitalise on this response is partly dependent on oxygen extraction (Wagner, 2000).

One of the most documented changes across the MC, is the variation in BBT (de Jonge, 2003). For example, at the onset of menstruation BBT decreases to lower levels and remains relatively low throughout the follicular phase of the MC, then following ovulation, BBT increases by approximately 0.3 to 0.5°C and remains elevated throughout the luteal phase of the MC (Horvath & Drinkwater, 1982; Kelly, 2006; Stephenson & Kolka, 1993). This increase in BBT post ovulation has been linked to the thermogenic effect of progesterone (de Jonge, 2003) which rises and reaches its peak during the luteal phase. Theoretically, the rise in BBT during the luteal phase could remain elevated throughout exercise and/or heat stress, which could make women more susceptible to the development of heat illnesses during this phase of the MC (de Jonge, 2003). In turn, these effects could have subsequent negative implications for exercise performance, in particular prolonged endurance performance in hot and humid environments (Cheung *et al.*, 2000; González-Alonso *et al.*, 1999; Marsh & Jenkins, 2002). Additionally, there might also be indirect effects of this rise in BBT during the luteal phase, such as a higher HR, increases in minute ventilation (described above), and a greater perceived

exertion (Constantini *et al.*, 2005), as well as changes in skin blood flow, vasodilation, onset of sweating, and thermal conductance (Giersch *et al.*, 2020). Therefore, given both the potential direct and indirect effects of progesterone on BBT, women could be at a potential thermoregulatory disadvantage when performing endurance exercise in the luteal phase of the MC (Giersch *et al.*, 2020).

Substrate metabolism is also a large contributor to endurance performance. Indeed, in endurance activities, the ability to enhance fat metabolism, and therefore spare carbohydrate stores is deemed beneficial during moderate intensity exercise (*i.e.*, especially of a prolonged duration). Oestrogen and progesterone have been reported to play a role in regulating substrate metabolism during exercise (Boisseau & Isacco, 2022). For example, research highlights that during endurance exercise oestrogen initiates a shift from carbohydrate utilisation to fat oxidation, whereas progesterone has been suggested to have anti-estrogenic effects (D'Eon *et al.*, 2002; Hackney *et al.*, 1991; Hackney *et al.*, 2022; Willett *et al.*, 2021). As such, some studies have shown that during the follicular phase of the MC there is a greater reliance on carbohydrate metabolism as an exercise energy substrate, which transitions to a greater dependence on fat metabolism across the luteal phase (D'Eon *et al.*, 2002; Hackney *et al.*, 1991; Hackney *et al.*, 2022; Willett *et al.*, 2021). However, it is important to note that these findings are not always consistent (Frandsen *et al.*, 2020; Horton *et al.*, 2002). Interestingly, the magnitude of this transition appears to be mediated by the oestrogen to progesterone ratio, with a greater shift being reported in women with a larger hormone ratio change during the luteal phase (Hackney *et al.*, 2022). Therefore, the interaction of oestrogen and progesterone on substrate metabolism seems to be as critical as the individual and isolated effects of each sex hormone (Hackney *et al.*, 2022). Furthermore, it should also be noted that when investigating the effects of the MC on substrate metabolism during exercise, nutritional status is an important variable to consider, as fed conditions have been shown to blunt the above observed effect when compared to responses in fasted women (Campbell *et al.*, 2001; de Jonge, 2003).

Exogenous sex hormones in OCPs can also exert an influence on the systems and processes that play a vital role in endurance performance (Burrows & Peters, 2007; Constantini *et al.*, 2005). For example, OCPs have been shown to increase stroke volume and preload, caused by increased plasma volume during the pill-taking days, which might result in a greater cardiac output and theoretically influence endurance performance (Stachenfeld, 2008). Moreover, it is thought that OCPs can affect thermoregulatory responses at rest and during exercise in

sportswomen (Lebrun *et al.*, 2013). Specifically, studies have shown that OCPs increase BBT (by $\approx 0.2^{\circ}\text{C}$) during pill-taking days when compared to pill-free days (Grucza *et al.*, 1993; Martin & Buono, 1997; Rogers & Baker, 1996; Tenaglia *et al.*, 1999). As stated previously, this could have important implications as BBT has been associated with performance in long duration events. Thus, the rise in BBT with OCP use could interfere with endurance performance in a similar way to the influence of endogenous progesterone during the luteal phase of the MC (Lebrun *et al.*, 2013). Finally, OCP use might affect substrate metabolism at rest and/or during exercise (Boisseau & Isacco, 2022). Whilst some studies have found no differences in substrate metabolism at rest and during exercise with OCP use (Jensen & Levine, 1998), others have demonstrated an increase in lipolytic activity during endurance exercise without any substantial effect on substrate utilisation (Bemben *et al.*, 1992; Boisseau & Isacco, 2022; Bonen *et al.*, 1991).

2.4.4 Studies investigating the effects of the menstrual cycle and oral contraceptive pill use on endurance performance

Early literature by Nicolay *et al.* (2008) observed a greater exercise time to fatigue, in six healthy women, when cycling at 70% $\dot{V}\text{O}_{2\text{max}}$ in the luteal phase (7 to 8 days following ovulation) compared with the follicular phase (days 7 to 8 of MC), as verified using serum sex hormone analysis. Similarly, Bandyopadhyay and Dalui (2012) investigated running time to exhaustion (≈ 31 minutes) at 70% of HR_{max} during the early follicular, late follicular, and mid-luteal phases of the MC. The authors reported that time to exhaustion was reduced during the early follicular phase, but it is important to note that no MC phase verification was used. In contrast, Campbell *et al.* (2001) demonstrated a 13% improvement in time trial performance (≈ 24 to 28 minutes), completed following two-hours of cycling exercise at 70% $\dot{V}\text{O}_{2\text{peak}}$, in a fasted state, in the follicular compared to the luteal phase of the MC (as identified via urinary oestrogen and progesterone), in eight moderately trained women. Interestingly, this response was attenuated when participants repeated the time trial exercise with carbohydrate supplementation. The authors proposed that the potential effects of the MC on endurance performance can be reduced with ingestion of carbohydrates. This theory is supported in recent work by Hulton *et al.* (2021) who showed that a supraphysiological glucose dose curtails any likely metabolic influence of the MC during endurance exercise (90 minutes at 60% $\dot{V}\text{O}_{2\text{peak}}$). Despite having participants perform in a non-fasted state Oosthuysse *et al.* (2005) also showed a trend for a faster cycling TT finishing time in the late follicular phase, coinciding with the ovulatory surge in oestrogen, compared to the early follicular and mid-luteal phases of the MC.

In contrast with the previously discussed research, other studies pertaining to the effects of the MC on endurance performance have reported no change across the MC. For example, de Souza *et al.* (1990) reported no differences between the early follicular (days 2 to 4 following the onset of menses) and mid-luteal (6 to 8 days following a positive ovulation test) phases in exercise time to fatigue (\approx 15 minutes), during maximal exercise, in eight eumenorrheic women. Likewise, Casazza *et al.* (2002) demonstrated that MC phase does not affect endurance performance, with no changes found between the follicular (days 4 to 8 after the start of menses) and luteal (6 to 9 days after ovulation) phases of the MC (verified by serum sex hormone analysis) in time till volitional exhaustion (\approx 14 minutes) during a continuously graded exercise test on a cycle ergometer. Further, Thompson *et al.* (2012) investigated the effects of the MC on prolonged exercise performance (\approx 72 minutes) both in temperate (20°C, 45% relative humidity) and hot, humid (32°C, 60% relative humidity) conditions, in 12 recreationally active women. The authors reported no changes in prolonged exercise performance, in temperate conditions, between the early follicular (days 3 to 6) and mid-luteal (days 19 to 25) phases. In agreement with these studies, further studies have concluded that time to exhaustion during sub-maximal and maximal work, as well as time trial performance are not affected by the MC, in both trained and untrained naturally menstruating women (Bailey *et al.*, 2000; Beidleman *et al.*, 1999; Bryner *et al.*, 1996; Forsyth & Reilly, 2008; Lebrun *et al.*, 1995; McLay *et al.*, 2007; Takase *et al.*, 2002). More recently, Mattu *et al.* (2020) reported no difference in cycling time to exhaustion, at 85% peak power output, between the mid-follicular and mid-luteal phases. Although, it is interesting to note that the short exercise duration (*i.e.*, \approx 2.5 minutes) implemented by Mattu *et al.* (2020) might not have been long enough to benefit from the mechanisms proposed to enhance endurance performance across the MC, such as changes in substrate metabolism. Overall, the differences between studies investigating the effect of MC phase on endurance performance could be partly explained by the different procedures used to assess endurance performance, including different: 1) protocols (*i.e.*, incremental versus steady-state exercise and constant load versus self-paced time trial); 2) exercise durations (*i.e.*, ranging from \approx 2.5 minutes to \approx 72 minutes); 3) intensities (*i.e.*, differing percentages of aerobic capacity); and 4) modes of activity (*i.e.*, cycle ergometer versus treadmill running). Moreover, the standardisation of other variables, such as participant training status, time of day, prior exercise, and fuelling practices have also been inconsistent between studies. Finally, as with the strength performance literature, the current endurance literature is fraught with methodological inconsistencies specific to MC research (see *Section 2.2.5*).

In addition to the effects of the MC on endurance performance, several studies have also investigated the potential difference in endurance performance between naturally menstruating women and OCP users. For example, Bryner *et al.* (1996) assessed endurance performance (maximal treadmill test [$\dot{V}O_{2\text{max}}$] and an endurance run [≈ 12 minutes]) before and after 21 days of OCP supplementation in 10 women. The authors showed no effect of OCP consumption on run time to exhaustion between OCP use and non-use. In contrast, Casazza *et al.* (2002) tested participants before and after 4 months of triphasic OCP consumption in six moderately active women. Triphasic OCP use resulted in an 11% decrease in $\dot{V}O_{2\text{peak}}$ exercise capacity between the MC and OCP use, suggesting that exogenous sex hormones reduce endurance performance in moderately active women. Furthermore, studies that have investigated if endurance performance differs between pill-taking and pill-free days of the OCP *cycle*, have also reported conflicting findings. For example, Rechichi *et al.* (2008) investigated several measures (*i.e.*, power output, HR, ventilation, oxygen consumption, respiratory exchange ratio, rating of perceived exertion [RPE], blood lactate, and blood glucose) during a 1 h cycling test at three points across the OCP *cycle* in 13 cyclists and triathletes. Despite variation in some physiological variables, the authors concluded that there was no difference in endurance performance throughout an OCP *cycle*. Similarly, Vaiksaar *et al.* (2011b) examined whether variables commonly used in endurance testing (*e.g.*, power output, HR, oxygen consumptions, carbon dioxide production, minute ventilations, respiratory exchange ratio, and blood lactate) were influenced by OCP use in nine recreationally trained rowers. In this study, participants performed two incremental tests to voluntary exhaustion on a rowing ergometer at two time points across the OCP *cycle*. The authors concluded that sport-specific endurance performance was not influenced by pill-taking versus pill-free days. In agreement with the above findings recent research by Taipale-Mikkonen *et al.* (2021) also showed no difference in physiological variables monitored during incremental treadmill testing in women across different phases of an OCP *cycle* (*i.e.*, consumption phase 1 = day 8, consumption phase 2 = day 12, withdrawal phase = days 21 to 24 and bleeding = days 24 to 28). Again, like the research investigating the MC, discrepancies between studies investigating changes in measures of endurance performance between naturally menstruating women and OCP users, across the OCP *cycle*, could be partly explained by the different research designs, exercise protocols, participants characteristics, and poor methods specific to research in sportswomen (see *Section 2.2.5*).

2.4.5 Methodological considerations for menstrual cycle and oral contraceptive pill research in sport and exercise science

As discussed in *Sections 2.4.2 and 2.4.4* it appears that most research studies pertaining to the effect of MC and OCP use on exercise performance are conflicting. Whilst inconsistencies between findings might be partly attributed to an array of the usual study design variables (*e.g.*, sample size, participant characteristics, outcome measures etc.), there are several additional methodological factors that need to be considered when conducting research in sportswomen (Elliott-Sale *et al.*, 2021). Specifically, at present there is a lack of agreement on the terminology used when describing woman participants. For example, of the studies including women as participants, many have not defined what type of woman they are investigating (*i.e.*, naturally menstruating woman vs. HC user [Elliott-Sale *et al.*, 2021]). Additionally, many studies use the terms eumenorrheic woman (*i.e.*, a woman who has a MC length between 21 and 35 days, including evidence of an ‘LH surge’ and correct verified sex hormone profile) and naturally menstruating woman (*i.e.*, a woman who has a MC length between 21 and 35 days, including evidence of an ‘LH surge’, without verified sex hormone profile) interchangeably, with no real uniformity when defining reproductive status (Elliott-Sale *et al.*, 2021). Similarly, numerous studies have not specified different HC types and brands (Elliott-Sale *et al.*, 2021). Ultimately, this can lead to the grouping of non-homogenous participants which likely results in a large inter- and intra-individual variation in endogenous and exogenous sex hormone concentrations and makes interpreting results between studies difficult. Moreover, several studies have grouped naturally menstruating women with HC users, which does not allow for the independent effect of endogenous or exogenous sex hormones on specific outcomes to be deciphered. Furthermore, discrepancies within the literature might also be attributable to differences in the terminology used to define the different phases of the MC and HC use (Elliott-Sale *et al.*, 2021). For example, some studies state that testing occurred during the follicular phase of the MC, however it is unknown whether this term refers to the early follicular phase (*both* oestrogen and progesterone are low), the mid-follicular phase (potentially rising oestrogen and low progesterone) or the late-follicular phase (close to oestrogen peak and low progesterone). Moreover, terminology is often used interchangeably, such as the early follicular phase or menses or follicular phase (Elliott-Sale *et al.*, 2021). Therefore, it is important to determine the exact days of testing and preferably the sex hormone concentrations on those days (see below), to ensure that the same MC and HC phases are being compared between studies. To overcome these issues, future studies need to

adopt consistency in the terminology used to describe women as participants, and the testing phases for MC and HC research. Thus, the interested reader is directed to the work of Elliott-Sale *et al.* (2021).

Inconsistencies in MC research in sportswomen might also be partly attributed to the timing of testing (*i.e.*, phase of MC). As previously mentioned in *Section 2.3.3*, the MC can be divided into distinctly different phases each with different sex hormone concentrations of oestrogen and progesterone. It is thought that any potential effects of the fluctuations in endogenous sex hormones across the MC are most likely to be identified when testing is conducted during key points in the MC when hormone concentrations and/or ratios significantly differ. However, at present without clear and consistent timing of testing direct comparisons between studies cannot be made, and thus the true effect of studies investigating the effects of MC phase on set outcomes cannot be ascertained (Elliott-Sale *et al.*, 2021). Furthermore, _mOCP users can be used as a control group whereby the cyclical fluctuations in endogenous sex hormones across the MC can be compared to a more stable endogenous sex hormone environment due to _mOCP use (Elliott-Sale *et al.*, 2013). Alternatively, _mOCP users can also be considered as an experimental group (Elliott-Sale *et al.*, 2013), as _mOCP use introduces both exogenous hormones, and, albeit small, fluctuations in exogenous hormones between pill-taking and pill-free days. As with MC research, the timing of testing is an important consideration for either study design. For example, as described in *Section 2.3.6* _mOCP use results in four distinct hormonal environments which could have different implications on specific outcomes. However, few studies have communicated which _mOCP hormone profiles have been compared whether between naturally menstruating women and _mOCP users or across the _mOCP cycle (Elliott-Sale *et al.*, 2021). Collectively, without clear and consistent timing of testing direct comparisons between studies cannot be made, and thus the true effect of the MC and _mOCP use cannot be ascertained. Thus, a consensus is needed on the sex hormone profiles of interest and the criteria for subsequent testing timepoints (Elliott-Sale *et al.*, 2021).

Another key methodological consideration for MC and HC research is the subsequent verification of the respective cycle phases (Thompson & Han, 2019). Indeed, to ensure that the intended MC phases were examined, as well as avoid the inclusion of LPD and anovulatory cycles within MC research, it is recommended that a ‘three-step’ method is applied (Schaumberg *et al.*, 2017). Specifically, to assist in setting the timing of testing throughout the MC the calendar-based counting method should be applied in conjunction with urinary

ovulation detection kits to confirm the presence of an ovulatory cycle (Schaumberg *et al.*, 2017). This should be followed by serum measurement of oestrogen and progesterone to subsequently verify the phase of the MC. Across previous studies however, there appears to be large variability between the methods used to identify and then subsequently verify MC phase (*e.g.*, calendar-based counting, BBT, MC history questionnaires, and urinary ovulation detection kits, as well as salivary, urinary, and serum measurement of both oestrogen and progesterone), with very few studies using the recommended ‘three-step’ approach (Thompson & Han, 2019). Moreover, often the endogenous sex hormone concentrations have not been measured in HC users and, as such, the degree of downregulation during pill-taking days and possible upregulation during pill-free days, is assumed or estimated (Elliot-Sale & Hicks, 2018). Overall, it is theorised that most studies within the literature to date are of predominantly low-quality, thus there are no current guidelines for exercise performance (or training) specific for sportswomen which are underpinned by high-quality scientific evidence (Blagrove *et al.*, 2020). Although, it should be noted that a thorough grading of the quality of the current literature, specific to methodological considerations for sportswomen, has yet to be conducted. Methodological guidelines aimed at improving the quality of research on sport and exercise science studies with women participants have recently been published and researchers are recommended to comply with these (Elliott-Sale *et al.*, 2021). However, it is acknowledged that these guidelines are costly, time-demanding, and might not be compatible within some settings (*i.e.*, applied practice). Thus, these guidelines can create a paradox of increases in the quality and quantity of woman-specific research (Noordhof *et al.*, 2022). Ultimately, researchers are encouraged to conduct more studies on sportswomen, whilst maintaining the highest quality level available to them, and where applicable, authors should fully acknowledge any limitations of their study to allow for accurate interpretation.

2.4.6 Section summary

In summary, there are plausible mechanisms whereby sex hormones have the potential to exert either positive/negative effects on exercise performance, but whether these translate to changes in actual components of exercise performance across the MC and with OCP use are not well-understood. As discussed within this section, there is a divide within the literature between studies that support and refute an effect of fluctuations in endogenous sex hormones across the MC on measures of exercise performance, with no real consensus. This section also demonstrated that data pertaining to the effect of OCP use on measures of exercise performance are minimal and inconclusive. Specifically, it is unknown whether exercise performance differs

between naturally menstruating women and OCP users, nor if exercise performance differs between the pill-taking and pill-free days of the OCP *cycle*. As such, the direction and magnitude of the effect of the MC and OCP use on measures of strength and endurance performance remain unknown. Therefore, to fully understand the research landscape, a systematic review with meta-analysis will enable any true effect to be elucidated, hence the aims of *Chapters 3 and 4* in this thesis, to investigate the effects of the MC and OCP use on exercise performance, by performing two separate systematic reviews with meta-analyses. Additionally, as described in *Section 2.4.5* the current literature base is fraught with methodological inconsistencies, and at present most of the research to date is interpreted as low-quality, although a thorough grading has yet to be conducted. Therefore, the secondary aim of *Chapters 3 and 4* was to appraise the quality of previous studies, for the first time, using robust assurance tools.

2.5 The influence of the menstrual cycle and oral contraceptive pill use on the responses to and recovery from exercise

The scientific principle behind training is that an improvement in exercise performance results from an adequate balance between stress (*i.e.*, training) and the appropriate response and recovery post exercise (Kellmann *et al.*, 2018). Specifically, many aspects of the effect of exercise on physiology occur during the post exercise recovery times, which are critical timepoints relative to the adaptation process associated with training (Bishop *et al.*, 2008; Haddad & Adams, 2002). Therefore, whilst having an understanding on the effects of the MC and OCP use on exercise performance is an important consideration for sportswomen, it is not the only consideration. Indeed, even if changes in endogenous and exogenous sex hormones across the MC and with OCP use do not transpire to have any meaningful effects at a performance level, there is evidence to suggest that these fluctuations might affect the responses to, and recovery from exercise (Hackney *et al.*, 2019; Mackay *et al.*, 2019; Minahan *et al.*, 2015; Romero-Parra, Cupeiro, *et al.*, 2021; Romero-Parra, Rael, *et al.*, 2021; Savage & Clarkson, 2002). To date, however, most studies examining the effect of the MC and OCP use have focused on investigating what happens during exercise performance (see *Section 2.4*), or post a training programme (Dalgaard *et al.*, 2019; Myllyaho *et al.*, 2021; Nichols *et al.*, 2008; Oxfeldt, Dalgaard, Jørgensen, Johansen, *et al.*, 2020; Reis *et al.*, 1995; Riechman & Lee, 2021; Sakamaki-Sunaga *et al.*, 2016; Sung *et al.*, 2022; Sung *et al.*, 2014). As such, the effects of the

MC and OCP use on the responses to, and recovery from exercise are relatively unknown. Therefore, the following section will define recovery, examine the proposed influence of endogenous and exogenous sex hormones on aspects of the recovery process, and discuss whether these proposed influences translate into changes in the time course of recovery post exercise across the MC and with OCP use in sportswomen.

2.5.1 Defining recovery

Recovery is regarded as a multifaceted (*i.e.*, physiological, and psychological) restorative process relative to time for the re-establishment of performance abilities (Kellmann *et al.*, 2018). Different tests and measurements can be used to monitor recovery (Kellmann *et al.*, 2018), including: 1) physical performance tests (*e.g.*, jump, sprint, and strength tests); 2) physiological markers (*e.g.*, HR and/or HR variability); 3) biochemical markers (*e.g.*, creatine kinase [CK], cortisol, free testosterone, interleukin-6 [IL-6]); and 4) self-reported measures (*e.g.*, perception of an individual's readiness to perform and delayed onset of muscle soreness [DOMS]).

2.5.2 The 'normal' response and recovery profile following exercise

Initially described by Selye (1956), the general adaptation syndrome was the original model from which periodisation was designed. The general adaptation syndrome model describes the physiological response of an organism to stress, and proposes that all stressors result in similar responses: 1) the initial response, referred to as the alarm stage, whereby the physiological state of the organism decreases following the imposition of stress; 2) the resistance stage, where positive adaptations occur, returning the organism to homeostasis and possibly into a higher state, known as supercompensation; and 3) the exhaustion stage which occurs when the imposed stress is greater than the adaptive reserves of the organism or additional stressors occur (Cunanan *et al.*, 2018). Since, this pioneering work, a more comprehensive model of the responses to training stimuli has been proposed, named the fitness-fatigue theory (Banister *et al.*, 1991). The fitness-fatigue theory states that training results in two after-effects, which can positively or negatively influence performance: 1) fitness; and 2) fatigue (Chiu & Barnes, 2003). The traditional fitness-fatigue model starts with the observation that performance tends to reduce immediately after training and stays reduced for up to a few days because of fatigue (like Selye's alarm stage). Following this initial reduction there is a rebound and performance then improves because of dissipation in fatigue and improved fitness (like Selye's resistance stage). The interaction between these two after-effects results in the change in performance

following the stimulus. Collectively these models provide a simple framework for understanding the effects of a single training stimulus, which can help long-term training program design and periodisation (Chiu & Barnes, 2003; Kellmann *et al.*, 2018). Specifically, from this, it is evident that the responses to, and recovery from exercise are important drivers for long term adaptation (Bishop *et al.*, 2008). Thus, sufficient recovery from exercise is essential to allow optimal performance to be reached and to prevent negative developments, such as overtraining and injuries (Bishop *et al.*, 2008; Kellmann *et al.*, 2018). Whilst several variables influence the responses to, and recovery from exercise (*e.g.*, the intensity and duration of exercise and the type of activity), what remains to be determined is how endogenous and exogenous sex hormones in women affect these outcomes.

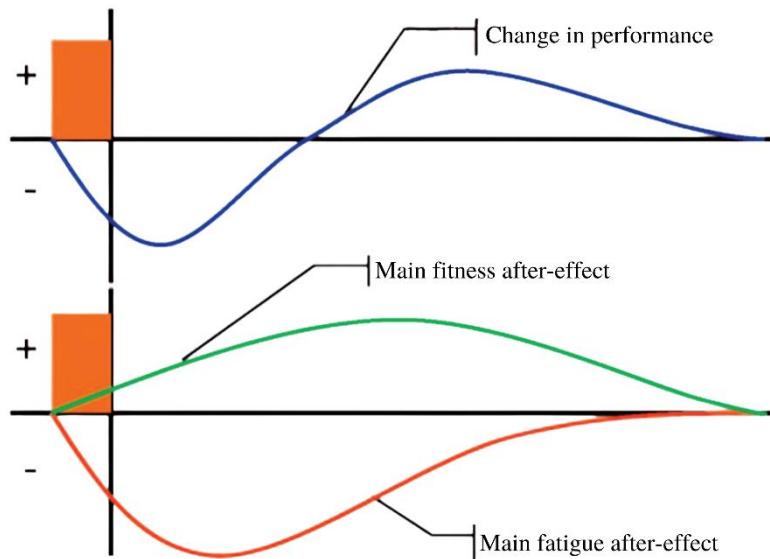


Figure 2-2 The original fitness-fatigue model proposed by Bannister in 1982, as shown in Chiu and Barnes (2003).

2.5.3 Potential mechanisms of endogenous and exogenous sex hormones on the responses to and recovery from exercise

As discussed in *Section 2.3.2*, ERs and PRs are present in most human tissues (Wierman, 2007). The expression of these receptors could influence target tissues within systems that drive the responses to, and recovery from exercise. For instance, oestrogen is reported to upregulate intracellular signalling pathways that stimulate skeletal muscle protein synthesis (Knowles *et al.*, 2019). Thus, a strengthened anabolic response to exercise might help increase skeletal

muscle repair and adaptation (Knowles *et al.*, 2019). Additionally, over the last two decades, evidence has accumulated, primarily from animal models, that suggests oestrogen might play a key role in the protection of skeletal muscle against exercise induced muscle damage (EIMD), as well as muscle repair and regeneration (Tiidus, 2005). Firstly, it is well known that oestrogen has antioxidant effects and helps membrane stability (Kendall & Eston, 2002). Therefore, it is plausible that the strong antioxidant and membrane stabilising properties of oestrogen might account for its ability to reduce EIMD (Enns & Tiidus, 2010; Tiidus, 2003). Likewise, oestrogen has been shown to inhibit the inflammatory response post exercise (Enns & Tiidus, 2010; Kendall & Eston, 2002; Tiidus, 2005; Tiidus, 2003), which might help to lessen any muscle disruption, leading to a potential quicker recovery time. Specifically, leucocytes (*i.e.*, neutrophils and macrophages) assist in the removal of damaged tissue during inflammation which plays an important role in muscle recovery following damage. However, neutrophils might further exacerbate EIMD through oxidising reactions (Enns & Tiidus, 2010; Tiidus, 2003). As such, limiting leucocytes (with oestrogen, although the exact mechanisms are not fully understood) into skeletal muscle during the inflammatory period might lesson muscle disruption and speed healing (Enns & Tiidus, 2010; Tiidus, 2003), as evidenced from studies on cardiac, neural, and other tissues (Harada *et al.*, 2001; Squadrito *et al.*, 1997; Wise *et al.*, 2001). In addition to the potential effects of oestrogen on reducing EIMD and inflammatory responses post exercise, there are also several theoretical reasons to suspect that oestrogen influences muscle repair, recovery, and regeneration (Enns & Tiidus, 2010; Tiidus, 2005; Tiidus, 2003). For example, one consequence of oestrogen attenuating leucocyte infiltration in skeletal muscle might be a change in skeletal muscle repair rates (Enns & Tiidus, 2010; Tiidus, 2005; Tiidus, 2003). Alternatively, infiltration of muscle by leucocytes might play a role in the activation and proliferation of satellite cells (Enns & Tiidus, 2010; Tiidus, 2005; Tiidus, 2003).

Progesterone might also play a role in skeletal muscle metabolism. For example, some studies have shown a proposed catabolic effect of progesterone (Knowles *et al.*, 2019), which could theoretically impair recovery post exercise. Moreover, most of the abovementioned research focused on the influence of oestrogen, and research investigating the significance of progesterone in the protection of muscle against EIMD, as well as muscle repair and regeneration is lacking (Tiidus, 2005). Of the available research however, there is little evidence to suggest that progesterone has any direct effect on EIMD, inflammation, or repair mechanisms (Tiidus, 2005). Although, as noted previously in *Section 2.3.2* several studies have reported an antagonistic effect of progesterone on oestrogen actions in other tissues (Tiidus,

2005). As such, the potential interactive effects of oestrogen and progesterone need to be further considered in relation to EIMD, as well as muscle repair and recovery. Overall, despite a potential effect of sex hormones on the mechanisms that underpin the responses to, and recovery from exercise it is important to acknowledge that most of the research to date has been conducted in animal models. Whilst at a mechanistic level, endogenous and exogenous sex hormones have the potential to affect the recovery response post exercise, whether the fluctuations in these hormones across the MC or with OCP use can create optimal/suboptimal hormonal environments to maximise/minimise the responses to and recovery from exercise in sportswomen is unclear.

2.5.4 Studies investigating the effects of the menstrual cycle and oral contraceptive pill use on the responses to and recovery from exercise

Theoretically, if oestrogen reduces EIMD and helps to promote muscle repair, then quicker recovery times following exercise might be reported during the mid- to late follicular and mid-luteal phases of the MC. Although, it is important to note that given the proposed antagonistic effects of progesterone on oestrogen actions (Tiidus, 2005), the presence of high progesterone in the mid-luteal phase might offset the positive effect of oestrogen and thus negatively impact recovery time in this phase. In contrast, when oestrogen is low during the early follicular phase of the MC it is hypothesised that recovery from exercise might take longer at this timepoint compared to other cycle phases, as the positive effects of oestrogen are lost. Furthermore, the suppression of endogenous oestrogen with OCP use might also result in a greater magnitude of EIMD and a slower recovery post exercise in OCP users compared to naturally menstruating women (Hicks *et al.*, 2017; Minahan *et al.*, 2015; Savage & Clarkson, 2002). Additionally, the influence of different concentrations of endogenous and exogenous sex hormones between pill-taking and pill-free days could influence EIMD and recovery responses across the OCP cycle (Romero-Parra, Rael, *et al.*, 2021). To date, however studies investigating the responses to and recovery from exercise across the MC and with OCP use in sportswomen have provided conflicting results, as discussed in greater detail below.

Hackney *et al.* (2019) examined biochemical responses (*i.e.*, blood CK and IL-6) throughout 72 h of recovery from endurance exercise in the mid-follicular and mid-luteal phases of the MC in healthy, exercise-trained women. Hackney and colleagues demonstrated that a longer recovery was required during the mid-follicular phase compared to the mid-luteal phase,

perhaps due to the antioxidant aspects of oestrogens being mitigated at this time. Although, interestingly, the authors did not investigate when oestrogen concentrations are at their highest/peaking and when progesterone concentrations are low (*i.e.*, the late follicular phase of the MC) despite previous research suggesting that oestrogen enhances recovery (see *Section 2.5.3*). In agreement with the findings by Hackney *et al.* (2019), Oosthuysen and Bosch (2017) investigated the CK and DOMS response to unaccustomed exercise (downhill running) across MC phases in 15 naturally menstruating women. The findings suggested that whilst the CK response to exercise did not differ across MC phases, the DOMS response did, with a delayed recovery of muscle soreness occurring in the early and late follicular phases of the MC compared to the mid-luteal phase. Similarly, Sipavičienė *et al.* (2013) investigated whether variations in oestrogen concentrations across the MC (*i.e.*, day 1 or 2 of the follicular phase and day 1 or 2 of the ovulatory phase) influenced the susceptibility to EIMD following stretch-shortening cycle exercise (100 maximal drop jumps) in physically active women. It was found that muscle strength returned to baseline levels faster after exercise in the ovulatory phase (high oestrogen) compared to the follicular phase (low oestrogen). However, the authors reported no differences in CK activity and perceived muscle soreness between MC phases. In contrast, Markofski and Braun (2014) examined the effect of MC phase on markers of EIMD following a single session of high-volume eccentric exercise. The authors demonstrated a higher CK response to exercise and a reduced strength recovery post the damaging exercise bout in the luteal phase (days 1 or 2 of luteal phase) when compared to the follicular phase (days 2 or 3 of the follicular phase) of the MC. Thus, the authors concluded that a higher concentration of oestrogen was not associated with an improvement in the signs and symptoms of EIMD. It is important to consider that the oestrogen concentration at the time of the exercise bout might not influence recovery responses, but rather the oestrogen concentration during the post exercise recovery time. For instance, in the study by Markofski and Braun (2014) during the recovery time oestrogen concentrations could have been rising during the follicular phase and reducing throughout the luteal phase. Additionally, naturally menstruating participants were pooled with those taking OCPs within the study by Markofski and Braun (2014), thus it is difficult to draw conclusions regarding the effect of the MC/OCP *cycle* on EIMD from this study. Certainly, the effects of oestrogen on the responses to and recovery from exercise appear positive, yet there remains conflict within the literature.

In addition to the studies that have reported an effect of the MC on recovery post exercise several studies have also reported no differences. For example, research by Chaffin *et al.* (2011) reported no difference in IL-6 and DOMS between the early follicular (approximately days 1 to 3 of the MC) and mid-luteal (roughly days 20 to 22 of the MC) phases of the MC in a group of competitive women distance runners following high-intensity interval running. Thus, the authors concluded that naturally menstruating women runners do not need to vary training across the MC to reduce DOMS. Further, Romero-Parra, Alfaro-Magallanes, *et al.* (2020) investigated the influence of the MC on indirect markers of muscle damage (*i.e.*, range of motion, muscle soreness, CMJ performance, and limb circumferences) post eccentric-based resistance exercise (*i.e.*, 10 × 10 back squats at 60% of each participants one-repetition maximum) in 19 well-trained naturally menstruating women. Whilst the protocol elicited EIMD, sex hormone fluctuations across MC phases did not affect any of the indirect markers of muscle damage, except for perceived muscle soreness. Specifically, the authors reported that muscle soreness was perceived to be greater in the early follicular phase when oestrogen concentrations were at their lowest. Using the same study design, Romero-Parra, Barba-Moreno, *et al.* (2020) determined whether the fluctuations in sex hormones across the MC between the early follicular, late follicular, and mid-luteal phases influence direct markers of muscle damage (*i.e.*, CK, myoglobin, lactate dehydrogenase, IL-6, tumoral necrosis factor- α , and C reactive protein). However, the damaging protocol utilised was not strenuous enough to elicit EIMD. Thus, the lack of MC phase differences in blood markers of muscle damage could be attributed to the exercise protocol as well as the use of well-trained participants, highlighting the importance of the training stimulus and participant training history in study designs assessing EIMD. Further, discrepancies between studies that support and refute an effect of the MC on the recovery process post exercise could be attributed to method considerations pertaining to MC research (see *Section 2.4.5*). For example, not all studies tested within the same phases of the MC, thus phases are not entirely comparable between studies. Similarly, the protocol used to verify MC phases was different between studies, with very few studies utilising the ‘three-step’ methodology to identify and verify MC phases. Finally, it should be considered that a large range of tests and measurements were used between the studies to monitor recovery (*i.e.*, direct physiological and biochemical markers versus subjective outcomes such as perceived muscle soreness) which could explain some of the heterogeneity within the literature.

Recently, a systematic review with meta-analysis was conducted to identify, evaluate, and summarise the available empirical evidence (Romero-Parra, Cupeiro, *et al.*, 2021). This meta-analysis suggested that fluctuations in endogenous sex hormones across the MC can affect EIMD in terms of DOMS and strength loss, whereas no differences were observed between MC phases for CK. Therefore, the authors highlight that practically, lower training loads or longer recovery periods could be considered during the early follicular phase, when sex hormone concentrations are at their lowest, and women might be more vulnerable to EIMD, whereas training loads can be enhanced in the late follicular and mid-luteal phases. However, it is evident from this review that further research is required. Indeed, the authors demonstrated that of the 19 studies included, only seven studies compared EIMD across MC phases (the other 12 reported responses to exercise at one timepoint of the MC), and only one study assessed EIMD across three phases of the MC, hence the need for future research (Romero-Parra, Cupeiro, *et al.*, 2021). Overall, whilst oestrogen might play an important role in the recovery process, the significance of this, particularly the potential for reduced or enhanced recovery post exercise in sportswomen across MC phases, is not yet fully known. As such, more research is needed before conclusions can be made pertaining to the optimal prescription of recovery post exercise in naturally menstruating women.

Given the different sex hormone profile experienced by _mOCP users, it is possible that _mOCP use might have different implications for the responses to, and recovery from exercise. For example, several studies have reported changes in muscle damage markers and recovery between naturally menstruating women and pill users. Indeed, Hicks *et al.* (2017), Minahan *et al.* (2015), and Roth *et al.* (2001) all reported higher post exercise levels of CK in OCP users compared with naturally menstruating women. In contrast, Hayward *et al.* (1998) reported higher post exercise levels of serum CK in naturally menstruating women compared to OCP users, and one study reported no difference between the groups (Savage & Clarkson, 2002). These conflicting findings might be attributable to the timing of testing and the different sex hormone environments assessed between the studies. For instance, Hayward *et al.* (1998) unexpectedly found a higher endogenous oestrogen concentration in OCP users compared to naturally menstruating women in their study, which might be explained by the timing of their testing (*i.e.*, day two of bleeding in both groups). Specifically, day two of menses is the lowest point of endogenous oestrogen in naturally menstruating women, whereas it is possible that at day two of withdrawal bleeding endogenous oestrogen had increased due to the suppressing

effect of exogenous hormones being removed during the pill-free days in OCP users. Therefore, currently it appears that endogenous oestrogen might be protective against EIMD and could enhance recovery post exercise, but further research is necessary. Moreover, given the changing sex hormone profile across the m OCP cycle, it could be theorised that the recovery response to exercise might differ between pill consumption and pill withdrawal days (Romero-Parra, Rael, *et al.*, 2021). Indeed, there is a small amount of evidence to suggest that some markers of EIMD are greater during the pill-free days compared to pill-taking days which might indicate a change in recovery across the OCP cycle (Romero-Parra, Rael, *et al.*, 2021), although the lack of differences in other EIMD variables between OCP phases warrants further investigation.

2.5.5 Section summary

To summarise, recovery from exercise is an important aspect of improving performance, and evidence suggests that there is a potential role for endogenous and exogenous sex hormones in the recovery process from exercise. Therefore, understanding the effect of the MC and OCP use on the responses to and recovery from exercise is essential to optimise the support provided to sportswomen. At present, there is a paucity of studies that have examined the role of endogenous and exogenous sex hormones on recovery from exercise, thus it is difficult to draw evidenced-based guidelines for sportswomen, and those working with them. Despite this, an absence of evidence is not evidence of absence, and the current evidence suggests that exercise scientists should pursue studying these potential effects. As such, *Chapter 6* investigates the effect of the MC and m OCP use on physical and perceptual measures of recovery time post an exercise session in recreationally active women.

2.6 The lived experiences of the menstrual cycle and oral contraceptive pill use and their influence on exercise performance and recovery post exercise

The concentration of endogenous and exogenous sex hormones, and the fluctuations in these, are not the only considerations when it comes to exercise performance and the recovery process post exercise in sportswomen. Indeed, another plausible reason for any potential effect could be the influence of an individuals lived experiences of their MC or OCP use, such as the experience of cycle related symptoms and perceived effects. Firstly, cycle related symptoms (both physical and psychological) are commonly reported in recreationally active women and

have the potential to influence an individual's ability to perform and train (Bruinvels *et al.*, 2021; Martin *et al.*, 2018). Secondly, an individual's perceived effect of performance and recovery are important considerations, with research showing that an individual's beliefs towards a factor which could theoretically influence performance might result in an actual change in performance (Carmichael *et al.*, 2021). Of relevance for this thesis is that many active women perceive that their MC or HC use influences their ability to perform or train (Armour *et al.*, 2020; Bruinvels *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Read *et al.*, 2021; Solli *et al.*, 2020). However, the literature to date has mainly concentrated on the differences in sex hormone concentrations alongside objective markers of exercise performance and recovery across the MC and with OCP use (see *Sections 2.4 and 2.5*), and thus the influence of cycle related symptoms alongside perceived effects have infrequently been investigated. Therefore, the following section will discuss the potential influence of cycle related symptoms and perceived effects of the MC and HC use on exercise performance and recovery time post exercise.

2.6.1 Cycle related symptoms and their impact on exercise performance and training outcomes in sportswomen

The cyclic fluctuations in endogenous sex hormones across the MC have been associated with a variety of cycle related symptoms (Table 2.1; [Bruinvels *et al.*, 2021]). These cycle related symptoms can be categorised broadly into two main types: 1) physical symptoms, including period pain, breast pain, and bloating; and 2) psychological symptoms, such as mood changes, anxiety, and irritability (Dickerson *et al.*, 2003; Ferries-Rowe *et al.*, 2020; Yonkers *et al.*, 2008). Typically, a similar pattern of symptoms is reported by naturally menstruating women, whereby symptoms predominately appear in the days preceding and during menses (Dickerson *et al.*, 2003; Ferries-Rowe *et al.*, 2020; Yonkers *et al.*, 2008). From a sporting perspective, it is evident that common negative symptoms, such as period pain, are likely to be antagonistic with optimal exercise performance and training (Bruinvels *et al.*, 2022). Often, the OCP is prescribed to women to help reduce negative cycle related symptoms within general and athletic populations (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). In turn, the use of OCPs, could help to limit any potential negative effects of symptoms on performance and training (Martin *et al.*, 2018). Therefore, it is evident that the experience of cycle related symptoms by sportswomen should be considered within sporting environments, and those working with sportswomen should recognise the impact these symptoms can have on aspects of performance and training. However, despite these potential effects, the magnitude

of symptoms (*i.e.*, the type, frequency, and severity, as well as common symptom footprints) and the direction of their effects (*i.e.*, impact on exercise performance and recovery outcomes) have yet to be fully documented.

Table 2-1 Commonly reported cycle related symptoms as described by Bruinvels *et al.* (2021).

Cycle related symptoms	
<i>Physical symptoms</i>	<i>Psychological symptoms</i>
Cravings/ increased appetite	Mood changes/ anxiety
Breast pain/ tenderness	Poor concentration/ memory
Tiredness/ fatigue	
Stomach cramps	
Bloating/ increased gas	
Water retention	
Lower back pain	
Headache/ migraine	
Diarrhoea	
Disturbed sleep	
Temperature fluctuations	
Joint pain/ muscle cramps	
Dizziness/ light-headedness/ reduced coordination	
Constipation	
Nausea/ sickness/ vomiting	
Changes to/ difficulties breathing	

Of the research that is currently available it appears that cycle related symptoms are prevalent in naturally menstruating active women (Armour *et al.*, 2020; Brown *et al.*, 2021; Bruinvels *et al.*, 2021; Findlay *et al.*, 2020; Martin *et al.*, 2018; Nolan *et al.*, 2022; Read *et al.*, 2021). For example, studies investigating the influence of cycle related symptoms on performance and training outcomes using individual semi-structured interviews report that most sportswomen, from recreationally active women to elite woman athletes, experience symptoms (Brown *et al.*, 2021; Findlay *et al.*, 2020; Read *et al.*, 2021). Indeed, Brown *et al.* (2021) showed that all women athletes included in their study reported symptoms associated with the MC including

period pain/cramps, bloating, and irritability. Interestingly, the authors also highlighted that these symptoms were reported to occur at set times across the cycle, with the lead up to and during menses being the timepoints in which more negative symptoms were experienced. Specifically, the woman athletes included in this study reported negative psychological symptoms that affected their ability to perform and train in the week before menstruation (feelings of fatigue and low energy resulting in reduced motivation to train) and physical symptoms lasting until the end of menses (period pain and bloating) that were perceived to impact actual performance outputs. Moreover, studies that have used large-scale survey-based approaches report similar findings, with between 77 to 84% of sportswomen experiencing cycle related symptoms, the most common including period pain, mood swings, changes in appetite, headaches, breast pain, and bloating (Armour *et al.*, 2020; Bruinvels *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022). Additionally, these studies also highlight that experiencing cycle related symptoms potentially contributes to changes in perceived exercise performance and training outcomes (Armour *et al.*, 2020; Bruinvels *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022). Specifically, Bruinvels *et al.* (2021) used a novel approach (the Menstrual Symptom Index [MSi]) to quantify the type, number, and frequency of cycle related symptoms and their relationship with performance and training outcomes. The authors reported that symptoms are commonly experienced by regularly exercising women, and that a greater prevalence and frequency of symptoms (*i.e.*, a higher MSi score) was associated with an increased likelihood of negative outcomes, such as missing training or competition. It is important to note that the abovementioned studies have several limitations. Firstly, all previous studies have relied on retrospective self-reported symptom data and are therefore potentially limited by memory recall. Additionally, the abovementioned studies have presented a general overview of symptoms throughout the entity of the MC, as such key timepoints where specific symptoms might be experienced were not examined in real-time, only retrospectively. Moreover, the MSi tool developed by Bruinvels *et al.* (2021) did not capture the severity of symptoms, which could theoretically influence exercise performance and training outcomes, in addition to the type and frequency of symptoms experienced. Furthermore, none of the previous studies have examined the influence of symptomology on objective markers of performance and recovery. Thus, given the recognised methodological shortcomings of the literature that is available, further research into cycle related symptoms in sportswomen is warranted.

As mentioned previously, it is thought that in addition to their use as a birth control measure, OCPs might help to alleviate the cycle related symptoms experienced across the MC within

sporting populations (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). For instance, Martin *et al.* (2018) reported that HC users experienced greater perceived positive effects specifically relating to the ability to predict and/or manipulate the timing, frequency, and amount of bleeding. On the other hand, it is possible that some individuals using OCPs might still experience negative symptoms related to their use (Armour *et al.*, 2020; Brown *et al.*, 2021; Nolan *et al.*, 2022), which might also affect performance and training. For instance, it has been reported that in OCPs exogenous ethinyl oestradiol has a higher oestrogen receptor affinity and is several times more potent than endogenous oestradiol (Bennink, 2004), which might play a role in the aetiology of cycle related symptoms during the pill-taking days. Additionally, it could be theorised that the downregulation of endogenous hormones and sudden withdrawal of exogenous hormones might play a role in the aetiology of cycle related symptoms during the pill-free days (Sulak *et al.*, 2000). Indeed, studies by Armour *et al.* (2020), Brown *et al.* (2021), and Nolan *et al.* (2022) report that $\approx 50\%$ of HC users still contend with cycle related symptoms. Despite this, most studies examining symptoms in sportswomen have excluded those using HCs, and very few have compared the symptoms experienced between naturally menstruating women and OCP users. Moreover, like the studies assessing cycle related symptoms in naturally menstruating women, the above studies are also limited by memory recall, and restricted to retrospective examination of symptoms. As a result, at present, the full extent of symptoms experienced by OCP users, alongside their potential impact on exercise performance and training, and how this compares with naturally menstruating women, has yet to be determined.

2.6.2 Perceived effects of the menstrual cycle and hormonal contraceptive use on exercise performance and recovery from exercise in sportswomen

It is reported that between 36 to 93% of sportswomen perceive that their MC or HC use influences their ability to perform or train (Armour *et al.*, 2020; Bruinvels *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Read *et al.*, 2021; Solli *et al.*, 2020). For example, studies examining perceived effects in naturally menstruating women commonly report perceived performance and training to be improved in all phases of the MC excluding the time leading up to, and during, menses, whereas perceived performance and training are reduced during this time (Armour *et al.*, 2020; Brown *et al.*, 2021; Findlay *et al.*, 2020; Read *et al.*, 2021; Solli *et al.*, 2020). Interestingly, it appears negative effects (*i.e.*, reduced performance etc.) are predominately reported in conjunction with cycle related symptoms (Armour *et al.*, 2020; Brown *et al.*, 2021; Findlay *et al.*, 2020; Read *et al.*, 2021; Solli *et al.*,

2020). In HC users, despite the reported perceived advantages of HC use in some sportswomen (Bennell *et al.*, 1999) no previous studies have examined the perceived effects of HC use on performance and training outcomes. Indeed, of particular interest to this thesis are the potential perceived changes in performance and training across the OCP *cycle* (*i.e.*, between pill-taking and pill-free days). Overall, the literature available shows that a large proportion of sportswomen report feeling that their performance and training is impaired during certain phases of their MC (Carmichael *et al.*, 2021), and it is theorised that HC use could also impact perceived outcomes (both positively and/or negatively). Despite this, research has effectively ignored individual lived experiences when investigating the effect of the MC and HC use on objective markers of exercise performance and the recovery process post exercise. Therefore, to provide a more comprehensive understanding of the effect of the MC and OCP use on performance and recovery outcomes in sportswomen, it is essential that future research considers the impact of perceived effects rather than solely focusing on the sex hormone concentrations themselves.

2.6.3 Section summary

In summary, these findings highlight the importance of considering not only the reproductive hormonal milieu on exercise performance and training outcomes, but also the individual lived experiences of the MC and OCP use. Specifically, cycle related symptoms and perceived effects are frequently reported by sportswomen and could be some of the mechanisms underpinning any performance and training effects. However, this individual lived experience of the MC and OCP use, and any association with performance and training outcomes, has been relatively overlooked within the literature. Moreover, the existing research has focused on investigating within well-established pre-defined cycle phases where endogenous and exogenous sex hormone concentrations are significantly different. Whilst this is an optimal design for investigating the impact of significantly different sex hormone concentrations on outcomes, it does not paint a full picture of the holistic impact of the MC and _mOCP *cycle*, as often cycle related symptoms and their perceived impact are reported to be highest during the shifts between cycle phases (Bruinvelds *et al.*, 2022). Thus, by using this type of design, the impact of any residual effects of cycle related symptoms, and perceived effects, on exercise performance and the recovery process post exercise are potentially missed. Establishing whether there is a residual effect of cycle related symptom frequency and severity, irrespective of cycle phase is important as sportswomen need to be able to perform and train regardless of sex hormone concentrations. Overall, no previous studies have adopted such a multifaceted

approach when investigating the influence of the MC and OCP on exercise performance and recovery outcomes. As such, *Chapter 5* of this thesis examines the symptoms experienced by naturally menstruating women and OCP users, and their perceived influence on exercise performance and recovery time post exercise. Subsequently, *Chapter 6* ties together the impact of endogenous and exogenous sex hormones, cycle related symptoms, and perceived effects to fully investigate the influence of the MC and OCP use on exercise performance and recovery time post exercise in sportswomen.

2.7 Investigations, aims, and hypotheses arising from the review of the literature

As this literature review has outlined, research investigating the effect of the MC and OCP use on exercise performance is currently conflicting, hence the first aims of this thesis to conduct two systematic reviews with meta-analyses to determine the direction and/or magnitude of the effects of: 1) MC phase; and 2) OCP use on exercise performance (see *Chapters 3 and 4*). Additionally, given that most of the research to date is interpreted as low quality, despite no formal grading, the secondary aim of *Chapters 3 and 4* was to appraise the quality of previous studies using robust assurance tools. As previously highlighted, understanding the effects of the MC and OCP use on exercise performance are not the only considerations for sportswomen. Indeed, even if MC phase and OCP use do not transpire to have any meaningful effects at a performance level, there is evidence to suggest that the responses to, and recovery from an exercise session might be affected. As such, understanding the effect of MC and OCP use on the responses to, and recovery from exercise was the latter aim of this thesis (see *Chapter 6*). Finally, whilst exercise performance and the recovery process post exercise might change across the MC and OCP *cycle*, and between naturally menstruating women and OCP users, via hormonally mediated changes, another plausible reason could be the influence of cycle related symptoms, as well as perceived effects. To date, however, the individual lived experiences of women have been relatively overlooked, and few studies have adopted such a hybrid approach to investigating the effects of the MC and OCP on performance and recovery outcomes. Thus, *Chapters 5 and 6* explored the effects of cycle related symptoms and perceived effects of the MC and OCP use on performance and recovery outcomes. Overall, in consideration of the review of the literature, four studies were conducted and are presented over *Chapters 3 to 6*. The titles, aims, and hypotheses of each study are outlined below:

Chapter 3. Study one.

Title: The Effects of Menstrual Cycle Phase on Exercise Performance in Naturally Menstruating Women: A Systematic Review and Meta-Analysis.

Aim: To critically examine existing studies investigating changes in exercise performance across the MC, in naturally menstruating women, and to appraise the quality of previous studies using robust assurance tools.

Hypothesis: Exercise performance would be reduced and improved when ratios of oestrogen and progesterone were low: low (*i.e.*, early follicular phase) and high: low (*i.e.*, late follicular/ovulatory phase), respectively. Additionally, it was hypothesised that most of the previous studies included in this Chapter would be judged as poor quality.

Chapter 4. Study two.

Title: The Effects of Oral Contraceptives on Exercise Performance in Women: A Systematic Review and Meta-Analysis.

Aim: To explore the effects of OCP use on exercise performance in women in two ways. First, by making a between group comparison of OCP users and non-users (*i.e.*, naturally menstruating counterparts) and second, by making a within group comparison of OCP consumption and withdrawal. Moreover, the secondary aim of this Chapter was to assess the quality of previous studies using robust assurance tools.

Hypothesis: Exercise performance would be reduced in OCP users compared with naturally menstruating women, due to the downregulation of endogenous sex hormones. Additionally, given the small changes in endogenous sex hormones and the presence and withdrawal of exogenous hormones between pill-taking and pill-free days, it was also hypothesised that exercise performance would change across the OCP cycle. Finally, it was hypothesised that most of the previous studies included in this Chapter would be judged as poor quality.

Chapter 5. Study three.

Title: Cycle Related Symptoms and Their Perceived Influence on Exercise Performance and Recovery Time Post Exercise.

Aim: To: 1) retrospectively describe and compare the type, frequency, and severity of symptoms experienced by naturally menstruating women and _mOCP users; 2) investigate in real-time the effect of MC and _mOCP phases on the type, frequency, and severity of symptoms; and 3) determine whether the symptoms experienced by naturally menstruating women and

_mOCP users during pre-defined MC and _mOCP *phases* are associated with perceived exercise performance and recovery time post exercise.

Hypothesis: Naturally menstruating women would experience a greater magnitude of cycle related symptoms compared to pill users. It was also hypothesised that the experience of cycle related symptoms would change across the MC and _mOCP *cycle*, and subsequently perceived negative exercise performance and recovery times post exercise would be reported when the magnitude of symptoms was greater.

Chapter 6. Study four.

Title: The Effect of The Menstrual Cycle, Oral Contraceptive Pill Use, and Related Symptoms on Exercise Performance and Recovery Time Post an Exercise Session in Recreationally Active Women.

Aim: To: 1) determine whether MC and _mOCP *phase* influence physical and perceptual measures of exercise performance and recovery time following an exercise session; and 2) evaluate whether the symptoms experienced by recreationally active women in the days before and after an exercise session are associated with exercise performance and recovery time post exercise.

Hypothesis: Both physical and perceptual measures of exercise performance and recovery time post exercise would be impaired when concentrations of endogenous sex hormones are low (*i.e.*, during the early follicular phase of the MC, and with _mOCP use compared to naturally menstruating women). Additionally, it was hypothesised that the symptoms experienced in the days leading up to and post the exercise session would negatively affect performance and recovery time in both naturally menstruating women and pill users.

CHAPTER 3 – THE EFFECTS OF MENSTRUAL CYCLE PHASE ON EXERCISE PERFORMANCE IN NATURALLY MENSTRUATING WOMEN: A SYSTEMATIC REVIEW AND META-ANALYSIS

This Chapter has been published previously in:

McNulty, K.L.*, Elliott-Sale, K.J.*., Dolan, E., Swinton, P.A., Ansdell, P., Goodall, S., Thomas, K., & Hicks, K.M. (2020). The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. *Sports Medicine*, 1-15.

*Joint author

Author contributions: KLM, KES, KMH, PA, SG and KT designed the research question. KLM conducted the searches and screening and KLM, KES, and KMH completed the three-phase screening process. KLM extracted the data, which were verified by KES and KMH. PAS performed all the statistical analysis. PAS, KLM, KMH, KES, and ED interpreted the data analysis. KLM and KES wrote the manuscript with critical input from KMH, ED, PAS, PA, SG and KT. All authors read and approved the final manuscript.

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McNulty, K.L., Elliott-Sale, K.J., Dolan, E., Swinton, P.A., Ansdell, P., Goodall, S., Thomas, K., & Hicks, K.M. (2020). The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. Poster presentation at: Future Physiology Conference; 19th – 22nd April 2021; Virtual event.

McNulty, K.L., Elliott-Sale, K.J., Dolan, E., Swinton, P.A., Ansdell, P., Goodall, S., Thomas, K., & Hicks, K.M. (2020). The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis. 15-minute oral presentation at: Women in Sport and Exercise Academic Network (WiSEAN) Conference; 19th – 22nd April 2021; Virtual event.

3.1 Introduction to Chapter 3

As demonstrated in *Chapter 2, Section 2.2.1*, there has been a rise in the number of women participating in exercise, from physical activity to elite sport, attributable to the increasing development of, and investment in, women's professional sport (Fink, 2015; Forsyth & Roberts, 2018). Specifically, the percentage of women competing at the Olympic Games has increased from 26% in Seoul in 1988 to 49% in Tokyo in 2021 (International Olympic Committee, 2021). However, performance-based research in women has not kept pace with this exponential rise in participation (Costello *et al.*, 2014; Cowley *et al.*, 2021). Indeed, it would be naive to assume that all research in men can be directly applied to women, given the anatomical, physiological, and endocrinological differences between the sexes (Ans dell *et al.*, 2020; Emmonds *et al.*, 2019; Sheel, 2016). As such, sportswomen will benefit from sex-specific research and guidelines, which consider the effects of women's physiology, such as the MC, on performance outcomes (Pitchers & Elliott-Sale, 2019).

The MC is an important biological rhythm, whereby large cyclic fluctuations in endogenous sex hormones, such as oestrogen and progesterone, are observed (Davis & Hackney, 2017; Landgren *et al.*, 1980; Owen Jr, 1975). As described in *Section 2.3.3*, the fairly predictable (and measurable) fluctuations in oestrogen and progesterone across the MC create significantly different transient sex hormone profiles, which are used to differentiate between MC phases (de Jonge, 2003; Mihm *et al.*, 2011). In brief, the MC is commonly divided into three phases: 1) the early follicular phase, characterised by low oestrogen and progesterone; 2) the late follicular/ovulatory phase, characterised by high oestrogen and low progesterone; and 3) the mid-luteal phase, characterised by high oestrogen and progesterone (Thompson & Han, 2019). Whilst the primary function of these sex hormones is to support reproduction, research has highlighted that the changing concentrations of endogenous oestrogen and progesterone across the MC, also exert a myriad of diverse and complex effects on multiple physiological systems, including cardiovascular, respiratory, metabolic, and neuromuscular parameters (Ans dell *et al.*, 2019; Chrousos *et al.*, 1998; Davis & Hackney, 2017), which play an integral role in exercise performance. As such, it is plausible that changes in exercise performance might be observed due to the different sex hormone profiles experienced across the MC (Constantini *et al.*, 2005; de Jonge, 2003; Frankovich & Lebrun, 2000; Lebrun, 1993; Lebrun *et al.*, 2013).

To date, and as highlighted in *Chapter 2 Section 3*, the effects of fluctuations in oestrogen and progesterone across the MC on exercise performance outcomes are conflicting, with some

studies reporting improved performance outcomes during the early follicular (Campbell *et al.*, 2001; Pallavi *et al.*, 2017; Tenan *et al.*, 2016), ovulatory (Bambaeichi *et al.*, 2004), and mid-luteal (Ekenros *et al.*, 2013; Oosthuysse *et al.*, 2005) phases, whereas others have shown no changes in exercise performance across MC phases (Casazza *et al.*, 2002; de Jonge *et al.*, 2001; Dibrezzo *et al.*, 1988; Elliott *et al.*, 2003; McLay *et al.*, 2007; Thompson *et al.*, 2012; Vaiksaar *et al.*, 2011a). Therefore, it is evident that a consensus is yet to be reached regarding the effects of the MC on exercise performance. Additionally, despite no formal evaluation, it is perceived that most of the research conducted in this area is of low quality, which further compounds the ability to draw a consensus. Subsequently, no evidence-based guidelines for managing exercise performance across the MC currently exist for both sportswomen and practitioners working with them. Therefore, the purpose of this Chapter was to perform a systematic review with meta-analysis to critically examine existing studies investigating changes in exercise performance across the MC, in naturally menstruating women. Additionally, the secondary aim of this Chapter was to appraise the quality of previous studies, for the first time, using robust assurance tools. The information provided in this Chapter can be used to inform practical recommendations for sportswomen, practitioners, and researchers interested in managing exercise performance across the MC.

3.2 Method

This review conforms to the preferred reporting items for systematic reviews and meta-analyses (PRIMSA) statement guidelines (see *Appendix A*; [Moher *et al.*, 2009]).

3.2.1 Study inclusion and exclusion criteria

Consideration of Population, Intervention, Comparator, Outcomes, and Study design (PICOS) was used to determine the parameters within which the review was conducted.

3.2.1.1 Population

Participants included healthy women who were: 1) between the ages of 18 and 40 years; 2) naturally menstruating; 3) not taking any HCs or medication known to affect the HPO axis; 4) free from any menstrual-related dysfunctions (*e.g.*, amenorrhea) or any other conditions (*e.g.*, pregnancy, eating disorders or disordered eating), known to affect the HPO axis; and 5) free

from any injury that would affect participation. No restrictions were placed on activity level or training status.

3.2.1.2 Intervention

No specific intervention was investigated, but all participants were required to have a natural MC; defined as having a minimum of nine cycles per calendar year and a MC that ranged between 21 and 35 days in length.

3.2.1.3 Comparator

Comparisons were made between the early follicular phase (acting as a ‘control’ phase) of the MC and all other MC phases, in line with the following predetermined MC phase classification as shown in Figure 3.1: early follicular (days 1 to 5); late follicular (days 6 to 12); ovulation (days 13 to 15); early luteal (days 16 to 19); mid-luteal (days 20 to 23); and late luteal (days 24 to 28).

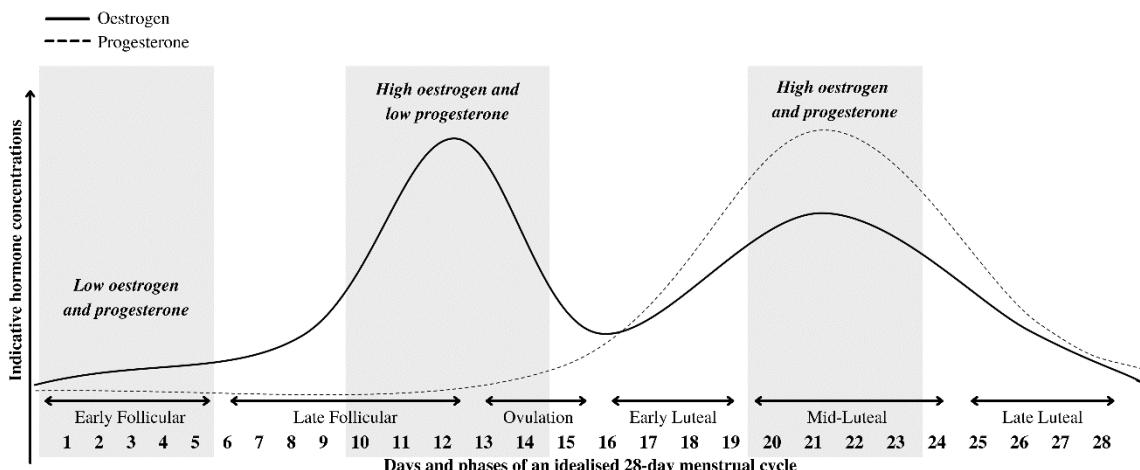


Figure 3-1 Schematic displaying the sex hormone fluctuations across an idealised 28-day menstrual cycle, with ovulation occurring on day 14, and corresponding study phases. Adapted from Pitchers and Elliott-Sale (2019).

3.2.1.4 Outcomes

The primary outcome was exercise test performance. For the purposes of this Chapter, exercise test performance was defined as total work done, time to completion, time to exhaustion, mean, peak and ratio outputs, rate of force production and decline, and indices of fatigue. Although $VO_{2\text{max}}$ and $VO_{2\text{peak}}$ tests are not performance tests, this physiology-based outcome was

included. A full list of considered outcomes can be found in *Appendix B*. Performance outcome data were allocated into broad categories to allow for subgroup analysis; namely endurance (power and capacity) and strength (maximal expression of force and rate of force development). All exercise outcomes were extracted, and effect size duplication of multiple outcomes from the same test accounted for within the statistical analysis, as described below.

3.2.1.5 Study design

Experimental studies were considered for analysis if they met the following inclusion criteria: 1) published, in full, in a peer-reviewed journal; 2) had the primary or secondary objective of assessing exercise performance across the MC; 3) included within group comparisons; and 4) outcome measure(s) were taken in two or more defined MC phases. As such, case studies, review articles, study protocol papers, and conference abstracts were excluded. Moreover, only full texts that were published in English or had an existing translation were retrieved and examined. There was no limit on the date of publication.

3.2.2 Search strategy for identification of studies

A systematic electronic literature search was conducted by one reviewer to identify all relevant articles using four online databases (PubMed, CENTRAL, SPORTDiscus, and ProQuest). The searches were performed using medical subject headings terms, free-text, and thesaurus terms, as well as keywords from existing relevant papers (Constantini *et al.*, 2005; de Jonge, 2003; Frankovich & Lebrun, 2000; Lebrun, 1993; Lebrun *et al.*, 2013). The following search terms and their combinations were used: ('menstrual cycle', OR 'menstrual phase', OR 'follicular phase', OR 'luteal phase') AND ('strength', OR 'power', OR 'torque', OR 'force', OR 'neuromuscular', OR 'max* voluntary contraction', OR 'isometric', OR 'isokinetic', OR 'skeletal muscle' OR 'muscular performance', OR 'aerobic', OR 'aerobic power', OR 'aerobic capacity', OR 'endurance', OR 'endurance power', OR 'endurance capacity', OR 'anaerobic', OR 'anaerobic power', OR 'anaerobic capacity', OR 'athletic performance', OR 'sports performance'). An example of a full electronic search for one database (PubMed: 14/01/2019) is presented in *Appendix C*. Databases were searched from inception until April 2020. The reference lists of obtained relevant articles and review articles were hand-searched to identify any further studies and were added manually. Following the same search criteria and strategy, an updated electronic and manual hand-search for relevant literature was subsequently conducted in July 2022 to identify any further articles published between April 2020 and July

2022 that fit the inclusion/ exclusion criteria. Articles identified in the updated search are not included in the analysis but are presented in Table 3.1 to provide the reader with an up-to-date review of the literature.

Table 3-1 Overview of the studies found during the updated electronic and manual hand-search for relevant literature that could be included in the present Chapter based on inclusion/exclusion criteria.

Author (date)	Aim	Population (participant health, training status and sample size)	MC phases	Methods of determining	Outcome measure(s)	Study conclusion	Quality rating
Barba- Moreno <i>et al.</i> (2022)	To investigate the effects of the MC on cardiorespiratory responses during steady-state exercise	Healthy endurance-trained women (n = 15)	EF, LF, and ML	MC history, counting of days, and serum oestrogen and progesterone	$\dot{V}O_{2\max}$ (ml.min) $\dot{V}O_{2\max}$ during the LF phase compared with the EF phase of the MC	Increase in $\dot{V}O_{2\max}$ during the LF phase compared with the EF phase of the MC	Moderate
Freemas <i>et al.</i> (2021)	To investigate whether aerobic exercise performance is impaired in the ML compared to the MF phase of the MC	Recreationally active women (n = 12)	LF and ML	Counting of days, and salivary oestrogen and progesterone	8-km TT cycling performance (mins)	Aerobic exercise performance was reduced in the ML phase compared with the MF phase	Very low

García-Pinillos <i>et al.</i> (2022)	To examine the effect of the MC when estimating one repetition maximum from the individual load-velocity relationship during the bench press exercise	Resistance-trained women (n = 9)	EF, LF, and ML	Counting of days	Estimated one repetition maximum during the bench press exercise (kg)	Estimation of the exercise one repetition maximum does not vary across MC phases	Low
García-Pinillos <i>et al.</i> (2021)	To examine the effects of the MC on vertical jumping, sprint performance, and force-velocity profiling	Resistance-trained women (n = 9)	EF, LF, and ML	Counting of days	Jumping tests (<i>i.e.</i> , squat jump height [cm], CMJ height [cm], Drop jump height from a 30 cm box [cm] and the reactive strength index 30 m sprint running test (s))	Vertical jump, sprint performance, and force-velocity profiling remained constant in trained women, regardless of MC phase	Low
Ghazel <i>et al.</i> (2020)	To evaluate the effect of music on short-term exercise performance	Women handball players,	EF, LF, and ML	Counting of days	Squat jump height performance (cm)	Phase of the MC does not affect	Very low

	during different MC phases	moderately trained (n = 14)			CMJ height performance (cm)	vertical jump performance	
Nakamura and Nose-Ogura (2021)	To examine the effects of administration of monophasic oral contraceptives on body composition and aerobic and anaerobic capacities	Women athletes (n = 10)	EF and ML	Counting of days, and serum oestrogen and progesterone	Aerobic parameters (<i>i.e.</i> , $\dot{V}O_{2\max}$ [L/min] and TTE [minutes]) Anaerobic parameters (<i>i.e.</i> , peak power output and average power output decline from a Wingate Test (W))	The phase of the MC did not affect any of the aerobic or anaerobic outcomes measured	Low
Paludo <i>et al.</i> (2020)	To investigate salivary oestradiol and cortisol concentrations, mood, anxiety, and exercise (aerobic and anaerobic) performance across two MC phases	Physically active women (n = 12)	EF and ML	Unknown	Aerobic (<i>i.e.</i> , $\dot{V}O_{2\max}$ [mL/kg/min]) and anaerobic (<i>i.e.</i> , peak power, average power, and fatigue index)	There was a small reduction in $\dot{V}O_{2\max}$ in the ML phase, but there was no difference across the MC in any other variable performance	Very low

Romero-Parra <i>et al.</i> (2021)	To determine whether the fluctuations in sex hormones across the MC influence muscle damage	Well-trained women (n = 19)	EF, LF, and ovulation	Counting of days, MC history, urinary ovulation detection test, and serum oestrogen and progesterone	CMJ height (cm) performance	No changes were observed across the MC for CMJ height	Moderate
Thompson <i>et al.</i> (2021)	To investigate the potential effect of the MC on various aspects of muscle performance	Active women (n = 12)	EF, LF, and ML	Counting of days, urinary ovulation detection test, and serum oestrogen and progesterone	CMJ performance (<i>i.e.</i> , average power [W/kg], and flight time [ms]) Bilateral hop jump performance (<i>i.e.</i> , contact time [ms], flight time [ms], and average power [W/kg]) Handgrip strength (kg)	Most variables showed no changes over the MC; however, isokinetic knee flexion, bilateral hopping and CMJs were greater in the ML phase compared to the LF phase	Moderate

					Isometric knee extensor strength (Nm)		
					Isokinetic knee flexion and extension 60° and 240° s ⁻¹		
Weidauer <i>et al.</i> (2020)	To determine changes in neuromuscular performance throughout the MC	Physically active college women (n = 25)	EF, ovulation, and ML	Counting of days, urinary ovulation detection test, and serum oestrogen and progesterone	Isokinetic peak torque at the knee at 60°, 180° and 240° s ⁻¹ (Nm) Handgrip strength (kg)	Muscular performance was diminished in the EF phase of the MC compared with all other phases	Moderate

CMJ, countermovement jump; EF, early follicular; LF, late follicular; MC, menstrual cycle; MF, mid-follicular; ML, mid-luteal; TTE, time to exhaustion; TT, time trial; $\dot{V}O_{2\max}$, maximal oxygen uptake.

3.2.3 Data selection, extraction, and study quality assessment

3.2.3.1 Selection of studies

Three reviewers independently reviewed the titles, abstracts, and full-text paper of the identified articles for inclusion and any duplicates were removed, using Covidence systematic review software (v1251, Veritas Health Innovation, Australia). All searches followed a two-phase screening strategy. Phase one assessed the eligibility of the title and abstract of every manuscript generated from the electronic searches and hand-searching against the predetermined inclusion and exclusion criteria. Studies that either clearly did not meet the inclusion criteria or met at least one exclusion criterion were excluded at this phase. In phase two, the full-text paper was retrieved for the articles identified in stage one and assessed against the predetermined inclusion and exclusion criteria. Any conflicts between reviewers relating to study eligibility were resolved in consensus meetings.

3.2.3.2 Data extraction and management

Data extraction was conducted by one reviewer, using a pre-piloted data extraction form, and independently verified by two members of the review team. Any discrepancies were resolved by reviewing the original article and consensus achieved by discussion during consensus meetings, or, if needed, in consultation with a fourth reviewer. When data were presented in graphical, and not in numerical format, DigitizeIt software (v2.3, DigitizeIt, Germany) was used to convert the relevant data. Further, where data were incomplete, authors were contacted to obtain the relevant information. Authors were given four weeks to respond, if the authors failed to respond after this date, the paper was excluded if no relevant data could be extracted from the published version of the paper.

3.2.3.3 Quality assessment of included studies

Study quality was assessed by one reviewer and independently verified by two members of the review team, using a strategy based on the recommendations of the Grading of Recommendations Assessment Development and Evaluation (GRADE) working group (Guyatt *et al.*, 2011). This strategy considers quality of evidence for any one outcome based on five domains, namely risk of bias, indirectness, inconsistency, imprecision, or evidence of publication bias. Both risk of bias and indirectness were initially conducted at the individual study level, with mode ratings used to describe whole outcomes. The initial appraisal tool used

was based on the Downs and Black checklist for measuring study quality (Downs & Black, 1998) and was specifically modified for use in this Chapter (see *Appendix D*). The modified Downs and Black checklist comprised 15 outcomes, from five domains: 1) reporting; 2) external validity; 3) internal validity – bias; 4) internal validity – confounding; and 5) power. A maximum attainable score of 16 could be awarded, whereby study quality was categorised as following: “high” (14 – 16); “moderate” (10 – 13); “low” (6 – 9); or “very low” (0 - 5). The results of the Downs and Black assessment were used to assign an *a-priori* quality rating to each study. This *a-priori* rating was then either maintained, or downgraded a level, based on the response to two questions that were considered key to the *directness* of these research studies: Q.1) was the MC phase confirmed using urinary ovulation detection kits? If the authors reported the use of a urinary ovulation detection kit to identify MC phase, the *a-priori* rating was maintained and if not, the study was downgraded a level (*e.g.*, a study that started out as “high” in quality but did not use a urinary ovulation detection kit to identify MC phase drops to “moderate” in quality). and Q.2) was the MC phase confirmed using blood samples? If the authors reported using blood samples to confirm MC phase, the Q.1 rating was maintained, if not, the study was downgraded a level (as such, the maximum rating for any study that does not use urinary ovulation detection kits or serum analysis to identify and verify MC phase is “low”). The inclusion of these specific questions was based on methodological conclusions made in previous studies (Elliott-Sale *et al.*, 2021; Thompson & Han, 2019). Consistency was ascertained using the meta-analysis results and was based on visual inspection of effect size estimates, whether confidence intervals overlapped, and on statistical tests for heterogeneity. Precision was judged based on the number of outcomes available (with outcomes based on < 5 data points downgraded) and on visual analysis of the width of the confidence intervals. Publication bias was assessed using Egger’s test along with visual inspection of funnel plots. Overall, this procedure allowed the final quality of evidence for each outcome to be categorised as either “high”, “moderate”, “low” or “very low” in quality. This quality appraisal was not used to exclude any study, although a sensitivity analysis was conducted using only those individual studies deemed to be of “high” or “moderate” in quality, based on the risk of bias and directness assessments. Any differences between the reviewers were resolved by discussion during consensus meetings, or, if needed, in consultation with a fourth reviewer.

3.2.4 Data synthesis

Data were extracted from studies comprising both between- and within-group designs. Pairwise effect sizes were calculated by dividing mean differences by pooled standard deviations. At the study level, variance of effect sizes was calculated according to standard distributional assumptions (Morris, 2008). All meta-analyses were conducted within a Bayesian framework enabling the results to be interpreted more intuitively compared to a standard frequentist approach through use of subjective probabilities (Kruschke & Liddell, 2018). With a Bayesian framework, dichotomous interpretations of the results of a meta-analysis with regards to the presence or absence of an effect (*e.g.*, with P values) can be avoided, and greater emphasis placed on describing the most likely values for the average effect and addressing practical questions such as, the probability the average effect is beyond a certain threshold (Kruschke & Liddell, 2018). The Bayesian framework is also particularly suited to hierarchical models and sharing information within and across studies to improve estimates (Kruschke & Liddell, 2018). In the present meta-analysis, three-level hierarchical models were conducted to account for covariance in multiple outcomes presented in the same study (Saunders *et al.*, 2017). For the initial analysis, individual effect sizes were calculated by comparing exercise performance in the early follicular phase (acting as a ‘control’ phase) with all other phases of the MC (late follicular, ovulation, early luteal, mid-luteal, and late luteal). Meta-regression was performed to assess whether the pooled effect size estimate was influenced by the testing category (endurance or strength outcomes). Where no evidence of a difference was identified, the model was rerun combining both categories of outcomes to increase data to better estimate model parameters. Given the expectation of relatively small effect sizes, an *a priori* threshold of ± 2 was identified for outliers. Primary analyses were completed with outliers removed, but results were also presented from the full complement of studies as sensitivity analyses. A sensitivity analysis was also conducted on data obtained from studies categorised as “high” or “moderate” in quality. Assessment of publication bias was made using a multilevel extension of Egger’s test with effect sizes regressed on the inverse of standard errors (Fernández-Castilla *et al.*, 2021). Inferences from all analyses were performed on posterior samples generated by Markov Chain Monte Carlo with Bayesian 95% credible intervals (CrIs) constructed to enable probabilistic interpretations of parameter values. Interpretations were based on visual inspection of the posterior sample, the median value ($ES_{0.5}$: 0.5-quantile) and 95% CrIs. Cohen (2013) standard threshold value of 0.8 was used to describe effect size as large, values between

0.5 and 0.8 as medium, values between 0.2 and 0.5 as small, and values between 0 and 0.2 as trivial.

After the initial analysis, a network meta-analysis approach was used to compare exercise performance measured across all MC phases (early follicular, late follicular, ovulation, early luteal, mid-luteal and late luteal) with each other. Network meta-analyses are becoming increasingly common in evidence synthesis and are most used to compare multiple experimental treatments where individual studies are unlikely to directly compare all relevant treatments (Greco *et al.*, 2015). The technique calculates pairwise effect sizes from studies comparing two treatments (direct evidence) and generates indirect evidence comparing other treatments through a common comparator (Greco *et al.*, 2015). The technique was adopted in the present Chapter to supplement the initial pairwise meta-analysis and synthesise additional data comparing exercise performance using different combinations of MC phases. Study-specific treatment effects were drawn from multivariate normal distributions with up to five-arms included. To test the consistency assumption of the network meta-analysis, the fit of the base-case model was compared to that of the inconsistency model. To summarise potential differences in exercise performance outcomes across all MC phases, results from the network-meta-analysis were used to calculate the Surface Under the Cumulative Ranking curve (SUCRA; [Salanti *et al.*, 2011]). For each MC phase a SUCRA value expressed as a percentage was calculated representing the likelihood that exercise performance was maximised or near maximised relative to other MC phases. More formally, the SUCRA value can be interpreted as the average proportion of phases where exercise performance is lower than the phase considered, with the mean SUCRA value equal to 50% (Rücker & Schwarzer, 2015). Analyses were performed using the R packages R2WinBUGS (Sturtz *et al.*, 2005) and brms (Bürkner, 2017). Convergence of parameter estimates were checked with Gelman-Rubin R-hat values (Gelman *et al.*, 1995).

3.3 Results

3.3.1 Literature search

The literature search and selection of studies are presented in Figure 3.2.

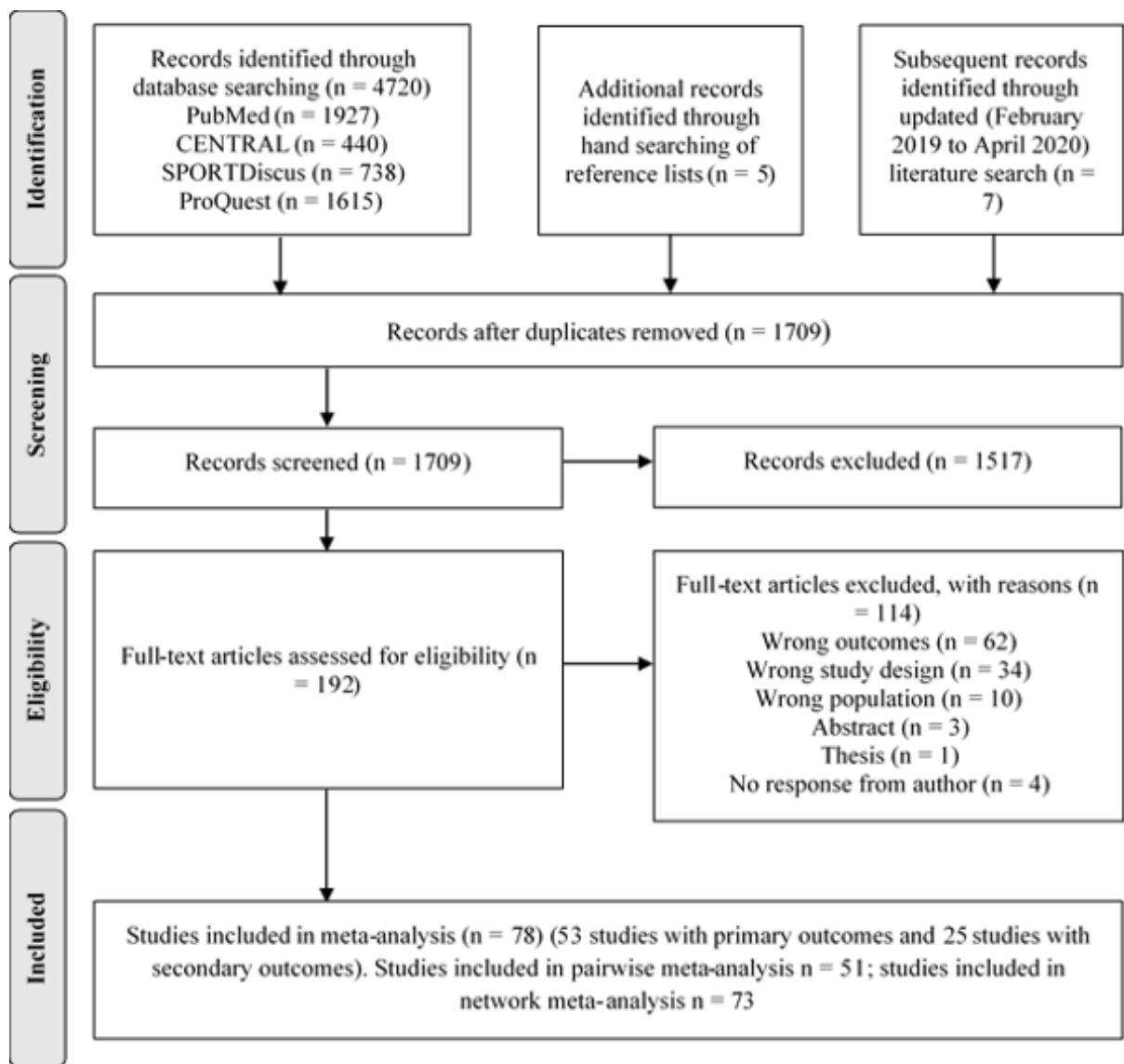


Figure 3-2 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines flow chart for literature search and study selection.

3.3.2 Study characteristics

In total 78 studies (Abt *et al.*, 2007; Ansdell *et al.*, 2019; Bailey *et al.*, 2000; Bambaeichi *et al.*, 2004; Bandyopadhyay & Dalui, 2012; Beidleman *et al.*, 1999; Bell *et al.*, 2011; Bemben *et al.*, 1995; Birch & Reilly, 1999; Birch & Reilly, 2002; Burrows & Bird, 2005; Bushman *et al.*, 2006; Campbell *et al.*, 2001; Casazza *et al.*, 2002; Davies *et al.*, 1991; De Bruyn-Prevost *et al.*, 1984; de Jonge *et al.*, 2001; de Souza *et al.*, 1990; Dean *et al.*, 2003; Dibrezzo *et al.*, 1988; Dombovy *et al.*, 1987a; Dombovy *et al.*, 1987b; Drake *et al.*, 2003; Ekenros *et al.*, 2013; Elliott *et al.*, 2005; Elliott *et al.*, 2003; Ettinger *et al.*, 1998; Frandsen *et al.*, 2020; Fridén *et al.*, 2003; Giacomoni *et al.*, 2000; Girija & Veeraiah, 2011; Gordon *et al.*, 2013; Gordon *et al.*, 2018;

Grucza *et al.*, 2002; Grucza *et al.*, 1993; Gür, 1997; Hertel *et al.*, 2006; Hoeger Bement *et al.*, 2009; Hoshi, 1997; Jarvis *et al.*, 2011; Julian *et al.*, 2017; Jurkowski *et al.*, 1981; Kaygisiz *et al.*, 2003; Kraemer *et al.*, 2006; Kubo *et al.*, 2009; Lara, Gutiérrez-Hellín, *et al.*, 2020; Lara, Gutiérrez Hellín, *et al.*, 2020; Lebrun *et al.*, 1995; Lee *et al.*, 2014; Lynch & Nimmo, 1998; Masterson, 1999; Mattu *et al.*, 2020; McCracken *et al.*, 1994; McLay *et al.*, 2007; Montgomery & Shultz, 2010; Okudan *et al.*, 2005; Oosthuysse *et al.*, 2005; Otaka *et al.*, 2018; Pallavi *et al.*, 2017; Petrofsky *et al.*, 2007; Quadagno *et al.*, 1991; Redman *et al.*, 2003; Rodrigues *et al.*, 2019; Romero-Moraleda *et al.*, 2019; Sarwar *et al.*, 1996; Shaharudin *et al.*, 2011; Sipavičienė *et al.*, 2013; Smekal *et al.*, 2007; Sunderland & Nevill, 2003; Sunderland *et al.*, 2011; Takase *et al.*, 2002; Tenan *et al.*, 2016; Thompson *et al.*, 2012; Tounsi *et al.*, 2017; Tsampoukos *et al.*, 2010; Vaiksaar *et al.*, 2011a; Wearing *et al.*, 1972; Wiecek *et al.*, 2016), with a total of 1,193 participants, were included. Details of the included studies are shown in *Appendix E*.

3.3.3 Methodological quality

3.3.3.1 Quality assessment of included studies

All quality classifications are presented in Figure 3.3. Analysis of quality based on the entire evidence base ($n = 78$) was ascertained at the individual study level, and according to the Downs and Black checklist, as well as the additional questions regarding MC phase confirmation. The quality of the evidence from the 78 studies included in this review was primarily classified as “low” in quality (8% “high”; 24% “moderate”; 42% “low”; 26% “very low”; Figure 3.3) such that, “our confidence in the effect estimate is limited: the true effect might be substantially different from the estimate of the effect” (Balshem *et al.*, 2011). Seventy-one percent of studies were initially allocated an *a-priori* rating of “moderate” quality, however following the application of questions pertaining to MC phase identification and verification, only 24% of these studies were allocated a final rating of “moderate” quality.

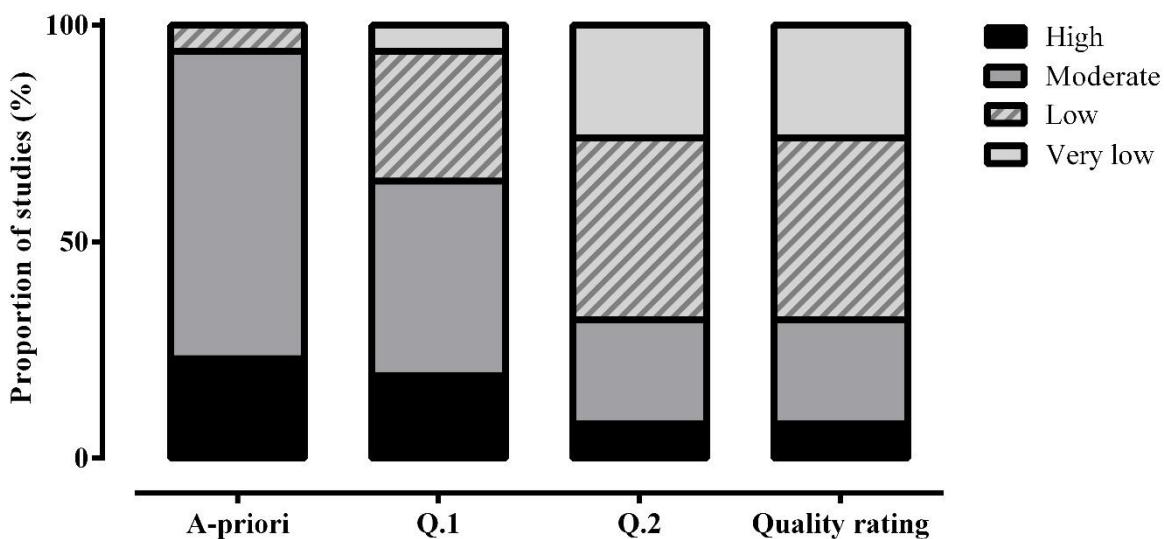


Figure 3-3 Quality rating of outcomes from all included studies ($n = 78$). Each bar represents the proportion of studies assigned a “high,” “moderate,” “low,” or “very low” quality rating. The x-axis represents the different stages of the quality appraisal process, with question one (Q. 1) and question two (Q. 2) indicating the questions asked to determine menstrual cycle phase identification and verification in each study, with the final bar representing the proportion of studies assigned to each quality rating category.

3.3.3.2 Menstrual cycle phase identification and verification

In the 78 included studies, an array of methods were used to identify MC phase: 1) a combination of methods (*e.g.*, counting of days, BBT, assessment of menstrual symptoms, MC history and serial follicular scanning] without urinary ovulation detection kits (45%); 2) a combination of methods (*e.g.*, counting of days, BBT, MC history, assessment of menstrual symptoms and urine ovulation detection kits) with urinary ovulation detection kits (31%); 3) counting of days (10%); 4) MC history (4%); 5) BBT (4%); and 6) urinary ovulation detection kits (1%). In addition, some studies (5%) did not provide any information on how MC phases were identified. In relation to MC phase verification, out of the 78 studies included in the review, most studies (59%) retrospectively verified MC phase using serum oestrogen and progesterone, a small number of studies retrospectively verified MC phase using saliva (4%) or urine (2%) oestrogen and progesterone, and the remaining studies provided no information on how they verified the identified MC phase (35%).

3.3.4 Outcomes

3.3.4.1 Analysis 1: Pairwise meta-analysis

The initial meta-analysis comprised pooling of pairwise effect sizes comparing exercise performance during the early follicular phase of the MC with all other MC phases (late follicular, ovulation, early luteal, mid-luteal, and late luteal). From the 78 studies that were eligible for the systematic review, 51 studies (Abt *et al.*, 2007; Ansdell *et al.*, 2019; Bailey *et al.*, 2000; Bandyopadhyay & Dalui, 2012; Beidleman *et al.*, 1999; Bell *et al.*, 2011; Bemben *et al.*, 1995; Birch & Reilly, 1999; Burrows & Bird, 2005; Bushman *et al.*, 2006; Campbell *et al.*, 2001; Casazza *et al.*, 2002; Davies *et al.*, 1991; De Bruyn-Prevost *et al.*, 1984; de Jonge *et al.*, 2001; de Souza *et al.*, 1990; Dean *et al.*, 2003; Dibrezzo *et al.*, 1988; Drake *et al.*, 2003; Ekenros *et al.*, 2013; Elliott-Sale, 2014; Elliott *et al.*, 2005; Ettinger *et al.*, 1998; Fridén *et al.*, 2003; Giacomoni *et al.*, 2000; Gordon *et al.*, 2013; Gordon *et al.*, 2018; Gür, 1997; Hoshi, 1997; Jarvis *et al.*, 2011; Julian *et al.*, 2017; Kraemer *et al.*, 2006; Kubo *et al.*, 2009; Lara, Gutiérrez-Hellín, *et al.*, 2020; Lara, Gutiérrez Hellín, *et al.*, 2020; Lebrun *et al.*, 1995; Lee *et al.*, 2014; Masterson, 1999; Montgomery & Shultz, 2010; Otaka *et al.*, 2018; Pallavi *et al.*, 2017; Petrofsky *et al.*, 2007; Quadagno *et al.*, 1991; Rodrigues *et al.*, 2019; Romero-Moraleda *et al.*, 2019; Sarwar *et al.*, 1996; Sipavičienė *et al.*, 2013; Tenan *et al.*, 2016; Thompson *et al.*, 2012; Tounsi *et al.*, 2017; Tsampoukos *et al.*, 2010; Vaiksaar *et al.*, 2011a; Wearing *et al.*, 1972) included assessment of exercise performance during the early follicular phase of the MC and included all other data required for calculations.

The 51 studies (mode quality rating = “low”; 8% “high”; 24% “moderate”; 37% “low”; 31% “very low”) generated 362 pairwise effect sizes (240 strength and 122 endurance) with an average of four outcomes per study and a range from 1 to 12 outcomes. Data were obtained from 709 participants with studies comprising a mean participant size of 14 (range n = 5 to 100). A total of nine outliers were identified (seven studies with effect sizes less than -2 [favouring the ‘other MC phases’] and two studies with effect sizes greater than +2 [favouring the early follicular phase]) and subsequently removed from the analysis. The three-level hierarchical model indicated a trivial effect with reduced exercise performance obtained in the early follicular phase of the MC, based on the median pooled effect size ($ES_{0.5} = -0.06$ [95% CrI: -0.16 to 0.04]; Figure 3.4). Large between study variance was identified ($\tau_{0.5} = 0.26$ [0.18 to 0.38]) and intraclass correlation coefficient estimates close to zero indicated little within-study correlation between outcomes. Pooling of strength and endurance outcomes was

conducted as no evidence was obtained that indicated a differential effect between these performance categories ($ES_{0.5/\text{Endurance-Strength}} = -0.01$ [95% CrI: -0.18 to 0.16]). Posterior estimates of the pooled effect size indicated close to zero probability of a small effect either in favour of the early follicular phase or all other MC phases ($d \geq 0.2$; $P \leq 0.001$). Egger's regression test provided no evidence of publication bias ($\text{Egger}_{0.5} = -0.01$ [95% CrI: -0.09 to 0.08]). Inclusion of outliers within the model had minimal influence on the average effect size ($ES_{0.5} = -0.08$ [95% CrI: -0.21 to 0.05]) and between study variance ($\tau_{0.5} = 0.30$ [95% CrI: 0.23 to 0.39]).

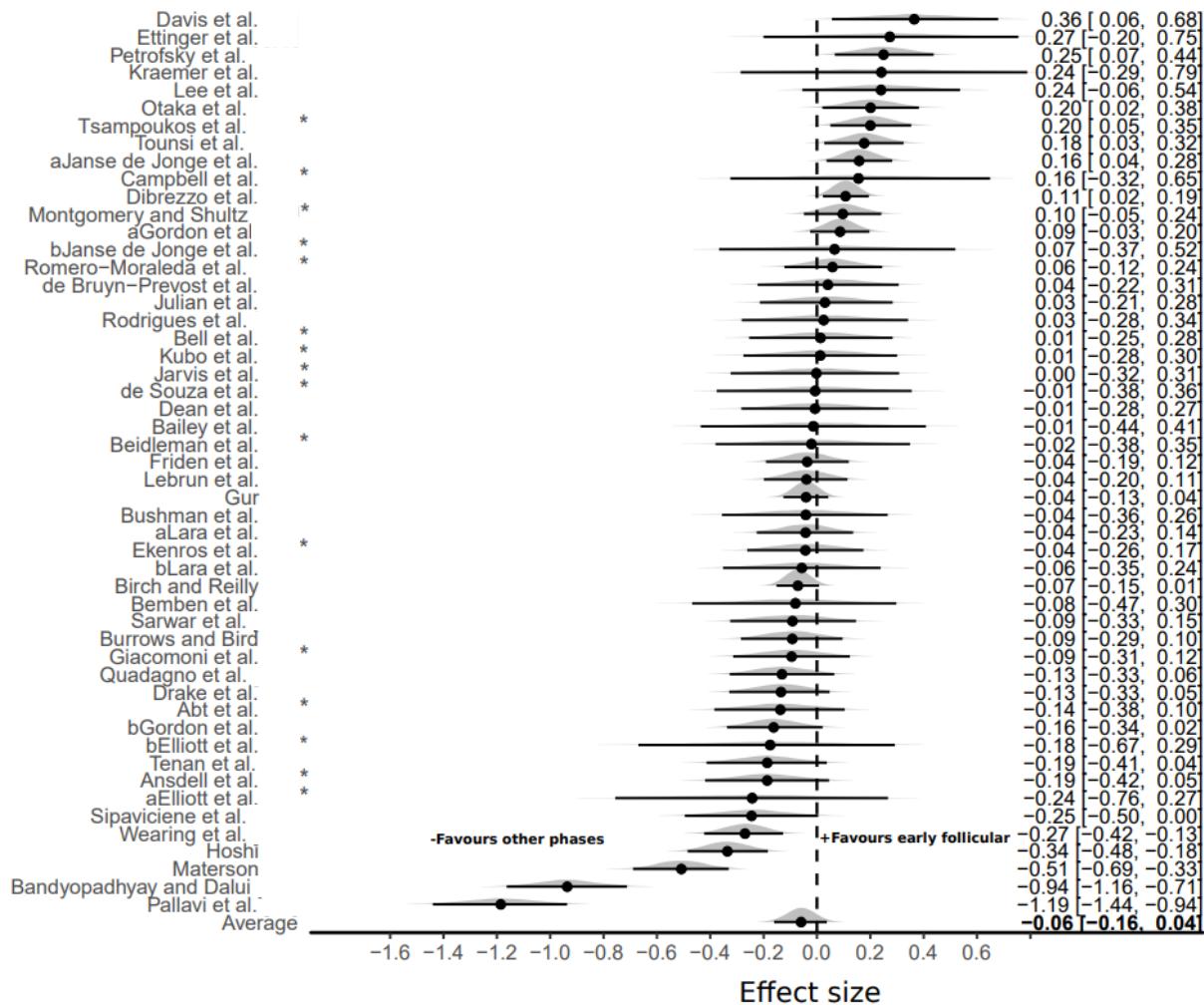


Figure 3-4 Bayesian Forest Plot of multilevel meta-analysis comparing exercise performance measured during the early follicular phase with all other menstrual cycle phases. The study-specific intervals represent individual effect size estimates and sampling error. The circle represents the pooled estimate generated with Bayesian inference along with the 95% credible interval. Negative values favour all other menstrual cycle phases (late follicular, ovulation,

early luteal, mid-luteal, and late luteal) compared to the early follicular phase. “High” and “moderate” quality studies are indicated with an asterisk (*).

A sensitivity analysis was completed with data obtained from studies classified as either “high” or “moderate” in quality. Sixteen studies compromising 38 strength effect sizes and 12 endurance effect sizes from 169 participants (Abt *et al.*, 2007; Ansdell *et al.*, 2019; Beidleman *et al.*, 1999; Bell *et al.*, 2011; Campbell *et al.*, 2001; de Souza *et al.*, 1990; Ekenros *et al.*, 2013; Elliott *et al.*, 2005; Elliott *et al.*, 2003; Giacomoni *et al.*, 2000; Jarvis *et al.*, 2011; Kubo *et al.*, 2009; Montgomery & Shultz, 2010; Romero-Moraleda *et al.*, 2019; Thompson *et al.*, 2012; Tsampoukos *et al.*, 2010) were included in the sensitivity analysis. Compared to the primary analysis, the reduced data set resulted in a relatively symmetric credible interval around the zero value ($ES_{0.5} = -0.01$ [95% CrI: -0.11 to 0.08]).

3.3.4.2 Analysis 2: Network meta-analysis

Figure 3.5 shows a network diagram illustrating the pairwise effect sizes calculated across the six MC phases (early follicular, late follicular, ovulation, early luteal, mid-luteal, and late luteal). Seventy-three studies (mode quality rating = “low”; 7% “high”; 26% “moderate”; 42% “low”; 25% “very low”) included enough data to be included in the network-meta-analysis (Abt *et al.*, 2007; Ansdell *et al.*, 2019; Bailey *et al.*, 2000; Bambaeichi *et al.*, 2004; Bandyopadhyay & Dalui, 2012; Beidleman *et al.*, 1999; Bell *et al.*, 2011; Bemben *et al.*, 1995; Birch & Reilly, 1999; Birch & Reilly, 2002; Burrows & Bird, 2005; Bushman *et al.*, 2006; Campbell *et al.*, 2001; Casazza *et al.*, 2002; Davies *et al.*, 1991; De Bruyn-Prevost *et al.*, 1984; de Souza *et al.*, 1990; Dean *et al.*, 2003; Dibrezzo *et al.*, 1988; Dombovy *et al.*, 1987a; Dombovy *et al.*, 1987b; Drake *et al.*, 2003; Ekenros *et al.*, 2013; Elliott *et al.*, 2005; Elliott *et al.*, 2003; Ettinger *et al.*, 1998; Fridén *et al.*, 2003; Giacomoni *et al.*, 2000; Gordon *et al.*, 2013; Gordon *et al.*, 2018; Grucza *et al.*, 2002; Grucza *et al.*, 1993; Gür, 1997; Hertel *et al.*, 2006; Hoeger Bement *et al.*, 2009; Hoshi, 1997; Jarvis *et al.*, 2011; Julian *et al.*, 2017; Jurkowski *et al.*, 1981; Kaygisiz *et al.*, 2003; Kraemer *et al.*, 2006; Kubo *et al.*, 2009; Lara, Gutiérrez-Hellín, *et al.*, 2020; Lara, Gutiérrez Hellín, *et al.*, 2020; Lebrun *et al.*, 1995; Lee *et al.*, 2014; Lynch & Nimmo, 1998; Masterson, 1999; Mattu *et al.*, 2020; McCracken *et al.*, 1994; McLay *et al.*, 2007; Montgomery & Shultz, 2010; Okudan *et al.*, 2005; Otaka *et al.*, 2018; Pallavi *et al.*, 2017; Petrofsky *et al.*, 2007; Quadagno *et al.*, 1991; Redman *et al.*, 2003; Rodrigues *et al.*, 2019; Romero-Moraleda *et al.*, 2019; Sarwar *et al.*, 1996; Shaharudin *et al.*, 2011; Sipavičienė *et al.*, 2013; Smekal *et al.*, 2007; Sunderland & Nevill, 2003; Sunderland *et al.*, 2011; Takase

et al., 2002; Tenan *et al.*, 2016; Thompson *et al.*, 2012; Tounsi *et al.*, 2017; Tsampoukos *et al.*, 2010; Vaiksaar *et al.*, 2011a; Wearing *et al.*, 1972; Wiecek *et al.*, 2016).

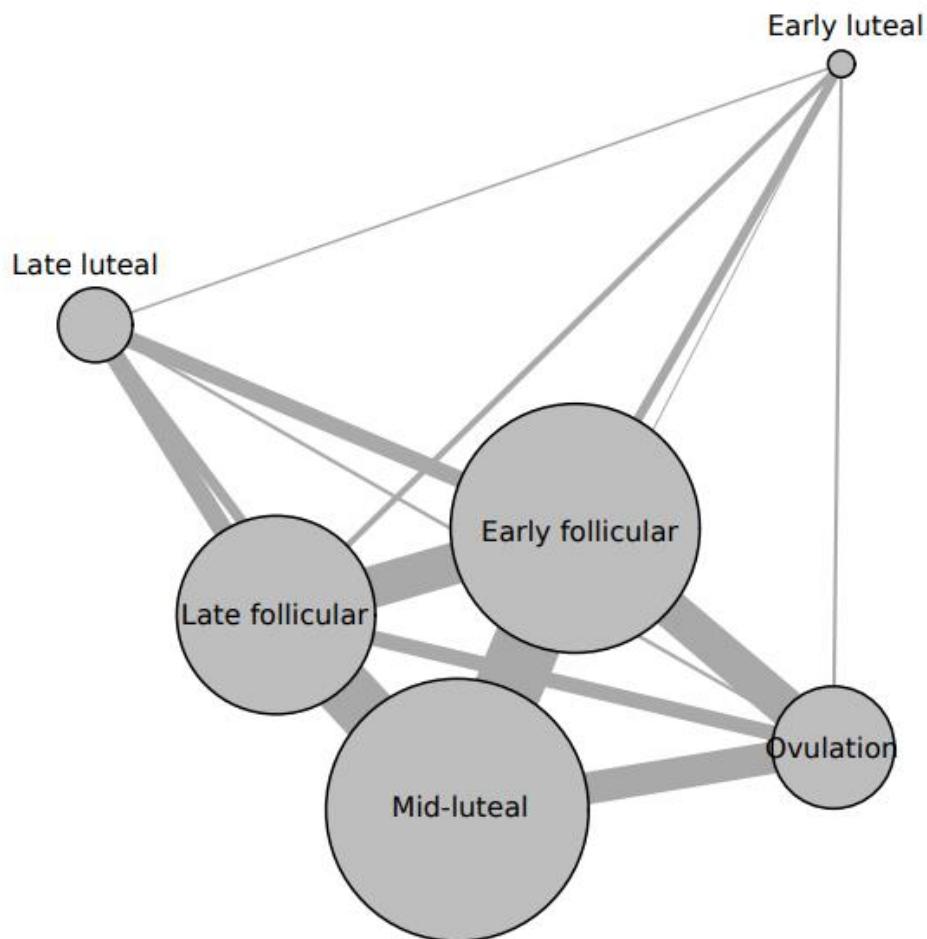


Figure 3-5 Network diagram illustrating the pairwise effect sizes calculated across the six menstrual cycle phases (early follicular, late follicular, ovulation, early luteal, mid-luteal, and late luteal). The analysis included direct and indirect pairwise effect sizes from 73 studies. The relative size of nodes and relative thickness of connecting lines illustrate the frequency of outcomes measured in each menstrual cycle phase and the number of direct comparisons between two phases, respectively.

A total of 220 performance outcomes were included across 954 participants, with the number of comparisons across MC phases equal to: comparison between two phases = 87; comparison between three phases = 93; comparison between four phases = 27; comparison between five phases = 10; and comparison between six phases = 3. The most frequent comparisons made

were between the early follicular and mid-luteal phase of the MC (21% of comparisons), followed by the late follicular and mid-luteal phases of the MC (18% of comparisons). Pairwise estimates including the early follicular phase as a reference are presented in Table 3.1, with negative median pooled effect sizes ('other MC phases') obtained for all comparisons and the largest effect identified between the early follicular and the late follicular phase of the MC ($ES_{0.5} = -0.14$ [95% CrI: -0.26 to -0.03]). The lowest SUCRA value was obtained for the early follicular phase (30%) with all other MC phase values ranging between 53 and 55%.

Table 3-2 Summary of network meta-analysis results from 73 studies using the early follicular phase as a reference.

Comparison to early follicular phase	Effect size [95% CrI]	SUCRA (%)
Early follicular	—	30
Late follicular	-0.14 [-0.26 to -0.03]	54
Ovulation	-0.07 [-0.15 to 0.07]	55
Early luteal	-0.07 [-0.19 to 0.16]	54
Mid-luteal	-0.04 [-0.11 to 0.08]	55
Late luteal	-0.01 [-0.18 to 0.17]	53

CrI, credible intervals; SUCRA, the surface under the cumulative ranking curve. Negative values for effect sizes favour all other menstrual cycle phases (late follicular, ovulation, early luteal, mid-luteal, and late luteal) compared to the early follicular phase.

3.4 Discussion

The purpose of this Chapter was to examine if MC phase affects exercise performance in naturally menstruating women. The results indicate that on average, exercise performance might be trivially reduced during the early follicular phase of the MC, when compared with all other MC phases. Performance was consistent between all other MC phases. In addition to the estimated trivial average effect, results from the meta-analysis models showed relatively large between-study variance indicating that research design, participant characteristics, and type of performance measured might influence any effect. Furthermore, most studies included in this meta-analysis were classified as "low" in quality, and as such, the confidence in the evidence reported in this meta-analysis is also low and should be interpreted with caution. Due to the trivial effect size, the large between-study variation, and the number of poor-quality studies

included in this review, general guidelines on exercise performance across the MC cannot be formed; rather, it is recommended that a personalised approach should be taken based on each individuals' response to exercise performance across their MC.

There are a range of suggested mechanisms by which the lower levels of oestrogen and progesterone in the early follicular phase of the MC might negatively affect exercise performance. Although a detailed mechanistic review is beyond the scope of this Chapter, the following points can be noted. Firstly, oestrogen is known for its anabolic effects (Alexander *et al.*, 2021; Chidi-Ogbolu & Baar, 2019; Lowe *et al.*, 2010b), as well as its role in regulating substrate metabolism through increasing glycogen uptake and sparing glycogen stores (Boisseau & Isacco, 2022; Hackney, 2021). Additionally, oestrogen is thought to have neuroexcitatory effects, whereby it reduces inhibition and increases voluntary activation (Ans dell *et al.*, 2019). Therefore, when oestrogen rises during the late follicular and ovulatory phases and remains elevated in the mid-luteal phase it is plausible that this might positively affect muscular performance or maximal and submaximal intensity exercise performance. Moreover, progesterone is thought to have anti-oestrogenic effects (Frankovich & Lebrun, 2000), therefore it could be speculated that the beneficial performance effects of oestrogen are likely to be greater in the late follicular and ovulatory phases when oestrogen is high without the interference of progesterone, compared to the mid-luteal phase when *both* oestrogen and progesterone are high. This speculation is supported by the finding presented here, that the biggest difference in exercise performance was reported between the early follicular and late follicular phases of the MC. However, the average effect calculated was trivial and there was considerable overlap between each of the pairwise comparisons with the early follicular phase. Whilst the current meta-analysis cannot identify the mechanisms responsible, it does indicate that, on average, exercise performance might be reduced by a trivial amount in the early follicular phase of the MC compared with all other phases. Interestingly, in a recent systematic review and meta-analysis by Elliott-Sale *et al.* (2020) which investigated the effects of OCP use on exercise performance, the available evidence indicated that compared with naturally menstruating women, OCP users have on average slightly inferior exercise performance (see *Chapter 4*). Oral contraceptive use results in significantly downregulated concentrations of endogenous sex hormones when compared with the ovulatory and mid-luteal phases of the MC (Elliott *et al.*, 2005). Indeed, the endogenous sex hormone profile of OCP users is comparable to the profile seen during the early follicular phase of the MC (Elliott *et al.*, 2005). Thus, both Chapters show slightly impaired, group level, exercise performance when *both* oestrogen and

progesterone are at their lowest, collectively suggesting that exercise performance might be mediated by the concentration of endogenous sex hormones in some sportswomen.

Within the literature to date, the most common comparison used when investigating the effects of the MC on performance was between the early follicular and mid-luteal phase. This is not surprising, as the difference in the reproductive hormonal milieu is typically at its greatest between these phases (early follicular: when *both* oestrogen and progesterone are low; and mid-luteal: when *both* oestrogen and progesterone are high; [Thompson & Han, 2019]). As such, if performance was altered by synergistic fluctuations in oestrogen and progesterone levels, the comparison between these two phases would maximise the chance of observing an effect. This bi-phasic comparison, however, ignores the late follicular/ovulatory phases of the MC, when oestrogen concentrations are high/ moderate, respectively, and progesterone is low. Indeed, the network analysis indicated that the largest difference in performance might be expected between the early follicular and the late follicular phases of the MC, when *both* oestrogen and progesterone are low and when oestrogen rises without a concurrent increase in progesterone. Therefore, the effects of oestrogen, without the interference of progesterone, might be overlooked if the late follicular or ovulatory phases are not included within the phase comparisons. Future studies should therefore consider multiple phase comparisons so that the effects of different ratios of oestrogen and progesterone can be explored. It should be noted that the inclusion of multiple phase comparisons will result in more variability, and as such, more participants will be needed to conclude any potential effects.

This systematic review included 78 studies and 1,193 women (range n = 5 to 100), yet very few studies were classified as “moderate” or “high” in quality, which implies that the confidence in the evidence used in this meta-analysis should be low. Specifically, only 24% of studies were allocated a quality rating of “moderate”, and only 8% of studies were allocated a quality rating of “high”. Our quality assessment approach included consideration of the methods used to identify and verify the MC phase in the included studies, which is key to the trustworthiness of the results obtained (*i.e.*, Q1. was the MC phase identified using urinary ovulation detection kits?; and Q2. was the MC phase verified using blood samples?). Across the included studies there was large variability in the methods used to identify and then verify MC phase, namely calendar-based counting, BBT, MC history questionnaires, urinary ovulation detection kits, and salivary, urinary, and serum measurement of both oestrogen and progesterone. Calendar-based counting is an indirect method to identify MC phase, whereby the self-reported onset of menses is set as day one, and the phases are then established by

counting days from this point (Thompson & Han, 2019). However, this method assumes that all participants with regular menstruation experience ovulatory cycles with a mid-cycle peak in oestrogen, which is not always the case (Schaumberg *et al.*, 2017; Sherman & Korenman, 1975). As such, the use of calendar-based counting methods in isolation is not recommended when accurate identification of MC phase is required (Wideman *et al.*, 2013). Similarly, BBT is a widely used method for identifying ovulation, and the length of the follicular and luteal phases (Thompson & Han, 2019), but this method does not provide information regarding actual sex hormone concentrations (Bauman, 1981), and temperature readings might also be influenced by a range of factors such as illness, stress, sleep patterns, and medication (Barron & Fehring, 2005). Hence, BBT in isolation is not considered a reliable method for MC phase verification (Thompson & Han, 2019). Studies using these methods were downgraded on this basis. Indeed, very few studies used a combination of the recommended methods by Thompson and Han (2019) which include the use of the calendar-based counting method in conjunction with urinary ovulation detection kits, to assist in setting the timing of testing throughout the MC and to confirm the presence of an ovulatory cycle, followed by serum measurement of both oestrogen and progesterone to subsequently verify the phases of the MC. Given that the rationale for exploring the effect of the MC on exercise performance is underpinned by changes in oestrogen and progesterone, it is essential that studies should accurately verify the changes in endogenous sex hormones during each phase of the MC to ensure that the intended phase is being examined. Overall, without verification it is unclear which sex hormone milieu is being investigated, thus making it difficult to draw accurate conclusions regarding changes in exercise performance across the MC and to make direct comparisons between studies. These recommendations echo recent publications (Elliott-Sale *et al.*, 2021; Thompson & Han, 2019), demonstrating an increasing awareness of the nuances of this type of research, and collectively providing researchers with ample tools to make methodological decisions for future investigations.

To limit the influence of poor-quality papers on the analyses, a sensitivity analysis was conducted with data obtained from studies that were classified as either “moderate” or “high” in quality (Abt *et al.*, 2007; Ansdell *et al.*, 2019; Beidleman *et al.*, 1999; Bell *et al.*, 2011; Campbell *et al.*, 2001; de Souza *et al.*, 1990; Ekenros *et al.*, 2013; Elliott *et al.*, 2005; Elliott *et al.*, 2003; Giacomoni *et al.*, 2000; Jarvis *et al.*, 2011; Kubo *et al.*, 2009; Montgomery & Shultz, 2010; Romero-Moraleda *et al.*, 2019; Thompson *et al.*, 2012; Tsampoukos *et al.*, 2010). Due to the limited amount of data available, only the pairwise meta-analysis comparing exercise

performance during the early follicular phase of the MC, with all other MC phases was conducted. The sensitivity analysis provided no evidence of any effect, with a relatively symmetric credible interval centred close to zero. Whilst studies that were allocated a higher quality rating were better able to identify and verify the MC phase, there was no association between study quality and average sample size. Given the reduced amount of data included within the sensitivity analysis and the low sample sizes, the result is consistent with the primary analyses and conclusion that if an average effect exists, it is likely to be trivial in magnitude.

The results from the meta-analysis models consistently showed large between-study variance, which might be attributable to several factors: 1) inconsistent research design, as shown by the network analysis that highlights the discrepancy in the number of phase comparisons made between studies; 2) poor methodological practices, as emphasised by the quality assessment, whereby the majority of studies included in the meta-analysis were classified as “low” (42%) in quality primarily due to inadequate MC phase identification and verification; 3) non-homogenous participant groups, as shown in *Appendix E* participants in this meta-analysis ranged from sedentary, to healthy, to physically active, to well-trained individuals; and 4) large variation in the type of exercise performance outcome measured, as detailed in *Appendix B*. As such, the breadth of this research area, without the corresponding depth, makes it difficult to apply a meaningful, yet generalisable, interpretation of the current data.

3.5 Conclusion

This is the first systematic review with meta-analysis to examine the effect of MC phase on exercise performance in naturally menstruating women. These data provide new information that exercise performance might on average be reduced by a trivial amount during the early follicular phase of the MC, compared with all other MC phases. The current meta-analysis also identified large between study variance in the effect of the MC on exercise performance. This might have been influenced by a range of methodological factors and small participant numbers, as well as associated high sampling variance. Participant characteristics, such as training history, might also have contributed to the large between-study variance observed. From a practical perspective, as the effects tended to be trivial and variable between studies, the implications of these findings are likely to be so small as to be meaningless for most sportswomen. These trivial effects might, however, be of greater relevance to elite woman

athletes, where the difference between winning and losing is marginal. Specifically, we recommend that practitioners working with sportswomen need to consider the MC and be aware of the potential times across the cycle whereby exercise performance might be reduced (early follicular phase) or enhanced (all other MC phases), but this approach should be tailored to, and informed by, the individual. In the future, it would be interesting to identify which factors might cause some women to experience reduced exercise performance during the early follicular phase of the MC, when compared with all other MC phases and identify strategies to monitor these effects. For example, one plausible reason for the reduction in exercise performance within this Chapter could be the impact of cycle related symptoms and their perceived effects. Specifically, it appears that both physical and psychological cycle related symptoms are common in sportswomen and might be associated with changes in various aspects of exercise performance and training (Bruinvels *et al.*, 2021). Therefore, *Chapters 5* and *6* will consider not only the reproductive hormonal milieu, but also the symptoms experienced and their perceived effects to facilitate a deeper understanding of the MC on exercise performance in sportswomen.

CHAPTER 4 – THE EFFECTS OF ORAL CONTRACEPTIVES ON EXERCISE PERFORMANCE IN WOMEN: A SYSTEMATIC REVIEW AND META-ANALYSIS

This Chapter has been published previously in:

Elliott-Sale, K.J.*., McNulty, K.L.*., Ansdell, P., Goodall, S., Hicks, K.M., Thomas, K., Swinton, P.A., & Dolan, E. (2020). The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. *Sports Medicine*, 1-28.

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Author contributions: KES, KLM, PA, SG, KMH, and KT designed the research question. KES conducted the searches and screening and KLM and KMH completed the three-phase screening process. ED extracted the data, with critical input from KLM, which were verified by KES and KMH. PAS performed the statistical analysis. PS, KES, KLM, and ED interpreted the data analysis. KES and KLM wrote the manuscript with critical input from ED, KMH, PA, SG and KT. All authors read and approved the final manuscript.

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Elliott-Sale, K.J., McNulty, K.L., Ansdell, P., Goodall, S., Hicks, K.M., Thomas, K., Swinton, P.A., & Dolan, E. (2020). The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. 15-minute oral presentation at: Future Physiology Conference; 19th – 22nd April 2021; Virtual event.

Elliott-Sale, K.J., McNulty, K.L., Ansdell, P., Goodall, S., Hicks, K.M., Thomas, K., Swinton, P.A., & Dolan, E. (2020). The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis. 15-minute oral presentation at: Women in Sport and Exercise Academic Network (WiSEAN) Conference; 19th – 22nd April 2021; Virtual event.

4.1 Introduction to Chapter 4

As demonstrated in *Chapter 3*, MC phase can affect exercise performance, whereby performance might be reduced by a trivial amount during the early follicular phase. However, it is important to acknowledge that the MC is susceptible to internal (*e.g.*, amenorrhea and oligomenorrhea) and external (*e.g.*, HCs) perturbations, highlighting the diversity in sex hormone profiles between women (Elliott-Sale *et al.*, 2021). For example, a study by Martin *et al.* (2018), showed that out of 430 elite UK-based sportswomen, 213 were HC users, meaning that almost half of the population surveyed did not have a natural MC. Of these 213 HC users, 145 (68%) reported taking an OCP, making them the most common type of HC used and the second most common reproductive hormonal profile, after naturally menstruating women. Therefore, whilst it is essential to understand the effect of the MC on exercise performance, to be able to support the other half of sportswomen, the effects of HCs (namely the OCP) need to be considered. These differences in sex hormone profiles between naturally menstruating women and OCP users, and across the OCP *cycle* will be considered within this Chapter.

Oral contraceptive pills alter the MC by changing a women's internal hormonal milieu, to reduce the risk of unplanned pregnancy (Elliott-Sale & Hicks, 2018). As described in *Chapter 2 Section 2.3.6*, most OCPs are _mOCPs which contain exogenous hormones delivered in a fixed amount every day for 21 pill-taking days (*i.e.*, consumption phase) followed by seven pill-free days (*i.e.*, withdrawal phase; [Elliott-Sale & Hicks, 2018]). In brief, _mOCP use results in four distinct hormonal environments: 1) a downregulated endogenous oestradiol profile for 21 days that rises during the seven pill-free days; 2) a chronically downregulated endogenous progesterone profile; 3) a daily surge of synthetic oestrogen and progestin that peaks within one hour after ingestion, with baseline values accumulating slightly over the 21 pill-taking days; and 4) seven exogenous hormone free days (Rechichi *et al.*, 2009). These profiles, reflecting pill consumption and withdrawal, are referred to as pseudo-phases, as they are 'artificial' phases in comparison with the phases of the MC, and might impact differently on exercise performance compared to naturally menstruating women and across the OCP *cycle*.

Despite the prevalence of OCP use in sportswomen (Martin *et al.*, 2018), the effects of OCPs on exercise performance remain poorly understood. Although many experimental studies (see *Chapter 2, Section 2.4*), numerous narrative and systematic reviews (Burrows & Peters, 2007; Constantini *et al.*, 2005; Lebrun *et al.*, 2013; Rechichi *et al.*, 2009), and books (Forsyth & Roberts, 2018; Hackney, 2016) have addressed this topic, few in the area of sport and exercise

science (*e.g.*, sportswomen, coaches, practitioners, or researchers) truly understand the implications of OCP use on exercise performance. Indeed, as described in *Chapter 2, Section 3*, previous research has shown conflicting findings on the directional effects of OCPs on outcomes such as, muscle function (Rechichi & Dawson, 2009; Sarwar *et al.*, 1996), aerobic and anaerobic (Bryner *et al.*, 1996; Casazza *et al.*, 2002; Giacomoni *et al.*, 2000) capacity, as well as performance-based tests (Lebrun *et al.*, 2003; Rechichi & Dawson, 2012). As such, at present, there are no evidence-based guidelines for managing exercise performance in OCP users. Further, the perceived low quality of the current literature limits the ability to adopt an evidence-based approach when working with sportswomen. Accordingly, the purpose of this Chapter was to investigate the effects of OCP use on exercise performance in women by: 1) making a between group comparison of OCP users and naturally menstruating women; and 2) a within group comparison of OCP consumption and withdrawal. To our knowledge, this is the first systematic review with meta-analysis on the effects of OCPs on exercise performance. Additionally, this Chapter will appraise the quality of previous studies, for the first time, using robust assurance tools. The information provided by this Chapter can be used to inform practical recommendations for sportswomen, practitioners, and researchers interested in managing exercise performance in OCP users.

4.2 Method

This review conforms to the PRISMA statement guidelines (*Appendix F*; [Moher *et al.*, 2009]).

4.2.1 Study inclusion and exclusion criteria

As in *Chapter 3*, consideration of PICOS was used to determine the parameters within which this review was conducted.

4.2.1.1 Population

Participants included healthy women who were between the ages of 18 and 40 years. No restrictions were placed on activity level or training status.

4.2.1.2 Intervention

All participants were required to take an OCP, either habitually or experimentally. ‘Habitual’ was defined as OCP use prior to the commencement of the study and not for the purposes of the study. ‘Experimentally’ was defined as starting OCP use for the purposes of the study. All forms of combined OCPs were considered.

4.2.1.3 Comparator

Four broad types of comparisons were considered: 1) between group comparison of habitual OCP users to naturally menstruating women. Women were phase matched in two ways for this comparison: 1_a) OCP withdrawal versus the early follicular phase of the MC and 1_b) OCP consumption versus all other phases of the MC except for the early follicular phase; 2) within group comparison of OCP consumption phase with the OCP withdrawal phase; 3) comparison of active OCP use with non-use (*e.g.*, within-group comparison of women who were habitual users or naturally menstruating women who stopped and/or started taking the OCP for the purpose of the study); and 4) randomised control trials of OCPs versus placebo intake (*e.g.*, between group comparison of naturally menstruating women who were randomly assigned to either an OCP or placebo pill).

4.2.1.4 Outcomes

The primary outcome was exercise test performance, based on the comparisons described above. Exercise performance was defined as in *Chapter 3*, including total work done, time to completion, time to exhaustion, mean, peak and ratio outputs, rate of force production and decline, and indices of fatigue, as well as $VO_{2\max}$ or peak $VO_{2\text{peak}}$. All exercise outcomes were extracted, and effect size duplication of multiple outcomes from the same test accounted for within the statistical analysis, as described below.

4.2.1.5 Study design

Experimental studies were considered for analysis if they were: 1) published, in full, in a peer-reviewed journal; and 2) had the primary or secondary objective of assessing changes in exercise performance. As such, case studies, review articles, study protocol papers, and conference abstracts were excluded. As in *Chapter 3*, only full texts that were published in English or had an existing translation were retrieved and examined, and there was no limit on the date of publication.

4.2.2 Search strategy for identification of studies

A systematic electronic literature search was conducted to identify all relevant articles using the same online databases as described in *Chapter 3*. The searches were performed using medical subject headings terms, free-text, and thesaurus terms, as well as keywords from existing relevant papers (Burrows & Peters, 2007; Rechichi *et al.*, 2009). The following search terms and their combinations were used: ('oral contraceptives') AND ('athletic performance', OR 'sports performance', OR 'muscle', OR 'skeletal muscle', OR 'strength', OR 'force', OR 'muscular strength', OR 'muscular force', OR 'power', OR 'anaerobic', OR 'anaerobic power', OR 'anaerobic performance', OR 'anaerobic capacity', OR 'aerobic', OR 'aerobic capacity', OR 'aerobic power', OR 'aerobic performance', OR 'endurance', OR 'endurance capacity', OR 'endurance power', OR 'endurance performance', OR 'fatigue', OR 'recovery'). Searches were limited to humans, English, and females. An example of a full electronic search, including limits, for one database (PubMed: 09/01/2019) is presented in *Appendix G*. Databases were searched from inception until April 2020. The reference lists of obtained relevant articles and review articles were hand-searched to identify any further studies and were added in manually. Following the same search criteria and strategy, an updated electronic and manual hand-search for relevant literature was subsequently conducted in July 2022 to identify any further articles published between April 2020 and July 2022. As in *Chapter 3*, articles found during the updated literature search are not included in the final analysis, but relevant details are displayed in Table 4.1.

Table 4-1 Overview of the studies found during the updated electronic and manual hand-search for relevant literature that could be included in the present Chapter based on inclusion/exclusion criteria.

Author (date)	Aim	Population	Oral	Naturally	Outcome	Study	Quality
		(participant	contraceptive	menstruating	measure(s)	conclusion	rating
		health,	pill type	group			
		training		description			
		status and					
		sample size)					
Barba-Moreno <i>et al.</i> (2022)	To investigate the effects of OCPs on cardiorespiratory responses during steady-state exercise	Healthy endurance- trained women (n = 23 [15 naturally menstruating women and 8 OCP users])	^m OCPs (Loette diario, Donabel, Drosure, Drosurelle, Yasmin, STADA Genericos, Gestinyl)	Women with regular MCs (24 to 35 days in length) for last year, tested at the EF, LF, and ML phases, verified using MC history, counting of days, and serum	$\dot{V}O_{2\max}$ (ml.min) $\dot{V}O_{2\max}$ across the OCP 'cycle'. No differences in $\dot{V}O_{2\max}$ between OCP users and naturally menstruating women	No changes in $\dot{V}O_{2\max}$ across the OCP 'cycle'. No differences in $\dot{V}O_{2\max}$ between OCP users and naturally menstruating women	Moderate

					oestrogen and progesterone		
Dalgaard <i>et al.</i> (2020)	To determine effects of using second generation OCPs on muscle adaptations to resistance training	Young, untrained women (n = 38 [18 menstruating women and 20 OCP users])	Second generation OCPs (30–35 µg ethinyl estradiol). Pill types included Femicept, Malonetta, Microgyn, Anastrella, and Cilest	Women who experienced a regular MC (menses every 24–35 days) at last 3 months, verified using serum oestrogen and progesterone	Maximal isometric muscle strength (N·m) 5 repetition maximum leg press strength (kg) CMJ height (cm) Average power using a modified Wingate test (W)	No differences between groups at baseline for any variable	Moderate
Nakamura and Nose-Ogura (2021)	To examine the effects of administration of _m OCPs on body composition and aerobic and	Women athletes (n = 10)	_m OCP (Lunabell)	Had not taken any OCPs for at least 1 year before testing, tested at EF and ML phases, verified using	Aerobic parameters (<i>i.e.</i> , $\dot{V}\text{O}_{2\text{max}}$ [L/min] and TTE [minutes]) Anaerobic parameters (<i>i.e.</i> , peak power output	Administration of _m OCPs did not affect aerobic and anaerobic capacities. There was no difference in	Moderate

	anaerobic capacities		serum oestrogen and progesterone	and average power output decline from a Wingate Test (W)	aerobic and anaerobic capacities across the OCP 'cycle'.		
Rael <i>et al.</i> (2021)	To assess the influence of different hormonal profiles on the cardiorespiratory response to exercise	85 endurance trained women (47 naturally menstruating and 38 OCP users)	Low dose ^m OCPs (Yasmin, Diane, Loette, Sibilla, Ceciliana, Linelle, Levobel, Melodene, Edelsin, Drosbellefex, Stada, and Drosure)	Naturally menstruating women (cycles of 24–35 days in length), tested in the EF phase, verified using serum oestrogen and progesterone	Maximal aerobic test ($\dot{V}O_{2\max}$ [ml/kg/min])	No differences between groups were observed	Moderate
Romero-Parra <i>et al.</i> (2021)	To evaluate the influence of the active pill phase versus	Resistance-trained women (n = 18)	^m OCPs	N/A	CMJ height (cm)	No difference in CMJ height across the OCP 'cycle'.	High

withdrawal
 phase of a _mOCP
 ‘cycle’ on
 exercise-induced
 muscle damage
 and
 inflammation
 after eccentric
 resistance
 exercise

Schaumberg <i>et al.</i> (2020)	To investigate the influence of OCP use on changes in time- to-fatigue, pulmonary oxygen uptake, cardiac output, and heart rate on-kinetics, as well as tissue	Healthy, recreationally active women (n = 47 [22 naturally menstruating women and 25 OCP users])	Low dose _m OCP	Naturally menstruating women who had ovulatory, regular MCs, tested in the ML phase, as verified using serum oestrogen and progesterone	Time to fatigue (seconds)	No difference in time to fatigue between groups	Moderate
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saturation index
to four-weeks of
sprint interval
training

Sung <i>et al.</i> (2022)	To investigate the effects of OCP use on muscle strength, muscle thickness, and fibre size and composition in young women undergoing 12 weeks of strength training	Healthy young women (n = 74 [40 naturally menstruating women and 34 OCP users])	Second- generation _m OCPs with ethinyl estradiol doses between 20 and 30 µg; Anastrella, Cilest, Femicept, Loette, and Microstad	Women who had regular MCs (28.3 ± 1.2 days in length), tested in the EF phase, verified using BBT	Muscle strength (maximum isometric force [kg])	Muscle strength at baseline was greater in OCP users compared with naturally menstruating women	Low
Thompson <i>et al.</i> (2021)	To investigate the potential effect of the MC and _m OCP	30 active women (12 naturally menstruating	_m OCPs (10 taking a _m OCP with high androgenicity,	Naturally menstruating women who had a regular	CMJ performance (<i>i.e.</i> , average power [W/kg],	Most variables showed no changes over the OCP	Moderate

'cycle' on and 18 OCP and 8 taking an MC (21 to 35 and flight time 'cycle'.
various aspects users) ^mOCP with low days), tested [ms]) However, for
of muscle androgenicity) during the EF, Bilateral hop the high-
performance LF, and ML jump performance androgenicity
verified using phases, (i.e., contact time OCP group,
counting of [ms], flight time isokinetic knee
days, urinary [ms], and average flexion was
ovulation power [W/kg]) higher in the
detection test, Handgrip strength late hormone
and serum Isometric knee compared with
oestrogen and extensor strength the early
progesterone (Nm) hormone
Isokinetic knee phase. For the
flexion and low-
extension 60° and androgenicity
240° s⁻¹ OCP group,
time of flight for the CMJs
was lower in
the late

Weidauer <i>et al.</i> (2020)	To determine changes in neuromuscular performance throughout the MC	50 physically active college women (25 naturally menstruating and 25 OCP users)	^m OCPs	Naturally menstruating women who had a regular (every 21-35 days) MC, tested in the EF, ovulation, and ML phases, verified by counting of days, urinary ovulation detection test, and serum	Isokinetic peak torque at the knee at 60°, 180° and 240° s ⁻¹ (Nm)	Handgrip strength (kg)	There were no differences between groups for any variable	Low

oestrogen and
progesterone

BBT, basal body temperature; CMJ, countermovement jump; EF, early follicular; LF, late follicular; MC, menstrual cycle; ML, mid-luteal; OCP, oral contraceptive pill; _mOCP, combined monophasic oral contraceptive pill; TTE, time to exhaustion; $\dot{V}O_{2\max}$, maximal oxygen uptake.

4.2.3 Data selection, extraction, and study quality assessment

4.2.3.1 Selection of studies

Studies were selected as in *Chapter 3*. In brief, three reviewers independently reviewed the titles, abstracts, and full-text paper of the identified articles for inclusion following a two-phase screening strategy. Phase one assessed the eligibility of the title and abstract of every manuscript and phase two assessed the full-text paper against the predetermined inclusion and exclusion criteria. Any conflicts between reviewers in the selection of studies were resolved in consensus meetings.

4.2.3.2 Data extraction and management

Data extraction was completed as in *Chapter 3*, whereby one reviewer extracted all relevant data into a pre-piloted data extraction form which was independently verified by two members of the review team. Any discrepancies were resolved by discussion during consensus meetings or, if needed, in consultation with a fourth reviewer. Where data was incomplete, authors were contacted to obtain the relevant information, and if no relevant data could be extracted the paper was excluded.

4.2.3.3 Quality assessment of included studies

The quality of each review outcome (defined as each of the statistical models undertaken) was assessed like *Chapter 3*. Briefly, a strategy based on the recommendations of the GRADE working group was used (Guyatt *et al.*, 2011). Each individual study was initially appraised using an appraisal tool based on the Downs and Black checklist for measuring study quality (Downs & Black, 1998) and was specifically modified for use in this Chapter (see *Appendix H*). The modified Downs and Black checklist comprised 15 outcomes, from five domains: 1) reporting; 2) external validity; 3) internal validity – bias; 4) internal validity – confounding; and 5) power. A maximum attainable score of 16 could be awarded, whereby study quality was categorised as following: “high” (14 – 16); “moderate” (10 – 13); “low” (6 – 9); or “very low” (0 - 5). The results of the Downs and Black assessment were used to assign an *a-priori* quality rating to each study. This *a-priori* rating was then either maintained, or downgraded a level, based on the response to two questions that were considered key to the *directness* of the research design: Q.1) was the natural MC phase confirmed using appropriate biochemical outcomes? and Q.2) was the type of OCP described to the level of detail required for

categorisation or replication? With regards to Q.1, for studies with OCP groups only, biochemical confirmation was not deemed necessary, as OCP users do not have cyclical fluctuations in endogenous sex hormones, in which case the *a-priori* score was maintained rather than downgraded. This rating was then either maintained, or downgraded a level based on whether the results obtained were consistent (determined by visual inspection of effect size estimates and the degree of CrI overlap); precise (with outcomes downgraded if they were based on < 5 data points) and whether publication bias was evidence (determined using Egger's test along with visual inspection of funnel plots as described below). The proportion of studies in each category was reported, with the mode considered to represent the overall quality rating for each individual review outcome.

4.2.4 Data synthesis

Data were extracted as in *Chapter 3*. In brief, pairwise effect sizes were calculated and variance of effect sizes at the study level was calculated according to standard distributional assumptions (Morris, 2008). All meta-analyses were conducted within a Bayesian framework. Three-level hierarchical models were conducted to account for covariance in multiple outcomes presented in the same study (Saunders *et al.*, 2017). Initial models were conducted including both strength and endurance outcomes with a regression coefficient assessing difference in the average effects, and where no evidence of a difference was identified, the model was rerun combining both categories of outcomes. Given the expectation of relatively small effect sizes, an *a priori* threshold of ± 2 was identified for outliers. Primary analyses were completed with outliers removed, but results were also presented from the full complement of studies as sensitivity analyses. Additionally, sensitivity analyses were conducted on data obtained from studies categorised as "high" or "moderate" in quality. Additional sensitivity analyses were conducted by restricting the analysis to studies that included exercise performance as the primary study outcome. Assessment of publication bias using Egger's multilevel test with effect sizes regressed on inverse standard errors (Fernández-Castilla *et al.*, 2021) identified no evidence of publication bias with median absolute intercept values less than 0.1 across all analyses. Inferences from all analyses were performed on posterior samples generated by Hamiltonian Markov Chain Monte Carlo with Bayesian 95% CrIs constructed to enable probabilistic interpretations of parameter values (Kruschke & Liddell, 2018). Interpretations were based on visual inspection of the posterior sample, the median value ($ES_{0.5}$: 0.5-quantile) and 95% CrIs. Cohen (2013) standard threshold values were used to describe effect size. Analyses were

performed using the R wrapper package brms, which was interfaced with Stan to perform sampling (Bürkner, 2017). Convergence of parameter estimates was obtained for all models with Gelman-Rubin R-hat values below 1.1 (Gelman *et al.*, 1995).

4.2.5 Rationale for between group comparisons

For the between group analyses of habitual OCP users to naturally menstruating women, the OCP withdrawal phase (days 1 to 7) was compared with the early follicular phase (days 1 to 5) of the MC, and the OCP consumption phase (days 8 to 28) was compared with all phases of the MC (days 6 to 28) except the early follicular phase. The OCP withdrawal phase was compared with the early follicular phase as during the withdrawal phase OCP users experience a withdrawal bleed and during the early follicular phase of the MC women experience menstruation. In addition, during both phases endogenous concentrations of oestrogen and progesterone are comparably low. During the remainder of the MC, endogenous concentrations of oestrogen and progesterone change over time (*e.g.*, the mid-cycle peak in oestrogen and the mid-luteal rise in *both* oestrogen and progesterone) and there is large variation in endogenous concentrations of oestrogen and progesterone because of different OCP formulations. As such, it is difficult to make meaningful comparisons during these phases and this could be considered a limiting factor of any meta-analysis making between group comparisons of naturally menstruating women and OCP users. To reduce the impact of this limitation, a sensitivity analysis was completed on the between group design data to better match the natural MC and OCP pseudo-phases. This was achieved by mapping days 1 to 5, 12 to 16, and 19 to 23 from both cycles, which correspond with the early follicular, ovulatory, and mid-luteal phases in a natural MC and represents the following hormonal profiles: low oestrogen and progesterone, medium/high oestrogen and low progesterone, and high progesterone and medium oestrogen. As such, this meta-analysis: 1) compared the two most stable phases of the OCP and MC in the first between group analysis; 2) compared the two least stable phases of the OCP and MC in the second between group analysis; and 3) performed an additional sensitivity analysis to better match OCP and MC phases.

4.3 Results

4.3.1 Literature search

The literature search and selection of studies are presented in Figure 4.1.

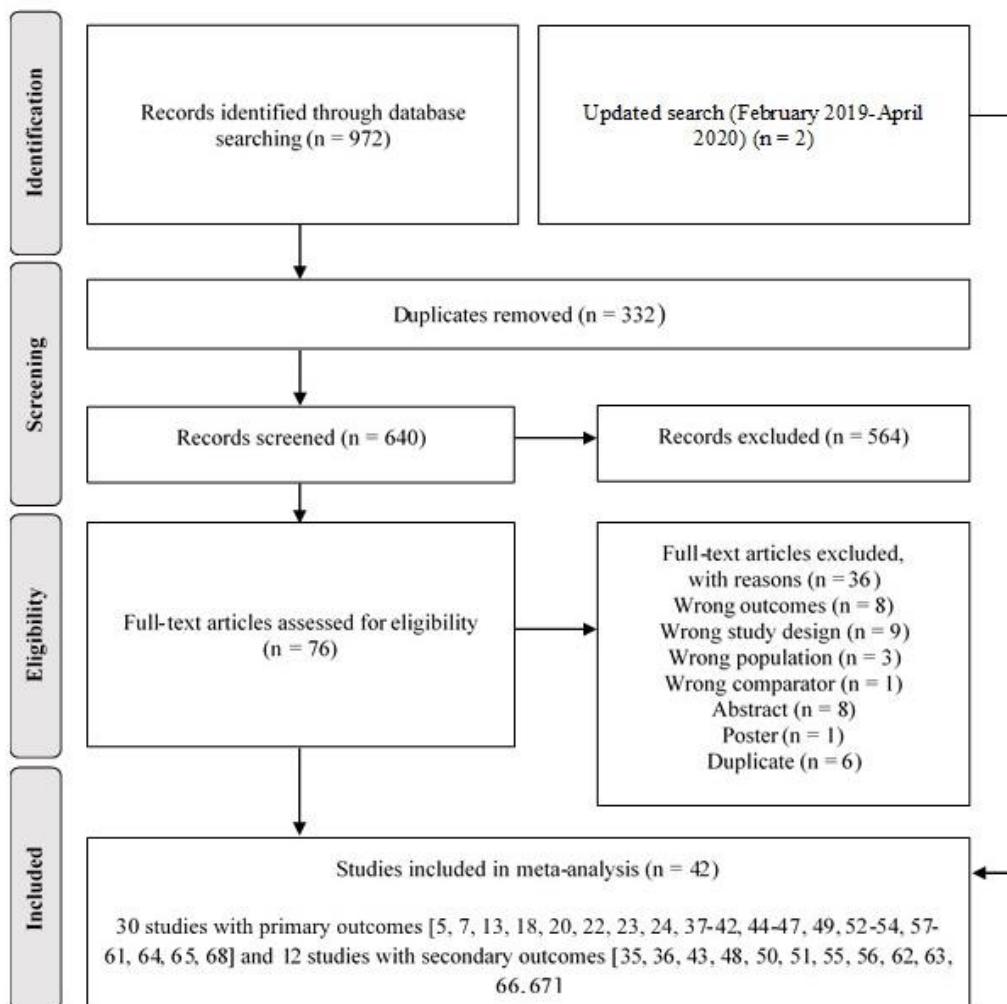


Figure 4-1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines flow chart for literature search and study selection.

4.3.2 Study characteristics

In total 42 studies (Anderson *et al.*, 2017; Armstrong *et al.*, 2005; Bell *et al.*, 2011; Bemben *et al.*, 1992; Bushman *et al.*, 2006; Casazza *et al.*, 2002; De Bruyn-Prevost *et al.*, 1984; Drake *et al.*, 2003; Ekenros *et al.*, 2013; Elliott *et al.*, 2005; Giacomoni *et al.*, 2000; Giacomoni & Falgairette, 1999; Gordon *et al.*, 2013; Gordon *et al.*, 2018; Grucza *et al.*, 2002; Grucza *et al.*,

1993; Hicks *et al.*, 2017; Isacco *et al.*, 2015; Joyce *et al.*, 2014; Lebrun *et al.*, 2003; Lee *et al.*, 2014; Lynch *et al.*, 2001; Lynch & Nimmo, 1998; Mackay *et al.*, 2019; Mattu *et al.*, 2020; Minahan *et al.*, 2015; Minahan *et al.*, 2017; Ortega-Santos *et al.*, 2018; Peters & Burrows, 2006; Quinn *et al.*, 2018; Rebelo *et al.*, 2010; Rechichi & Dawson, 2009, 2012; Rechichi *et al.*, 2008; Redman & Weatherby, 2004; Sarwar *et al.*, 1996; Schaumberg *et al.*, 2016; Sunderland *et al.*, 2011; Vaiksaar *et al.*, 2011a, 2011b; Wirth & Lohman, 1982) were included. Details of the included studies are shown in *Appendix I*.

4.3.3 Methodological quality

Methodological quality at the level of the individual study is presented in Figure 4.2. Eighty-three percent of studies were classified as “moderate”, “low”, and “very low” in quality, with 17% achieving “high” quality status. Specifically, four studies were graded as “very low”, 10 as “low”, 21 as “moderate”, and seven as “high” in quality.

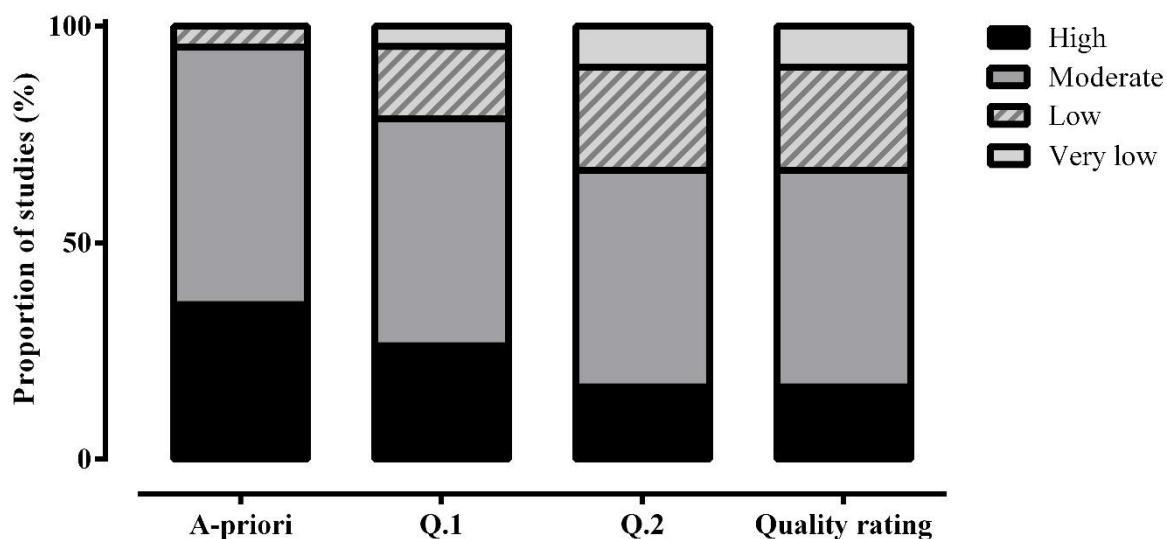


Figure 4-2 Quality rating of outcomes from all included studies (n = 42). Each bar represents the proportion of articles assigned a “high,” “moderate,” “low,” or “very low” rating. The x-axis represents the different stages of this process, with the first bar based on the assessment of risk of bias and study quality as determined by the Downs and Black checklist, while question one (Q. 1) and question two (Q. 2) were used to determine if the natural menstrual cycle phase comparison was verified using appropriate biochemical outcomes and whether the oral contraceptive pill under investigation was described in a sufficient level of detail. The final bar represents the proportion of studies assigned to each quality rating category.

4.3.4 Outcomes

4.3.4.1 Analysis 1: Between group analyses of habitual oral contraceptive users to naturally menstruating women

Thirty of the included studies (combined quality rating = “moderate”: specifically, 20% “high”; 37% “moderate”; 30% “low”; and 13% “very low”) generated 151 effects sizes from research designs comparing habitual OCP users with naturally menstruating women. The data were collected from 597 participants (habitual OCP n = 303 and naturally menstruating n = 294) with studies comprising a mean group size of 10 (range n = 5 to 25).

1a) Oral contraceptive pill withdrawal (days 1 to 7) versus the early follicular phase (days 1 to 5) of the menstrual cycle

Three outliers were identified with effect sizes greater than +2, and were removed from the analysis, leaving a total of 49 effect sizes (26 endurance and 23 strength) from 18 studies (combined quality rating = “moderate”: specifically, 17% “high”; 33% “moderate”; 28% “low”; and 22% “very low”; habitual OCP n = 176 and naturally menstruating n = 169). The three-level hierarchical model indicated a trivial effect with the median value associating greater exercise performances with naturally menstruating women ($ES_{0.5} = 0.18$ [95% CrI: −0.02 to 0.37]; Figure 4.3). Relatively large between-study standard deviation was identified ($\tau_{0.5} = 0.16$ [95% CrI: 0.01 to 0.44]) with estimates indicating moderate intraclass correlation ($ICC_{0.5} = 0.42$ [95% CrI: 0.00 to 0.80]) due to analysis of multiple outcomes reported within studies. Pooling of strength and endurance outcomes was conducted as no evidence was obtained that indicated a differential effect between the performance categories ($ES_{0.5/Endurance-Strength} = 0.04$ [95% CrI: −0.41 to 0.43]). Posterior estimates of the pooled effect size identified a moderate probability of a small effect favouring naturally menstruating women in the early follicular phase of the MC ($d \geq 0.2$; $P = 0.404$) and effectually a zero-probability favouring habitual OCP women ($d \leq -0.2$; $P = 0.001$). Inclusion of outliers within the model substantially increased the average effect size ($ES_{0.5} = 0.34$ [95% CrI: −0.04 to 0.72]) and between study variance ($\tau_{0.5} = 0.70$ [95% CrI: 0.24 to 1.23]).

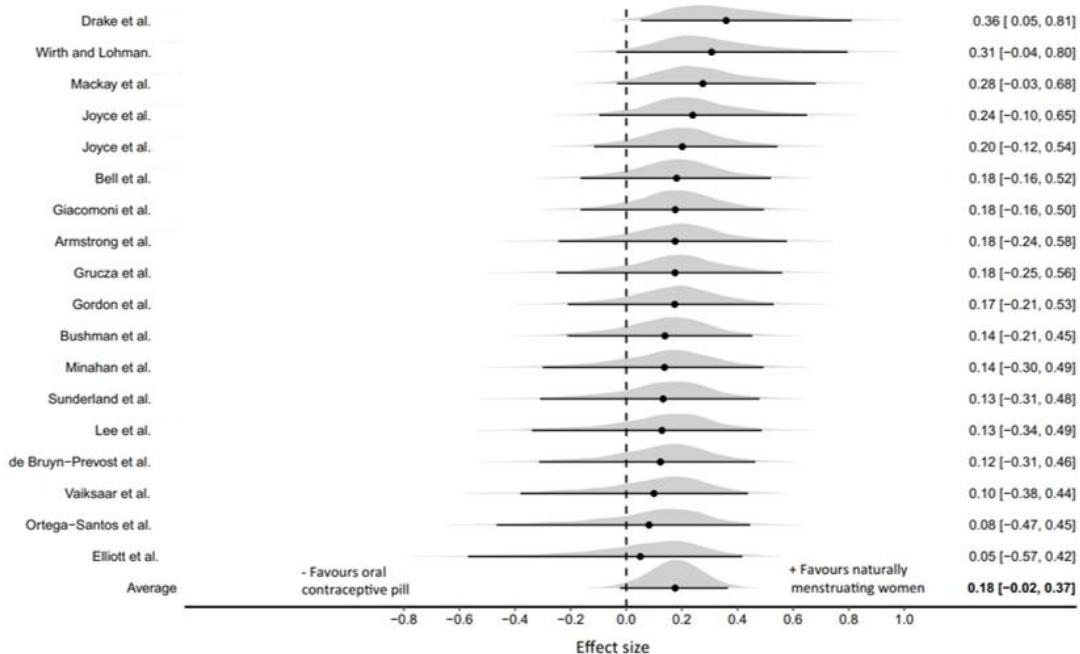


Figure 4-3 Bayesian Forest plot of multilevel meta-analysis comparing exercise performance measured during the oral contraceptive pill withdrawal phase and the early follicular phase (days 1 to 5) of the menstrual cycle. The study-specific intervals represent individual effect size estimates and sampling error. The circle represents the pooled estimate generated with Bayesian inference along with the 95% credible interval.

I_b) Oral contraceptive pill consumption (days 8 to 28) versus all phases of the menstrual cycle (days 6 to 28) except the early follicular phase (days 1 to 5)

Eleven outliers were identified with effects sizes greater than +2, and were removed from the analysis, leaving a total of 88 effect sizes (53 endurance and 35 strength) from 24 studies (combined quality rating = “moderate”: specifically, 21% “high”; 42% “moderate”; 25% “low”; and 13% “very low”; habitual OCP n = 244 and naturally menstruating n = 230). The three-level hierarchical model indicated a trivial effect with the median value associating greater exercise performances obtained in the naturally menstruating women ($ES_{0.5} = 0.13$ [95% CrI: -0.05 to 0.28]; Figure 4.4). Relatively large between study variance was identified $\tau_{0.5} = 0.22$ [95% CrI: 0.06 to 0.45] with central estimates indicating very low intraclass correlation $ICC_{0.5} = 0.08$ [95% CrI: 0.0 to 0.61] due to analysis of multiple outcomes reported within studies. Pooling of strength and endurance outcomes was conducted as no evidence was obtained that indicated a differential effect between the performance categories ($ES_{0.5/Endurance-Strength} = 0.02$ [95% CrI: -0.25 to 0.31]). Posterior estimates of the pooled effect size identified

a small probability of a small effect favouring naturally menstruating women ($d \geq 0.2$; $P = 0.188$) and effectively a zero-probability favouring habitual OCP women ($d \leq -0.2$; $P < 0.001$). Inclusion of outliers within the model increased the average effect size ($ES_{0.5} = 0.19$ [95% CrI: -0.14 to 0.51]) and between study variance ($\tau_{0.5} = 0.71$ [95% CrI; 0.49 to 1.07]).

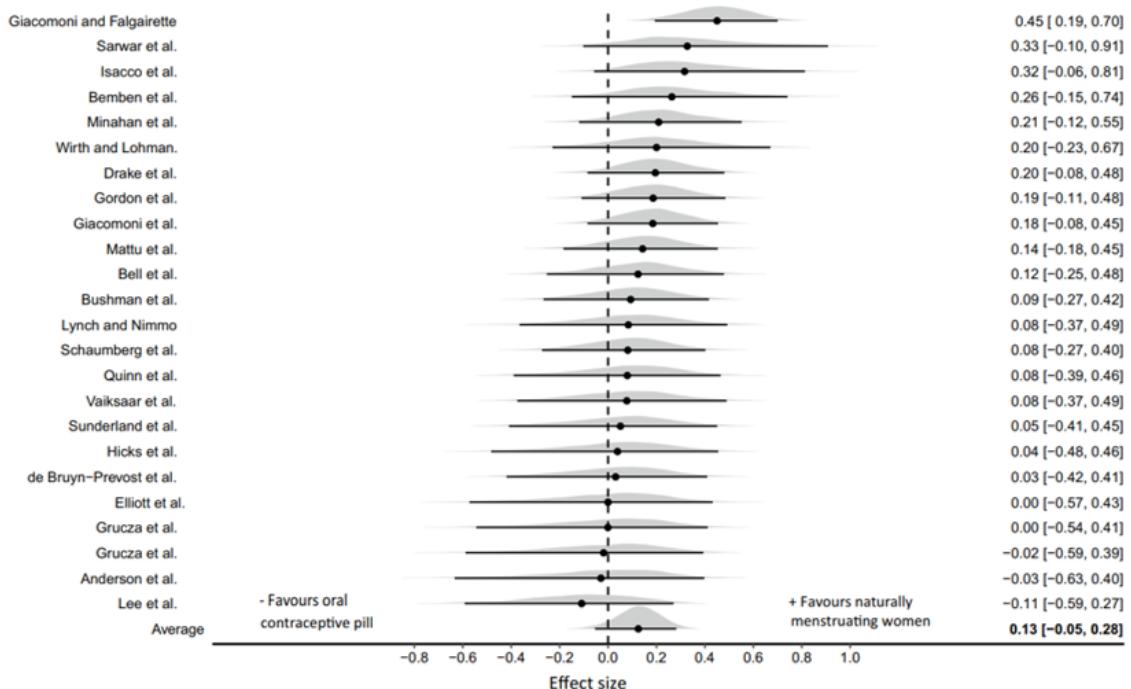


Figure 4-4 Bayesian Forest plot of multilevel meta-analysis comparing exercise performance measured during the oral contraceptive pill consumption phase with menstrual cycle phases days 6 to 28 (excluding the early follicular phase: days 1 to 5). The study-specific intervals represent individual effect size estimates and sampling error. The circle represents the pooled estimate generated with Bayesian inference along with the 95% credible interval.

1c) Sensitivity analyses: Primary outcome studies and “moderate” or “high” quality studies only

Sensitivity analyses were completed for between and within group designs using data from studies that included exercise performance as the primary study outcome (Table 4.2) and from studies categorised as “moderate” or “high” in quality (Table 4.3). No substantive differences were obtained from any of the previous analyses with pooled effects sizes identifying trivial effects with greater exercise performances obtained in naturally menstruating women.

Table 4-2 Results from sensitivity analyses with data from studies including exercise performance as the primary outcome.

Sensitivity analysis	Analysis details	Effect size	Between study variance	Intraclass correlation	Probability of small effect
Between group: oral contraceptive pill withdrawal versus the early follicular phase of the menstrual cycle	34 effect sizes from 11 studies (combined quality = H/M/L; 27% H; 27% M; 27% L; 18% VL)	0.14 [−0.14 to 0.38]	0.20 [0.01 to 0.59]	0.28 [0.0 to 0.82]	(d ≥ 0.2; P = 0.323; d ≤ −0.2; P = 0.014)
Between group: oral contraceptive pill consumption versus all phases of the menstrual cycle except the early follicular phase	57 effect sizes from 16 studies (combined quality = M; 26.7% H; 33.3% M; 26.7% L; 13.3% VL)	0.14 [−0.03 to 0.31]	0.10 [0.0 to 0.40]	0.42 [0.0 to 0.86]	(d ≥ 0.2; P = 0.257; d ≤ −0.2; P = 0.001)
Within group: oral contraceptive pill consumption versus oral contraceptive pill withdrawal	141 effect sizes from 21 studies (combined quality = H/M; 33.3% H; 33.3% M; 19.1% L; 14.3% VL)	0.05 [−0.03 to 0.11]	0.06 [0.0 to 0.17]	0.19 [0.0 to 0.66]	(d ≥ 0.2; P < 0.001)

Results are from multilevel random effects models with median parameter estimates and 95% credible intervals. H = “high”, M = “moderate”, L = “low”, and VL = “very low”.

Table 4-3 Results from sensitivity analyses with data from studies categorised as “moderate” or “high” in quality.

Sensitivity analysis	Analysis details	Effect size	Between study variance	Intraclass correlation	Probability of small effect
Between group: oral contraceptive pill withdrawal versus the early follicular phase of the menstrual cycle	22 effect sizes from 9 studies	0.12 [-0.24 to 0.43]	0.18 [0.01 to 0.61]	0.63 [0.0 to 0.88]	(d ≥ 0.2; P = 0.281; d ≤ -0.2; P = 0.041)
Between group: oral contraceptive pill consumption versus all phases of the menstrual cycle except the early follicular phase	60 effect sizes from 15 studies	0.14 [-0.09 to 0.33]	0.22 [0.05 to 0.48]	0.10 [0.0 to 0.55]	(d ≥ 0.2; P = 0.282; d ≤ -0.2; P = 0.006)
Within group: oral contraceptive pill consumption versus oral contraceptive pill withdrawal	89 effect sizes from 16 studies	0.03 [-0.06 to 0.10]	0.04 [0.0 to 0.16]	0.38 [0.0 to 0.69]	(d ≥ 0.2; P < 0.001)

Results are from multilevel random effects models with median parameter estimates and 95% credible intervals.

I_d) Sensitivity analysis of the natural menstrual cycle phases versus pseudo oral contraceptive pill phases; days 1 to 5, days 12 to 16, and days 19 to 23

An additional set of sensitivity analyses were completed on the between group design data to better match the natural MC and OCP pseudo-phases. This was achieved by mapping days 1 to 5, 12 to 16, and 19 to 23 from both cycles (Table 4.4). Collectively, findings were aligned with the more coarsely matched phases presented above. In days 1 to 5 and 19 to 23, pooled effect sizes again identified trivial effects with greater exercise performances obtained in naturally menstruating women. In days 12 to 16, pooled effect sizes were effectively zero with a wide CrI reflecting the limited data available (11 effect sizes from 5 studies).

Table 4-4 Results from sensitivity analyses comparing exercise performance outcomes comparing the natural menstrual cycle phases versus pseudo oral contraceptive pill phases.

Sensitivity analysis	Analysis details	Effect size	Between study variance	Intraclass correlation	Probability of small effect
Between group: days 1-5	42 effect sizes from 16 studies (combined quality rating = M; 18.75% H; 31.25% M; 25% L; 25% VL)	0.17 [-0.04 to 0.38]	0.15 [0.01 to 0.50]	0.60 [0.10 to 0.90]	(d ≥ 0.2; P = 0.368; d ≤ -0.2; P = 0.001)
Between group: days 12-16	11 effect sizes from 5 studies (combined quality rating = M; 60% M; 40% VL)	-0.04 [-0.73 to 0.58]	0.27 [0.01 to 1.28]	0.20 [0.10 to 0.70]	(d ≥ 0.2; P = 0.137; d ≤ -0.2; P = 0.291)
Between group: days 19-23	38 effect sizes from 14 studies (combined quality rating = M; 28.6% H; 35.7% M; 21.4% L; 14.3% VL)	0.13 [-0.13 to 0.34]	0.22 [0.02 to 0.56]	0.35 [0.01 to 0.65]	(d ≥ 0.2; P = 0.253; d ≤ -0.2; P = 0.009)

Results are from multilevel random effects models with median parameter estimates and 95% credible intervals. H = “high”, M = “moderate”, L = “low” and VL = “very low”.

4.3.4.2 Analysis 2: Within group analyses of the oral contraceptive pill consumption phase compared to the oral contraceptive pill withdrawal phase

Twenty-four of the included studies (combined quality rating = “high” and “moderate”: specifically, 33% “high”; 33% “moderate”; 17% “low”; and 17% “very low”) generated 148 effects sizes (positive values favouring OCP consumption) from research designs comparing OCP consumption with OCP withdrawal. The data were collected from 221 participants with studies comprising a mean group size of 10 (range n = 5 to 17). The three-level hierarchical model incorporating both strength (96 effect sizes) and endurance (52 effect sizes) provided some evidence of a trivial effect with the pooled effect size very close to zero ($ES_{0.5} = 0.05$ [95% CrI: −0.02 to 0.11]; Figure 4.5). Between study variance was relatively small $\tau_{0.5} = 0.06$ [95% CrI: 0.0 to 0.16] as was central estimates of intraclass correlation $ICC_{0.5} = 0.20$ [95% CrI: 0.0 to 0.62] due to analysis of multiple outcomes reported within studies. Pooling of strength and endurance outcomes was conducted as no evidence was obtained that indicated a differential effect between the performance categories ($ES_{0.5/Endurance-Strength} = 0.02$ [95% CrI: −0.22 to 0.33]). Posterior estimates of the pooled effect size identified almost zero probability of a small effect in either direction ($|d| \geq 0.2$; $P \leq 0.001$). Sensitivity analyses conducted with data from studies where performance was identified as a primary outcome had minimal effect on model outputs (Table 4.2) and from studies categorised as “moderate” or “high” in quality (Table 4.3) had no substantive influence on model outputs.

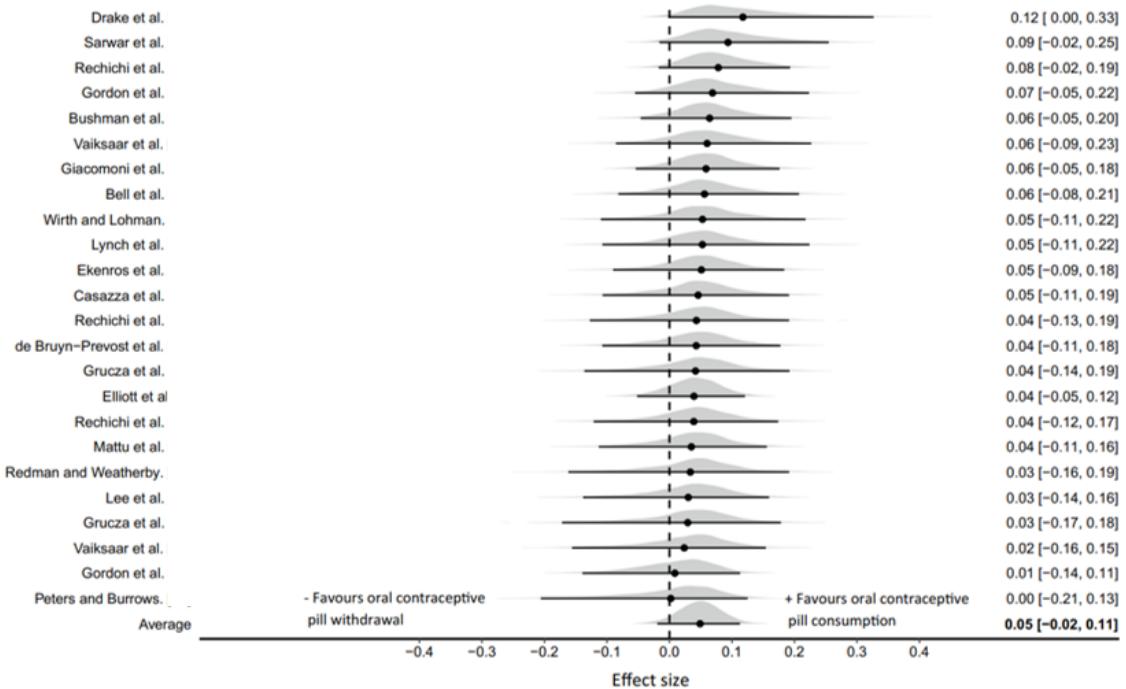


Figure 4-5 Bayesian Forest plot of multilevel meta-analysis comparing exercise performance measured during oral contraceptive pill consumption with the oral contraceptive pill withdrawal phase. The study-specific intervals represent individual effect size estimates and sampling error. The circle represents the pooled estimate generated with Bayesian inference along with the 95% credible interval.

4.3.4.3 Analysis 3: Within group comparison of oral contraceptive use and non-use

Only two studies (Casazza *et al.*, 2002; Ekenros *et al.*, 2013) met the inclusion criteria for this category and as such no meta-analysis was performed on these data. Casazza *et al.* (2002) tested participants during two phases (4 to 8 days and 17 to 25 after the start of menses) of the MC, in a randomised order. Following this, participants began taking the same triphasic OCP for four complete cycles (28 days per cycle) and were tested during the week of the inactive OCPs and during the second week of active OCP ingestion. Menstrual cycle phase had no effect on peak exercise capacity. Conversely, four months of OCP use, resulted in decreases in time to peak exercise (14%) and the peak power output attained (8%) during a continuously graded cycle test. In addition, all participants experienced an 11% decline in $\text{VO}_{2\text{peak}}$ ($\text{L}\cdot\text{min}^{-1}$). Ekenros *et al.* (2013) employed a cross-over design, such that participants taking an OCP upon recruitment were tested on day 2, 3, or 4 during the OCP free days and on days 7 or 8 and 14 or 15 during the OCP taking days, after which they stopped taking the OCP and were testing on day 2, 3, or 4, 48 hours after ovulation and 7 or 8 days after ovulation. Those who were

naturally menstruating at recruitment were tested on day 2, 3 or 4, 48 hours after ovulation and 7 or 8 days after ovulation and were re-tested following one OCP cycle on day 2, 3 or 4 during the OCP free days and on days 7 or 8 and 14 or 15 during the OCP taking days. There were no differences in muscle strength between groups, although maximum muscle strength of the knee extensors was different between the early follicular (days 2, 3, or 4) and luteal phase (7 or 8 days after ovulation) in the naturally menstruating group; 139 (28) N·m compared with 145 (26) N·m ($P = 0.02$).

4.3.4.4 Analysis 4: Randomised control trials of oral contraceptive use versus placebo intake

Only one study (Lebrun *et al.*, 2003) met the inclusion criteria for this category and as such no meta-analysis was performed on these data. Lebrun *et al.* (2003) employed a randomised, double-blind, placebo-controlled trial in naturally menstruating women. Testing was performed during the early follicular (days 3 to 8) and mid-luteal (days 4 to 9 after ovulation) phases of an ovulatory MC, after which participants were randomly assigned to either an OCP ($n = 7$) or placebo ($n = 7$) group and were tested between days 14 and 17 of the second cycle of OCP (*i.e.*, the same triphasic OCP) or placebo administration. Participants were active women, who regularly competed in aerobic activities such as running, cycling, triathlon, rowing, cross country skiing. Oral contraceptive pill use resulted in a mean decrease of 4.7% in $VO_{2\text{max}}$ compared with a 1.5% improvement in the placebo group. The decrease in absolute $VO_{2\text{max}}$ was accompanied by an increase in the sum of skinfolds, but not by changes in weight or measures of strength, anaerobic, or endurance performance.

4.4 Discussion

The purpose of this Chapter was to investigate the effect of OCP use on exercise performance in sportswomen. The results indicate a trivial performance effect on average with OCP use, whereby superior exercise performance was generally observed for naturally menstruating women compared to OCP users. In addition to the estimated trivial average effect, results from the meta-analysis models also indicated relatively large between study variance indicating that research design, participant characteristics, and type of performance outcome measured might influence any effect. Collectively, these findings demonstrate that OCPs might, on average, exert a slightly negative impact on exercise performance. However, from a practical perspective, the effect magnitude and variability support consideration of an individuals'

response to OCP use. Specifically, decisions as to the appropriateness of OCP use should be tailored to the individual requirements (*e.g.*, contraceptive, or medical need) and response (*i.e.*, to what degree their exercise performance might be affected) of each sportswoman. Furthermore, pooling of data comparing exercise performance between OCP consumption and withdrawal estimated an effect that was close to zero, indicating that exercise performance is unlikely to change across the OCP *cycle*.

As a result of combined OCP use, endogenous concentrations of 17- β -oestradiol and progesterone are significantly downregulated when compared with the late follicular/ovulatory (endogenous oestrogen is high) and mid-luteal phases (endogenous oestrogen and progesterone are *both* relatively high; [Elliott *et al.*, 2005]). This chronic downregulation might be responsible for the slightly impaired exercise performance demonstrated in OCP users when compared with naturally menstruating counterparts. Indeed, the endogenous sex hormone profile of an OCP user is comparable to the profile observed during the early follicular phase of the MC; correspondingly low levels of endogenous oestrogen and progesterone (Carol *et al.*, 1992; Elliott *et al.*, 2005; Spona *et al.*, 1996). In *Chapter 3*, which investigated the effects of MC phase on exercise performance in naturally menstruating women, the available evidence indicated that on average, exercise performance might be trivially reduced during the early follicular phase of the MC (low oestrogen and progesterone), when compared with all other phases of the MC (considerably higher concentrations of endogenous oestrogen and/or progesterone). Similarly, the within group results of the current Chapter showed that exercise performance between the OCP consumption and withdrawal phases of the OCP *cycle* was, on average, very unlikely to exhibit even a small effect, during which time the concentration of endogenous oestrogen and progesterone are consistently low (Elliott *et al.*, 2005). Collectively, these results indicate that exercise performance might be mediated by the concentration of endogenous sex hormones in some sportswomen, as reflected by evidence of slightly impaired performance, on average, at a time when these sex hormones are at their lowest.

The between-group findings from the present Chapter agree with those by Casazza *et al.* (2002) and Lebrun *et al.* (2003) who showed that experimental OCP use resulted in reduced peak exercise capacity and decreased maximal oxygen uptake, when compared with non-use. Specifically, Casazza *et al.* (2002) employed a cross-over design with data from two phases of the natural MC compared to data after four months of triphasic OCP use, and Lebrun *et al.* (2003) utilised a randomised, double-blind, placebo-controlled trial, with data from two phases of the natural MC compared with data after two months of triphasic OCP use. These

longitudinal intervention studies represent a change from inactive to active OCP use within the same individual, which is a stronger research design when compared to the cross-sectional observational studies included in the between-group analysis in the present meta-analysis. Thus, this further supports the notion that OCP use might result in small adverse effects on exercise performance, in some individuals, when compared with naturally menstruating women. Although, it is important to note that experimental OCP use might not always be carried out in consultation with a clinician who could monitor any potentially negative side effects, and possibly make changes to the OCP type or dose. As such, higher detrimental effects might be observed in experimental OCP users as opposed to habitual OCP users. In addition, some adverse side-effects, which are experienced during initial OCP use, can mitigate over time, potentially compounding the issue of comparing habitual OCP users with experimental OCP users. Contrary to the between-group findings from the present meta-analysis and those of Casazza *et al.* (2002) and Lebrun *et al.* (2003), Ekenros *et al.* (2013) showed no difference in performance between OCP and non-use. Although Ekenros *et al.* (2013) employed a longitudinal intervention study design, the original ‘non-OCP’ users only received a monophasic OCP for one month (*i.e.*, 21 OCP-taking days) before they were retested as habitual OCP users. Casazza *et al.* (2002) and Lebrun *et al.* (2003) retested after four and two months of OCP use, respectively, which might have resulted in a greater downregulation of endogenous oestrogen and progesterone than that seen by Ekenros *et al.* (2013). Additionally, the participants in the study by Ekenros *et al.* (2013) used a variety of OCPs, whereas Casazza *et al.* (2002) and Lebrun *et al.* (2003) used the same OCP, resulting in a more homogenous group, with potentially less inter-individual variation in endogenous sex hormone concentrations, thus reducing the possibility of type II errors (Elliott-Sale *et al.*, 2013). Moreover, Ekenros *et al.* (2013) used a strength-based performance measure, whilst Casazza *et al.* (2002) and Lebrun *et al.* (2003) employed endurance type performance measures, representing different physiological pathways for oestrogen and/or progesterone to exert their effects. These methodological differences might account for the disparity in results between Ekenros *et al.* (2013) and Casazza *et al.* (2002), Lebrun *et al.* (2003), and the present Chapter.

The within group analysis in the present Chapter demonstrated that exercise performance was relatively consistent across the OCP cycle. Thus, these results imply that exogenous supplementation of oestrogen and progesterone is unlikely to exert any substantive effect, and instead exercise performance is more likely mediated by the endogenous hormonal milieu because of OCP use (*i.e.*, the continuous downregulation of oestradiol and progesterone

between OCP consumption and withdrawal). As such, these data suggest that the ‘supplementary’ nature of OCPs should not be considered as performance-enhancing (Bennell *et al.*, 1999). As OCPs are also not ergolytic, the timing of the withdrawal bleed can be manipulated (*e.g.*, to avoid bleeding during competition) without negatively impacting performance, although the long-term health implications of continuous OCP consumption without any withdrawal are unknown. Indeed, Schaumberg *et al.* (2018) have noted that menstrual manipulation for exercise and sports performance reasons is a common practice amongst physically active women.

Although the results from the current meta-analysis align, and have solid mechanistic underpinnings, it is important to acknowledge that the practical implications of these findings are small. Indeed, all point estimates and outliers were in the same direction and indicated a potentially negative influence, on average, of endogenous sex hormone suppression on exercise performance. However, the real-life implications of these findings are likely to be so small, as to be trivial, and therefore not meaningful for most of the population. Additionally, a large range of moderating factors (independent of sex hormone changes; [Stewart & Bateson, 2016; Stewart & Black, 2015]) are likely to influence an individual’s response to, and requirement for, OCPs and we suggest that individuals do not solely make their decision to use, or not use, OCPs based on the performance related findings reported within this Chapter. For example, some individuals are prone to substantial cycle related symptoms due to the natural MC, such as cramps, bloating, and/or heavy menstrual bleeding, and for these individuals, the benefits of OCP use (Lethaby *et al.*, 2019; Naheed *et al.*, 2017) might outweigh the small detriments observed in this Chapter. Similarly, the consequences of unplanned pregnancy might be far greater than the trivial effects observed in the current Chapter. Conversely, large inter-individual variation exists in the response to most interventions (Hopkins, 2015; Swinton *et al.*, 2018), whereby some individuals might experience no performance-related side-effects whatsoever, whereas others might experience substantial performance-related side-effects from OCP use (Martin *et al.*, 2018). As such, we recommend that individuals consider all relevant factors (which might include physical, emotional, practical, financial, and health related aspects), before making decisions as to the appropriateness (or not) of OCP use.

The current Chapter was primarily conducted using non-randomised observational trials, which might be considered a limitation of its value. Randomised controlled trials are the preferred design to investigate the potential influence of a treatment (in this case OCPs) on an outcome (in this case exercise performance), however, they can be difficult to implement in this

population, as individuals tend to be habitual OCP users or non-users. Only one randomised controlled trial was identified from the relevant literature (Lebrun *et al.*, 2003) alongside two further trials wherein OCPs were prescribed to, or withheld from, non-users and habitual users in a cross-over design (Casazza *et al.*, 2002; Ekenros *et al.*, 2013). Withholding OCPs from a habitual OCP user has ethical and practical (*e.g.*, unplanned pregnancy) implications and as such, this type of research design is rarely employed. In addition, having the resources to conduct appropriately standardised and controlled studies across the time-periods required to adequately address this question is, in many cases, prohibitive (*i.e.*, an adequate wash-out and/or supplementation period). Instead, most data on OCP use versus non-use are based on between group investigations of independent parties, which might be impacted by a large range of confounding variables and does not permit causal inference to be made. The lack of randomised controlled trials will affect analyses within this area of study for the foreseeable future.

Following the Downs and Black quality assessment (Downs & Black, 1998) most studies (64%) included in this Chapter were classified as “moderate” or “low” in quality, which was largely due to a lack of standardisation (*e.g.*, prior activity and food intake) and inadequate familiarisation (*i.e.*, often no familiarisation took place or long periods of time had elapsed between testing sessions, potentially warranting re-familiarisation). Additionally, most studies had small samples (range: $n = 5$ to 25), with a mean group size of 10, meaning that many were likely to be under-powered. Rigorous control of these research design factors in future studies, along with consideration of individual response (Hopkins, 2015; Swinton *et al.*, 2018), and more randomised controlled trials (where possible), will provide further insight into the effects of OCP use on exercise performance and will allow sportswomen to make evidence-based decisions on OCP use within the context of sport and exercise. Moreover, consideration of the topic-specific methodological issues recommended by Elliott-Sale *et al.* (2021), namely hormone verification of MC phase, and adequate description of OCP type, resulted in a further reduction in “high” quality studies, from 36 to 17%, and an increase in “very low” quality studies, from 0 to 10%. Thus, future studies should use appropriate biochemical outcomes (*i.e.*, blood samples to determine the concentration of endogenous oestrogen and progesterone) to verify the reproductive hormonal milieu in OCP users, and naturally menstruating women, a tenet that is also supported by Thompson and Han (2019). Such measures would permit the relationship between specific sex hormone profiles and exercise performance to be established. In addition, future investigations should describe the type of OCP used to the level of detail

required for categorisation or replication, as different types of OCPs cause varying concentrations of exogenous and endogenous sex hormones, resulting in non-homogenous participant groups (Elliott-Sale *et al.*, 2013). The heterogeneity, caused by the non-homogenous populations plus the considerable variation in outcomes measured, likely contributed to the relatively large between study variance observed in the present Chapter. In the future, it would be interesting to tease out which factors might cause some women to have a negative effect, while others do not, but this was not possible with the current evidence base. Overall, future studies need to include homogenous populations, improve methodological quality, and limit confounders to facilitate a deeper understanding of individual effects.

4.5 Conclusion

Collectively, these results indicate that OCP use might result in slightly inferior exercise performance on average when compared to non-use, although any group level effect is likely to be trivial. Whilst most of the data used in this meta-analysis was rated as “moderate” to “low” in quality (83% of the total studies), a sensitivity analysis of “moderate” and “high” quality papers (67% of the total studies) did not change the general findings described, thus bolstering the confidence in the evidence. From a practical perspective, as the effects tended to be trivial and variable across studies, there appears to be no performance related evidence to warrant general guidance on OCP use compared with non-use. As such, an individualised approach should be taken, based on each individual’s response to OCP use, along with factors, such as their primary objective for using OCPs, and their experience of the natural MC. Moreover, the difference in exercise performance between OCP consumption and withdrawal phases was estimated on average to be close to zero, suggesting that the endogenous sex hormone profile is the prevailing driver of performance, rather than the supplementation of exogenous sex hormones. Thus, practically, there appears to be no performance related evidence to warrant general guidance on OCP consumption versus OCP withdrawal. *Chapter 3* alluded to the possible effects of factors beyond the reproductive hormonal profile on exercise performance. For example, the reduced exercise performance observed during the early follicular phase of the MC, in *Chapter 3*, might have been due to the experience of cycle related symptoms and their perceived effects at this timepoint. Oral contraceptives are often prescribed to women to manage the negative symptoms with the MC (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). Thus, it is possible that exercise performance did not

change across the OCP *cycle* in the present Chapter due to an attenuation of symptoms. Although, this theory does not explain the slightly inferior exercise performance observed in OCP users compared to naturally menstruating women. As such, *Chapters 5 and 6* will investigate this further, by considering the cycle related symptoms experienced by OCP users, and the perceived effects of OCP use, in addition to the reproductive hormonal milieu, on exercise performance.

CHAPTER 5 - CYCLE RELATED SYMPTOMS AND THEIR PERCIEVED EFFECTS ON EXERCISE PERFORMANCE AND RECOVERY TIME POST EXERCISE

This Chapter has been presented at the following conferences:

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). The menstrual cycle, oral contraceptive pill use, and associated symptoms on exercise performance and recovery. Pre-conference symposium at: Europhysiology 2022; 15th – 18th September; Copenhagen, Denmark.

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). Cycle related symptoms and their perceived effects on exercise performance and recovery time post exercise. Poster presentation at: Women in Sport Congress; 17th – 19th August; Melbourne, Australia.

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). The menstrual cycle, oral contraceptive pill use, and associated symptoms on exercise performance and recovery. Symposium at: The Physiological Society Physiology Symposium 2022; 11th May; Derby, United Kingdom.

5.1 Introduction to Chapter 5

As described in *Chapters 3 and 4* changes in endogenous and exogenous sex hormones across the MC and with OCP use might affect exercise performance. Additionally, as highlighted in *Chapter 2, Section 2.5*, these sex hormones can also potentially impact training outcomes, such as the recovery process post exercise. At present, the specific mechanisms behind these performance and training effects are not well-understood, however one plausible reason could be the impact of cycle related symptoms and their perceived effects (Bruinvels *et al.*, 2022). Indeed, common negative symptoms (*i.e.*, ‘period pain’ and mood changes) resulting from the MC are likely antagonistic with optimal performance and training, if not managed, in sportswomen (Bruinvels *et al.*, 2022). Moreover, previous work has shown that OCPs might help to reduce any negative MC related symptoms in sportswomen, thus limiting any potential negative effects on performance and training (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). Despite this, little is known about the type, frequency, and severity of cycle related symptoms, and how the symptoms experienced by naturally menstruating women and OCP users are perceived to influence exercise performance and training.

As described in *Chapter 2*, there are a range of suggested mechanisms by which the cyclical fluctuations in oestrogen and progesterone across the MC might affect exercise performance and training. However, the influence of cycle related symptoms and their perceived effects, are often overlooked (Bruinvels *et al.*, 2022). Of the available research it appears that MC related symptoms are prevalent in sportswomen, and most women perceive their symptoms to compromise their exercise participation and performance, particularly during or just prior to menstruation (Armour *et al.*, 2020; Brown *et al.*, 2021; Findlay *et al.*, 2020; Martin *et al.*, 2018). Recently, Bruinvels *et al.* (2021) developed a novel approach (MSi) that purports to quantify the type, number, and frequency of cycle related symptoms. The authors reported that a higher MSi score (greater prevalence and frequency of symptoms) was associated with an increased likelihood of missing training or competition. It is important to recognise, however that all previous studies have relied on retrospective self-reported data, thus are limited by memory recall. Additionally, retrospective recall presents a general overview of symptoms throughout the entity of the MC, overlooking key timepoints across the cycle where the type, frequency, and severity of symptoms might vary. Moreover, Bruinvels *et al.* (2021) did not capture symptom severity, which could theoretically influence exercise performance and training outcomes in addition to symptom type and frequency. As a result, the full extent of symptoms (*i.e.*, the type, frequency, and severity, as well as common symptom footprints) and

their potential impact on perceived exercise performance and training in sportswomen has yet to be examined.

The MC is susceptible to external perturbations; around 50% of sportswomen use some form of HC, with the OCP the most prevalent type (Elliott-Sale & Hicks, 2018; Heather *et al.*, 2021; Martin *et al.*, 2018). In addition to its use as a birth control measure, the OCP might help to alleviate the symptoms experienced across the MC (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). Consequently, this might help to reduce any potential negative effects of cycle related symptoms on performance and training outcomes (Martin *et al.*, 2018; Parker *et al.*, 2022). However, research to date highlights that some pill users still experience negative symptoms related to their OCP use, which could affect performance and training (Clarke *et al.*, 2021; Heather *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022; Parker *et al.*, 2022). Indeed, it has been reported that exogenous ethinyl oestradiol (found in OCPs) has a higher ER affinity and is several times more potent than endogenous oestradiol (Bennink, 2004), which might play a role in the aetiology of cycle related symptoms during pill-taking days. Additionally, it could be theorised that the downregulation of endogenous hormones and sudden withdrawal of exogenous hormones might play a role in the aetiology of cycle related symptoms during the pill-free days (Sulak *et al.*, 2000). Nevertheless, few studies have investigated the experience of cycle related symptoms in OCP users and their potential impact on perceived exercise performance and training outcomes.

Overall, given that sportswomen (irrespective of reproductive hormonal profile) might be affected by cycle related symptoms, and that these symptoms have the potential to influence aspects of exercise performance and training, it is important to gain a better understanding of symptomology within this population. Therefore, the purpose of this Chapter was to: 1) retrospectively describe and compare the type, frequency, and severity of symptoms experienced by naturally menstruating women and _mOCP users; 2) investigate in real-time the effect of MC and OCP *phases* on the type, frequency, and severity of symptoms; and 3) determine whether the symptoms experienced by naturally menstruating women and _mOCP users during pre-defined MC and _mOCP *phases* are associated with perceived exercise performance and recovery time post exercise.

5.2 Method

5.2.1 Participants

In total, 42 women volunteered to take part in this study. The sample included 21 naturally menstruating (mean \pm standard deviation [SD]: age, 29 ± 5 years; stature, 164.9 ± 5.7 cm; mass, 63.7 ± 9.1 kg) women and 21 $_m$ OCP users (age 28 ± 4 years; stature 165.2 ± 7.1 cm; mass 60.9 ± 11.6 kg). Participants in the naturally menstruating group self-reported having a regular MC between 21 and 35 days in length for at least one year prior to participation. Additionally, all naturally menstruating participants were not taking any form of HC for a minimum of three-months prior to the investigation, and self-reported being free from any other medication (*i.e.*, hormonal replacement therapy), MC related irregularity (*e.g.*, amenorrhea, anovulation, luteal phase deficiency), or condition (*e.g.*, polycystic ovarian syndrome, endometriosis, pregnancy, thyroid dysfunction, eating disorders or disordered eating) known to affect the HPO axis. To employ a homogenous design (see *Section 5.2.3.3*), all participants in the $_m$ OCP group reported taking the combined $_m$ OCP containing ethinyl oestradiol and a type of progestin (Table 5.1) taken for 21 days, followed by a seven-day pill free interval (or taken for 28 days, inclusive of a seven-day inactive/placebo pill interval) for a minimum of three-months prior to the study (Elliott-Sale *et al.*, 2013). All participants were deemed at least recreationally active, defined as meeting the *World Health Organisation's* activity guidelines of at least 150 to 300 minutes of moderate intensity activity per-week (or 75 to 150 minutes of vigorous intensity activity per-week), including muscle-strengthening activities at a moderate or high intensity, on a minimum of two days per-week (McKay *et al.*, 2022). Participants also reported taking part in multiple sports/forms of activity (*i.e.*, ‘Running’, ‘Cycling’, ‘Swimming’, ‘Gym-based classes’, and ‘Weight training’). A small percentage (19%) of participants were classified as trained, defined as regularly training and partaking in events in their chosen sport or activity (McKay *et al.*, 2022). No participants were deemed as highly trained, elite, or world class (McKay *et al.*, 2022). All participants were free from any injury in the past six months. Full ethical approval was granted from the Northumbria University, Health and Life Sciences ethics committee (HLSKM29409) and the study was conducted in accordance with the Declaration of Helsinki. Written, informed consent was obtained from all participants prior to participation. This Chapter uses the term ‘woman’ for people who self-report identifying with the sex they were assigned with at birth (Robinson *et al.*, 2022).

Table 5-1 The type of combined, monophasic, oral contraceptive used by each participant in the pill group.

Pill brand	Participants (n)	Oestrogen	Dosage (micrograms)	Progestin	Generation (based on type of progestin)	Dosage (micrograms)	Androgenicity
Yasmin®	n = 4	Ethinyl oestradiol	30	Dropspirenone	Fourth generation	300	-
Levest®	n = 3	Ethinyl oestradiol	30	Levonorgestrel	Second generation	150	++
Lucette®	n = 2	Ethinyl oestradiol	30	Dropspirenone	Fourth generation	300	-
Microgynon® 30	n = 2	Ethinyl oestradiol	30	Levonorgestrel	Second generation	150	++
Gedarel® 30/150	n = 2	Ethinyl oestradiol	30	Desogestrel	Third generation	150	+
Lizinna®	n = 1	Ethinyl oestradiol	35	Norgestimate	Third generation	250	+
Cilique®	n = 1	Ethinyl oestradiol	35	Norgestimate	Third generation	250	+
Rigevidon®	n = 1	Ethinyl oestradiol	30	Levonorgestrel	Second generation	150	++
Marlissa®	n = 1	Ethinyl oestradiol	30	Levonorgestrel	Second generation	150	++

Ovreena®	n = 1	Ethinyl oestradiol	30	Levonorgestrel	Second generation	150	++
Aranka®	n = 1	Ethinyl oestradiol	30	Dropspirenone	Fourth generation	300	-
Mercilon®	n = 1	Ethinyl oestradiol	20	Desogestrel	Third generation	150	+
Millinette® 20/75	n = 1	Ethinyl oestradiol	20	Gestodene	Third generation	75	+

++ = High androgenicity; + = Low androgenicity; - = Anti-androgenic

5.2.2 Research design

Data were collected for this Chapter using two approaches. Firstly, an initial 54-part online survey was created (Online Surveys, Jisc, United Kingdom) and distributed to all participants via email. The survey retrospectively assessed reproductive status, the type, frequency, and severity of symptoms typically experienced, and the perceived effects of the MC and _mOCP use on aspects of exercise performance and training. Information gathered from the initial 54-part online survey was used to ensure all participants met the *a priori* inclusion and exclusion criteria, and to answer aim one (*i.e.*, retrospectively describe and compare the type, frequency, and severity of symptoms experienced by naturally menstruating women and _mOCP users) and partly answer aim three (*i.e.*, determine whether the symptoms experienced by naturally menstruating women and _mOCP users during pre-defined MC and OCP *phases* are associated with perceived exercise performance and recovery time post exercise) of the present Chapter. Secondly, following a virtual pre-testing session to habituate participants to all procedures (*i.e.*, questionnaires), participants tracked cycle related data (*i.e.*, day of MC or _mOCP *cycle*, blood flow amount during the period or withdrawal bleed, as well as ovulation tracking in naturally menstruating participants), and their symptoms daily to further quantify symptom type, frequency, and severity across pre-defined MC and _mOCP *phases*. To do this, each participant received a unique link to an online form (Google Forms, Google, United Kingdom), consisting of 12 questions, which they completed daily, at a similar time of day (\pm two-hours), to minimise the effects of diurnal variation. Recording of daily cycle related data and symptom tracking began on day one of menses in naturally menstruating women, or day one of _mOCP withdrawal in pill users, and continued for the duration of one full MC (*i.e.*, until the onset of the next menstrual bleed) or _mOCP *cycle* (*i.e.*, until day 21 of _mOCP consumption). A daily text reminder was sent at the same time each day to all participants to ensure compliance. Results from this daily cycle related data, and symptom tracking were used to answer aim two (investigate in real-time the effect of MC and OCP *phases* on the type, frequency, and severity of symptoms) and partly answer aim three (*i.e.*, determine whether the symptoms experienced by naturally menstruating women and _mOCP users during pre-defined MC and OCP *phases* are associated with perceived exercise performance and recovery time post exercise) in the present Chapter.

5.2.3 Procedures

5.2.3.1 54-part online survey

Data gathered from the initial 54-part online survey included the following information: 1) demographic data (*i.e.*, age, sex, and medical history); 2) current MC and HC status (*i.e.*, MC length, period duration, regularity of cycles, type of HC used and duration of use); 3) the type, frequency, and severity of MC and _mOCP related symptoms; 4) training history; 5) MC and _mOCP monitoring and tracking; 6) the perceived effects of the MC and _mOCP use on aspects of performance and training (whereby participants were asked to indicate if their MC or _mOCP use led to perceived reduced/increased performance or a longer/quicker recovery post exercise across pre-defined MC and _mOCP *phases*, by marking either ‘Yes’ or ‘No’ or ‘I don’t experience this’); and 7) previous education on the MC and HC use. All survey questions were either multiple choice check boxes (some with a limit and others without a limit on the number of selections allowed), short/ long text answers, a matrix, or a linear scale. Free text answers were also requested where ‘Other’ was applicable. Logic was applied to the survey to ensure that only relevant questions were asked. The 54-part online survey was adapted specifically for this Chapter based on previous research in this area (see *Appendix J*; [Bruinvels *et al.*, 2021; Heather *et al.*, 2021; Solli *et al.*, 2020]). The survey was piloted with five researchers and five participants for language, comprehension, and compliance. To help content and face validity, as well as general clarity around questions, minor edits were made to the survey wording based on their feedback. To ensure a uniform understanding of the pre-defined MC and _mOCP *phases* and to assist in the answering of questions an idealised four-phase lay definition (and diagram) was provided to participants within the survey. Although only three pre-defined *phases* were used within the Chapter for those in the naturally menstruating group (Figure 5.1), a four-phase lay diagram was provided to help participant understanding. The survey was designed to take approximately 20 minutes to complete.

5.2.3.2 Daily cycle related data and symptom tracking

Data gathered from the daily cycle and symptom tracking form included: 1) day of MC or _mOCP *cycle*; 2) blood flow amount during the period or withdrawal bleed (*i.e.*, none, very light, light, moderate, heavy, and very heavy); and 3) symptom type, presence, and severity (*i.e.*, absent, mild, moderate, and severe) with 18 possible symptoms listed based on those reported in previous work (Bruinvels *et al.*, 2021), with the addition of symptom severity questions enhancing the form and the novelty of the current Chapter. Additionally, to identify MC *phases*

participants in the naturally menstruating group were asked to track ovulation using urinary ovulation detection kits (Advanced Digital Ovulation Test, Clearblue, Switzerland) and BBT using a digital thermometer (One Step Digital Basal Thermometer, Home Health UK Ltd, United Kingdom). Specifically, beginning on a predetermined day (depending on each participant's typical cycle length), using the start of menses as day one, participants in the naturally menstruating group used the ovulation detection kits once daily (at the same time each day with first urine void after their longest sleep), until a positive ovulation test was achieved. The urinary ovulation detection kit tracked changes in oestrogen and LH concentration (greater than $40 \text{ mIU} \cdot \text{mL}^{-1}$) and provided participants with a static smiley face when the 'LH surge' was detected. The urinary ovulation detection kit used had 99% accuracy in detecting the 'LH surge', as determined by the manufacturer. Participants were asked to record the status of the smiley face within the daily form. For BBT, participants were instructed to take this measure orally (under the tongue) every morning before arising and record the value in $^{\circ}\text{C}$, to two decimal places, within the daily form. Further information pertaining to cervical fluid (*i.e.*, none/dry phase, sticky phase, creamy phase, and clear phase) was also collected, but was not used to confirm ovulation and/or classify *phases* in the current Chapter. All questions in the form were either multiple choice check boxes, short text answers, a matrix, or a linear scale. The form was designed to take approximately five minutes to complete. The daily cycle and symptom tracking form can be found in *Appendix K*.

5.2.3.3 Menstrual cycle and combined monophasic oral contraceptive pill phase classification

The MC and mOCP cycle (Figure 5.1), were separated into pre-defined *phases*. Specifically, the MC was classified into three *phases* which were selected as those theoretically coinciding with low concentrations of oestrogen and progesterone (*phase* one, 'early follicular phase'), rising/high oestrogen and low progesterone concentrations (*phase* two, 'mid- to late follicular/ovulatory phase'), and high oestrogen and progesterone concentrations (*phase* three, 'mid-luteal phase'). Menstrual cycle *phases* were calculated based on the first day of menstruation. *Phase* one was defined as the first five days of the cycle from the onset of self-reported menstruation. *Phase* two was defined as four days prior to a positive ovulation test and the day of the positive ovulation test (Stricker *et al.*, 2006). *Phase* three was classified as the time between five to nine days post a positive ovulation test and was also indicated by BBT (*i.e.*, a rise in BBT [approximately 0.25 to 0.5 of a degree] following ovulation, that remains relatively constant for 10 to 16 days [Thompson & Han, 2019]). Participants that did not report a positive ovulation test or a biphasic rise in BBT were subsequently excluded from the

analysis. As such, our confidence in the sex hormone profiles captured during *phase* one and *phase* two of the MC in the present Chapter is high, however *phase* three of the MC is estimated rather than confirmed, thus our confidence in the hormone profile of *phase* three is limited. To ensure an equal number of days were used for each *phase*, the $m\text{OCP}$ cycle was classified into four *phases*: *phase* one (' $m\text{OCP}$ withdrawal', days 1 to 7 of pill-free days), *phase* two (' $m\text{OCP}$ consumption, days 1 to 7'), *phase* three (' $m\text{OCP}$ consumption, days 8 to 14'), and *phase* four (' $m\text{OCP}$ consumption, days 15 to 21). The *phases* of the $m\text{OCP}$ cycle were defined using counting from either the first day of the $m\text{OCP}$ free *phase* or the $m\text{OCP}$ taking *phase*. It is important to acknowledge that these profiles, reflecting $m\text{OCP}$ consumption and withdrawal, are pseudo-phases as they are 'artificial' *phases* in comparison with the *phases* of the natural MC, but for the purposes of this Chapter will be referred to as *phases*.

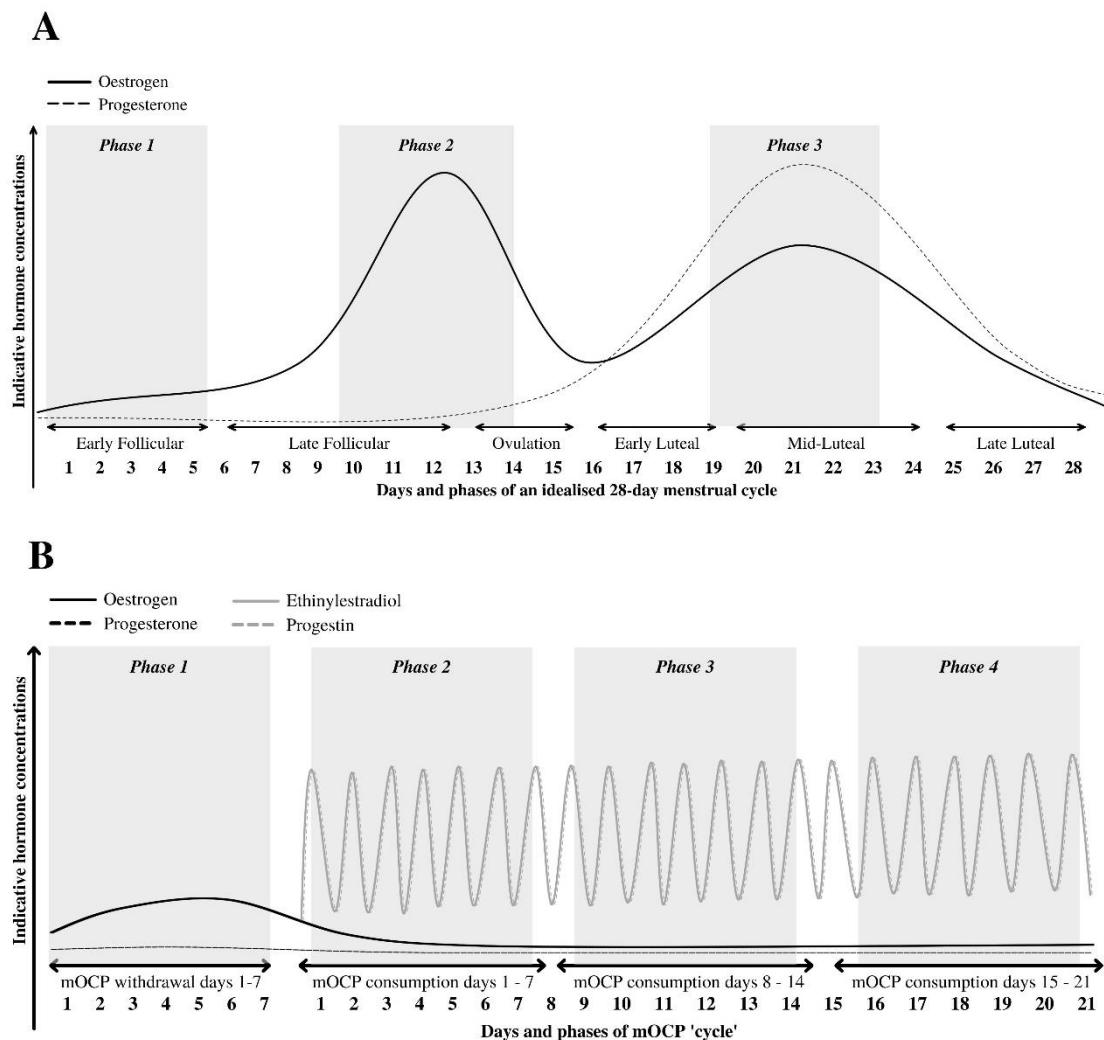


Figure 5-1 Schematic displaying: A) the endogenous sex hormone fluctuations across an idealised 28-day menstrual cycle, with ovulation occurring on day 14, and corresponding study

phases; and B) the endogenous and exogenous sex hormone fluctuations across the combined, monophasic, oral contraceptive pill (_mOCP) *cycle* and corresponding study *phases*.

5.2.4 Data analysis

5.2.4.1 54-part online survey

The raw data from the 54-part online survey were exported from Online Surveys directly to Microsoft Excel software for Windows. The sum of the number of symptoms reported was calculated to create the ‘total number of symptoms’, with a maximum value of 18. The average frequency of the symptoms reported, was then calculated using a Likert scale, based on previous research (Bruinvels *et al.*, 2021). Specifically, the following numerical value was attached to the Likert, “often” = 3 points, “sometimes” = 2 points, “rarely” = 1 point, and “never” = 0 points for each of the 18 symptoms reported. The ‘symptom index (Si) score’ was then calculated by totalling the frequency score (0 to 3) for each symptom (0 to 18) reported, with total scores ranging from 0 (minimum) to 54 (reporting every symptom, often). ‘Average symptom severity score’ was assessed using a Likert scale, with the following numerical values attached to the Likert, “absent” = 1, “mild” = 2, “moderate” = 3 and “severe” = 4. The ‘Si score’ was then multiplied by the ‘average symptom severity score’ to provide an overall ‘Si × severity score’.

5.2.4.2 Daily cycle and symptom tracking

The raw data from the daily cycle related data and symptom tracking form were exported from Google Forms directly to Microsoft Excel software for Windows. To quantify the type, frequency, and severity of symptoms across the MC and _mOCP *cycle*, cycles were first separated into pre-defined *phases* (see *Section 5.2.3.3*). The number of symptoms experienced in each *phase* were summed to create the ‘symptom frequency per *phase*’. The mode severity (*i.e.*, “absent” = 1, “mild” = 2, “moderate” = 3 and “severe” = 4) of each of the symptoms experienced per *phase* was then calculated to create the ‘symptom severity per *phase*’. Finally, the ‘symptom frequency per *phase*’ was then multiplied by the ‘symptom severity per *phase*’ to give an overall ‘*phase* symptom frequency × severity score’.

5.2.5 Statistical analysis

The statistical software package IBM SPSS Statistics (Version 24, SPSS Inc., USA) for Windows was used to conduct the statistical analysis. Data are presented as mean ± SD (for normally distributed, continuous data), medians (*Mdn*) ± interquartile range (*IQR*; for non-

normally distributed, or ordinal data), and number and percentages (for categorial data) unless otherwise stated. Normal distribution of data was confirmed using the Shapiro-Wilk test. If a normality breach was detected, a nonparametric Mann-Whitney U test was used. For data collected from the initial 54-part online survey an independent t-test was used to assess between group comparisons in the ‘total number of symptoms’ and the ‘Si score’. As data were ordinal, a nonparametric Mann-Whitney U test was used to assess for any between group comparison in ‘average symptom severity’. Additionally, as data were not normally distributed, a nonparametric Mann-Whitney U test was used to assess for any between group comparison in the overall ‘Si × severity score’. For data collected through daily tracking, one-way repeated measures ANOVAs were used to assess for differences in ‘symptom frequency per *phase*’, and the ‘*phase* symptom frequency × severity score’ across MC and _mOCP *cycle phases* (independently). Sphericity was assessed using Mauchly’s test of sphericity. Where sphericity was violated, a Greenhouse-Geisser correction was used. If a significant main effect was observed, a *post hoc* Bonferroni-corrected pairwise comparison was used. As data were ordinal, a nonparametric Friedman test was used to assess differences in ‘symptom severity per *phase*’ across MC and _mOCP *cycle phases* (independently). A binomial logistic regression was used to predict changes in perceived exercise performance and recovery post exercise in specific MC and _mOCP *cycle phases* (from the 54-part online survey), based on the ‘*phase* symptom frequency × severity score’ (from the daily cycle and symptom tracking form). The odds ratio for each variable and the accompanying 95% confidence intervals (CIs) were calculated. The α for all statistical tests was set at $P \leq 0.05$.

5.3 Results

5.3.1 Participant characteristics

Self-reported, descriptive, MC and _mOCP characteristics data for the participants included in the study are displayed in Table 5.2.

Table 5-2 Self-reported, descriptive, menstrual cycle and combined, monophasic, oral contraceptive pill characteristics data in naturally menstruating women ($n = 21$) and pill users ($n = 21$).

Descriptive menstrual cycle and combined monophasic oral contraceptive pill use characteristics

Naturally menstruating group (n = 21)

Mean age at menarche (years)	12 ± 1 (range 11 to 17)	
Cycle characteristics:	<i>n</i>	%
Menstrual cycle length		
Short (<20 days)	0	0
Regular (21 to 35 days)	21	100
Long (36< days)	0	0
Average period duration		
0 – 2 days	0	0
2 – 5 days	10	48
5 – 7 days	11	52
7+ days	0	0
Average period blood flow		
Very light/ spotting	1	5
Light	6	29
Moderate	12	57
Heavy	2	9
Very heavy	0	0
Variable cycle-to-cycle	0	0
Unsure	0	0
Average use of pain relief for menstrual cycle symptoms		
No, never	3	14
Yes, rarely (once/twice a year)	7	33
Yes, sometimes (roughly every 3 cycles)	9	43
Yes, often (every cycle)	2	10
Previous hormonal contraceptive use	17	81
Combined oral contraceptive pill use	13	76
Progestin-only oral contraceptive pill use	4	24
Contraceptive implant	5	29
Contraceptive injection	0	0
Contraceptive patch	0	0
Vaginal ring	0	0
Hormonal intrauterine system	0	0
Unsure	2	12
Mean duration since stopping hormonal contraceptive use (years)	3.8 ± 2.6	

Combined, monophasic, oral contraceptive pill group (n = 21)

Mean age at menarche (years)	13 ± 2 (range 10 to 16)	
Mean duration on current form of oral contraceptive pill (years)	7.9 ± 5.8	
Cycle characteristics:	<i>n</i>	%
Average time spent bleeding during withdrawal bleed		
0 – 2 days	0	0
2 – 5 days	16	76
5 – 7 days	5	24
7+ days	0	0
Average blood flow during withdrawal bleed		
Very light/ spotting	1	5
Light	12	57
Moderate	7	33

Heavy	1	5
Very heavy	0	0
Variable cycle-to-cycle	0	0
Unsure	0	0
Average use of pain relief for oral contraceptive pill symptoms	7	33
No, never	1	5
Yes, rarely (once/twice a year)	6	29
Yes, sometimes (roughly every 3 cycles)	7	33
Yes, often (every cycle)		
Reasons for current oral contraceptive pill use		
Birth control to avoid pregnancy	16	76
Manage menstrual cycle symptoms	10	48
Eliminate/ control bleeding	3	14
Other (<i>i.e.</i> , “acne”)	3	14

5.3.2 The type, frequency, and severity of symptoms from the initial 54-part online survey

The reported type and frequency of each symptom, for each group, are shown in Figure 5.2. There was no difference in the ‘total number of symptoms’ reported (naturally menstruating: 12 ± 4 symptoms; _mOCP: 11 ± 4 symptoms; $P = 0.353$), the ‘Si score’ (naturally menstruating: 26 ± 10 ; _mOCP: 22 ± 10 ; $P = 0.200$), ‘average symptom severity’ (naturally menstruating: 3 ‘moderate’ [Mdn]; _mOCP: 2 ‘mild’ [Mdn]; $P = 0.145$), and the overall ‘Si \times severity score’ (naturally menstruating: 68 [Mdn] ± 90 [IQR]; _mOCP: 50 [Mdn] ± 56 [IQR]; $P = 0.113$) between naturally menstruating women and _mOCP users.

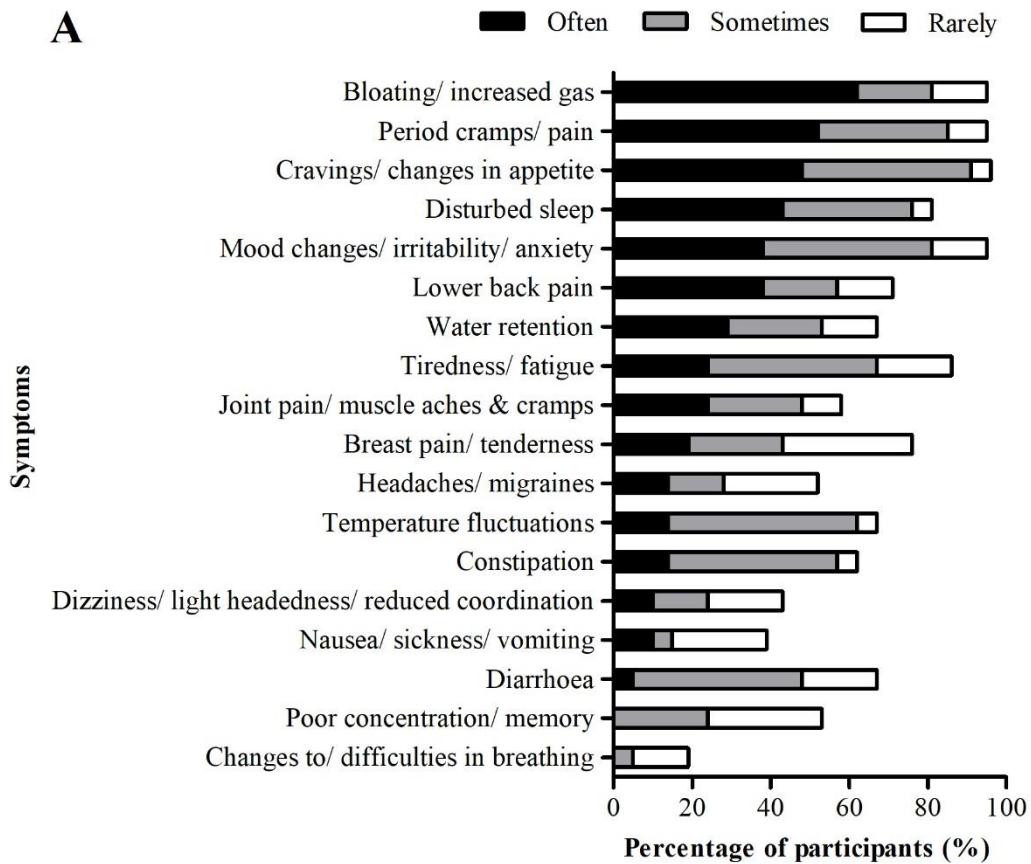
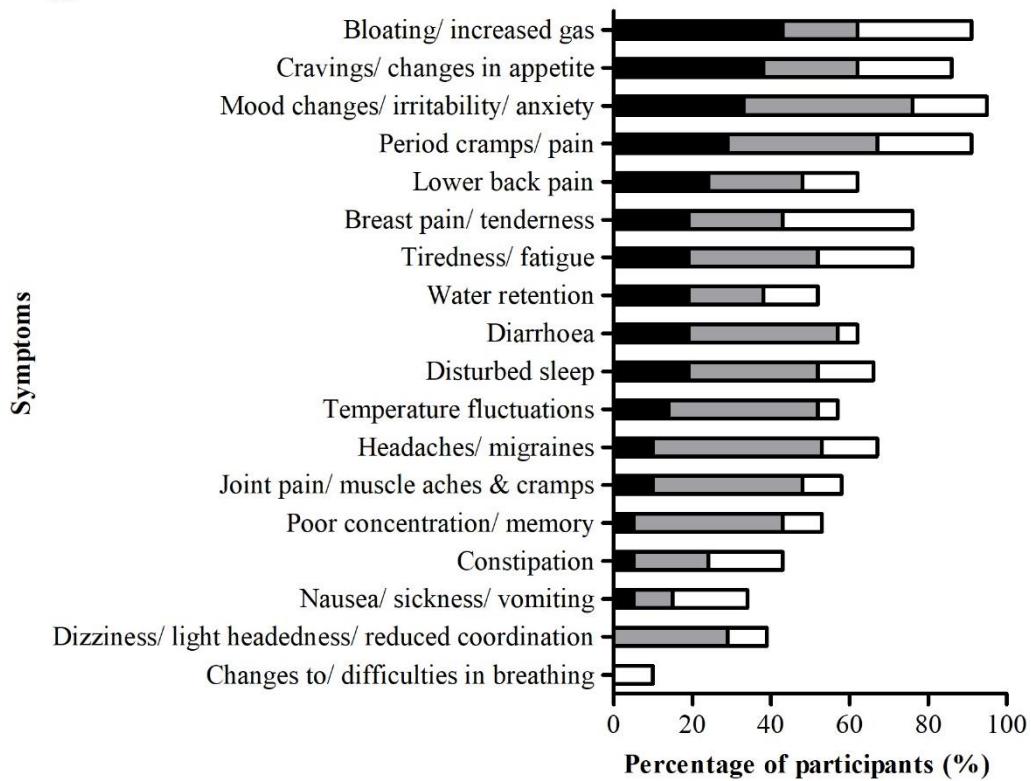
A**B**

Figure 5-2 The different types of symptoms experienced and the frequency of these symptoms (“often”, “sometimes”, and “rarely”) by: A) naturally menstruating women ($n = 21$); and B) combined, monophasic, oral contraceptive pill ($_m$ OCP) users ($n = 21$).

5.3.3 The type, frequency, and severity of symptoms across menstrual cycle and combined, monophasic, oral contraceptive pill phases from daily tracking data

Two naturally menstruating women were excluded from this analysis because one exhibited a LPD (defined by not having a luteal phase long enough to meet mid-luteal analysis classification in the present Chapter), and one was identified as anovulatory (defined by a lack of a positive ovulation test and no biphasic response in BBT). During the cycle whereby data was collected, participants in the naturally menstruating group had a mean cycle length of 30 ± 3 days, period duration of 6 ± 2 days, and ovulated on day 17 ± 3 days. The different types of symptoms experienced across MC and $_m$ OCP phases, for each group, are shown in Figure 5.3.

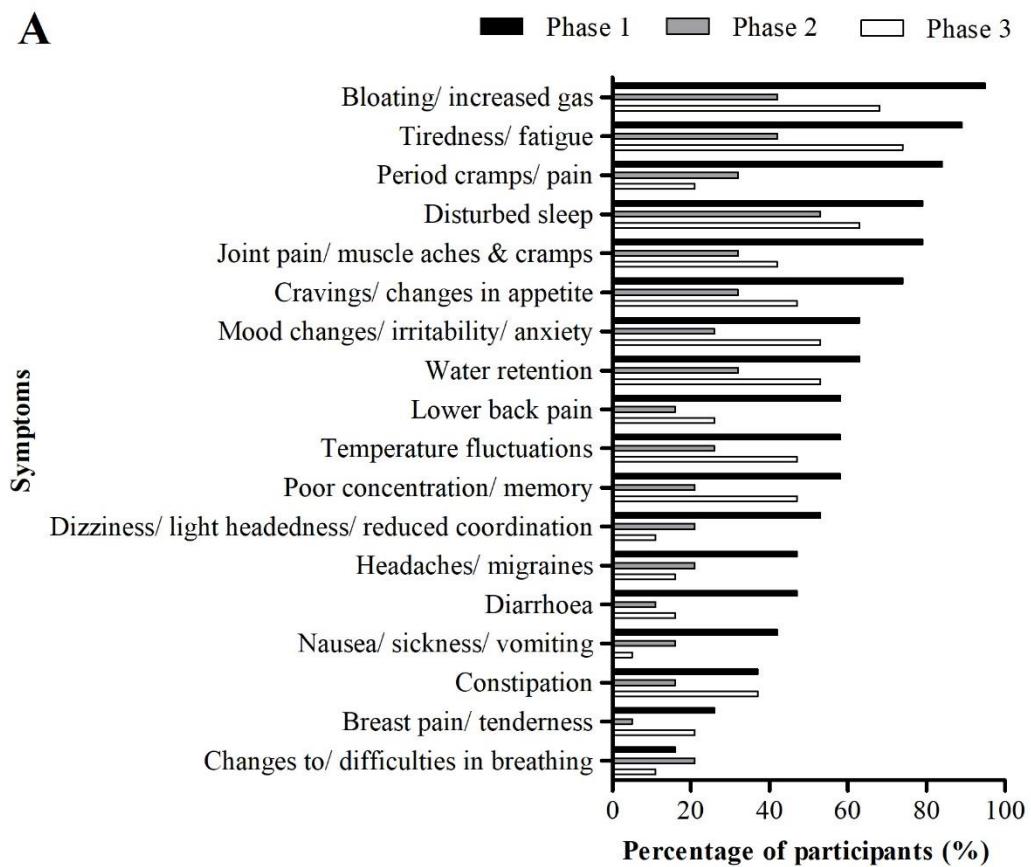
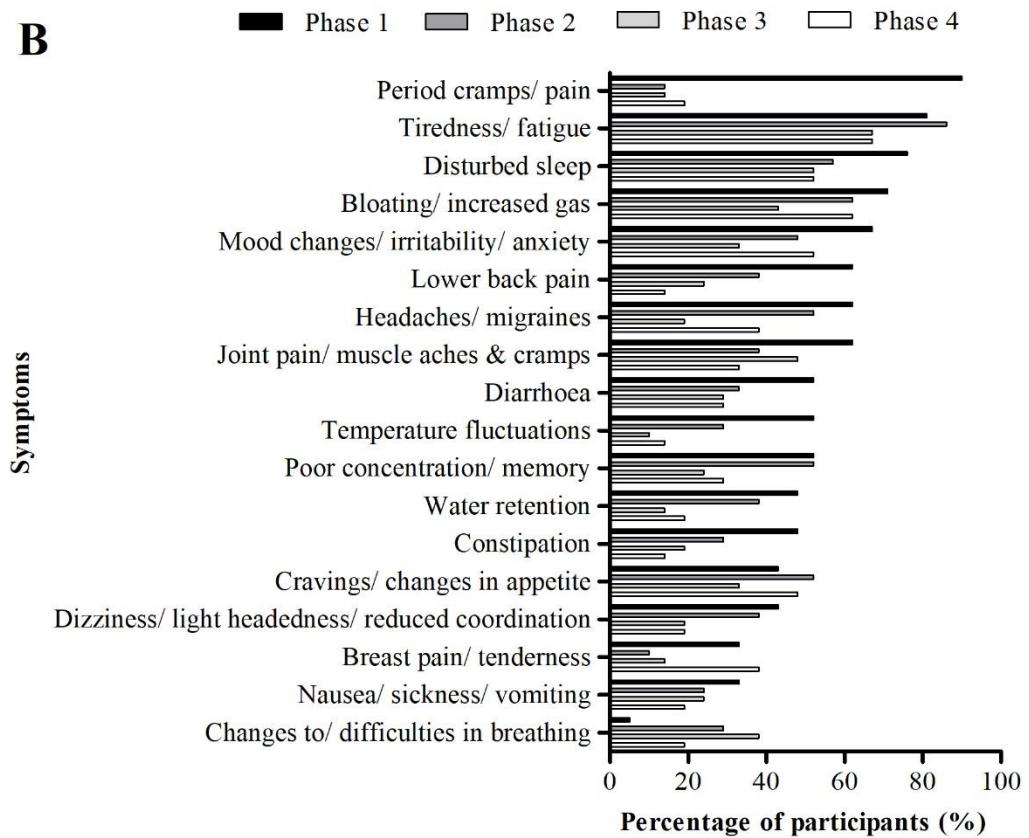
A**B**

Figure 5-3 The prevalence of the different types of symptoms experienced by: A) naturally menstruating women ($n = 19$) across menstrual cycle *phases* (*i.e.*, *phase* one: ‘early follicular phase’; *phase* two: ‘late follicular/ovulatory phase’; and *phase* three: ‘mid-luteal phase’); and B) combined, monophasic, oral contraceptive pill (_mOCP) users ($n = 21$) across pill *phases* (*phase* one: ‘_mOCP withdrawal’, days 1 to 7 of pill-free days; *phase* two: ‘_mOCP consumption, days 1 to 7’; *phase* three: ‘_mOCP consumption, days 8 to 14’; and *phase* four ‘_mOCP consumption, days 15 to 21’).

There was a difference in the frequency of symptoms experienced per *phase* across MC *phases* ($P = 0.001$; Figure 5.4, Panel A). Specifically, naturally menstruating women experienced a greater frequency of symptoms during *phase* one (28 ± 18 symptoms) of the MC compared to *phases* two (13 ± 13 symptoms; $P = 0.006$ [95% CI 4 to 27]), and three (16 ± 12 symptoms; $P = 0.010$ [95% CI 3 to 22]), whereas there was no difference between *phases* two and three ($P = 0.611$). There was no difference in symptom severity per *phase* between MC *phases* (*phase* one: $Mdn = 2$ [“mild”], *phase* two: $Mdn = 2$ [“mild”], and *phase* three: $Mdn = 2$ [“mild”]; $P = 0.084$). The ‘*phase* symptom frequency \times severity score’ differed across MC *phases* ($P < 0.001$; Figure 5.4, Panel B). Indeed, the ‘*phase* symptom frequency \times severity score’ was greater during *phase* one (62 ± 43 Au) of the MC compared to *phases* two (26 ± 25 Au; $P = 0.005$ [95% CI 10 to 62]) and three (37 ± 27 Au; $P = 0.026$ [95% CI 3 to 48]), but there was no difference between *phases* two and three ($P = 0.287$).

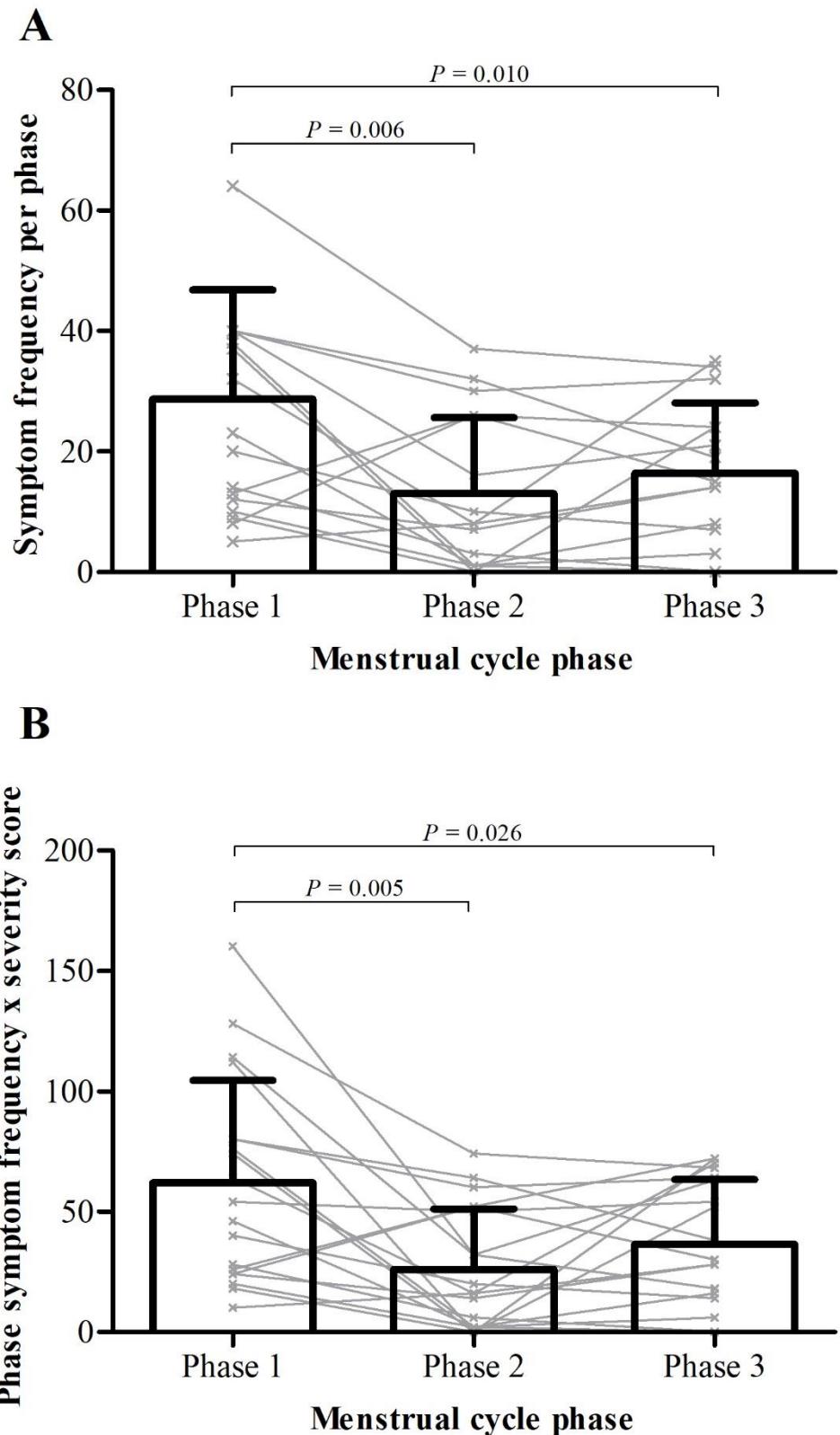


Figure 5-4 A) Symptom frequency per *phase*; and B) the ‘*phase symptom frequency x severity score*’ across menstrual cycle phases (*i.e.*, *phase one*: ‘early follicular phase’; *phase two*: ‘late

follicular/ovulatory phase'; and *phase* three: 'mid-luteal phase') in naturally menstruating women ($n = 19$). Values are individual means and bars with error lines represent the overall mean \pm standard deviation response.

There was a difference in the frequency of symptoms experienced per *phase* across _mOCP *phases* ($P = 0.001$; Figure 5.5, Panel A). Specifically, _mOCP users experienced a greater frequency of symptoms during *phase* one (35 ± 24 symptoms) of the _mOCP *cycle*, compared with all other _mOCP *phases* (*phase* two: 18 ± 20 symptoms, $P = 0.001$ [95% CI 6 to 28]; *phase* three: 13 ± 17 symptoms, $P = 0.001$ [95% CI 9 to 34]; *phase* four: 19 ± 21 symptoms $P = < 0.003$ [95% CI 5 to 27], respectively), but there was no difference between any of the _mOCP consumption *phases* ($P = 0.079$, $P = 1.000$, and $P = 0.376$, respectively). There was no difference in symptom severity per *phase* between _mOCP *phases* (*phase* one $Mdn = 2$ ['mild'], *phase* two $Mdn = 2$ ['mild'], *phase* three $Mdn = 2$ ['mild'], and *phase* four $Mdn = 2$ ['mild']; $P = 0.702$). The 'phase symptom frequency \times severity score' differed across _mOCP *phases* ($P < 0.001$; Figure 5.5, Panel B). Indeed, the 'phase symptom frequency \times severity score' was greater during *phase* one (73 ± 55 Au) of the _mOCP *cycle*, compared with all other _mOCP *phases* (*phase* two: 36 ± 39 Au, $P = 0.002$ [95% CI 11 to 61]; *phase* three: 30 ± 46 Au, $P = 0.005$ [95% CI 11 to 75]; *phase* four: 42 ± 51 Au, $P = 0.022$ [95% CI 4 to 59], respectively), however there was no difference between any of the _mOCP consumption *phases* ($P = 0.981$, $P = 1.000$, and $P = 0.477$, respectively).

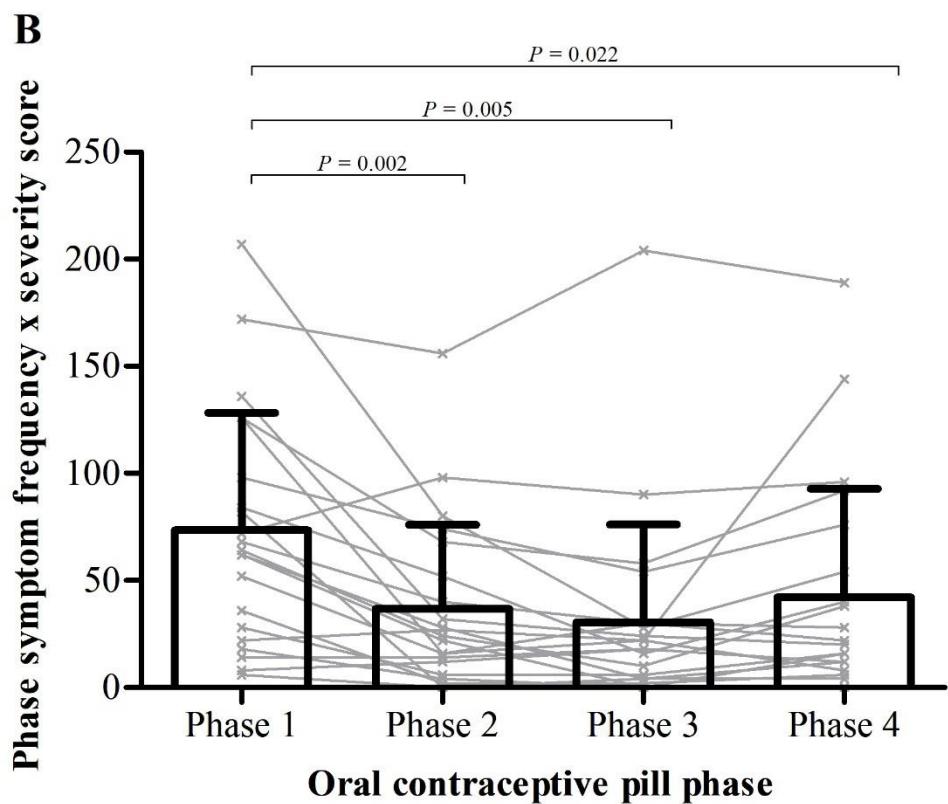
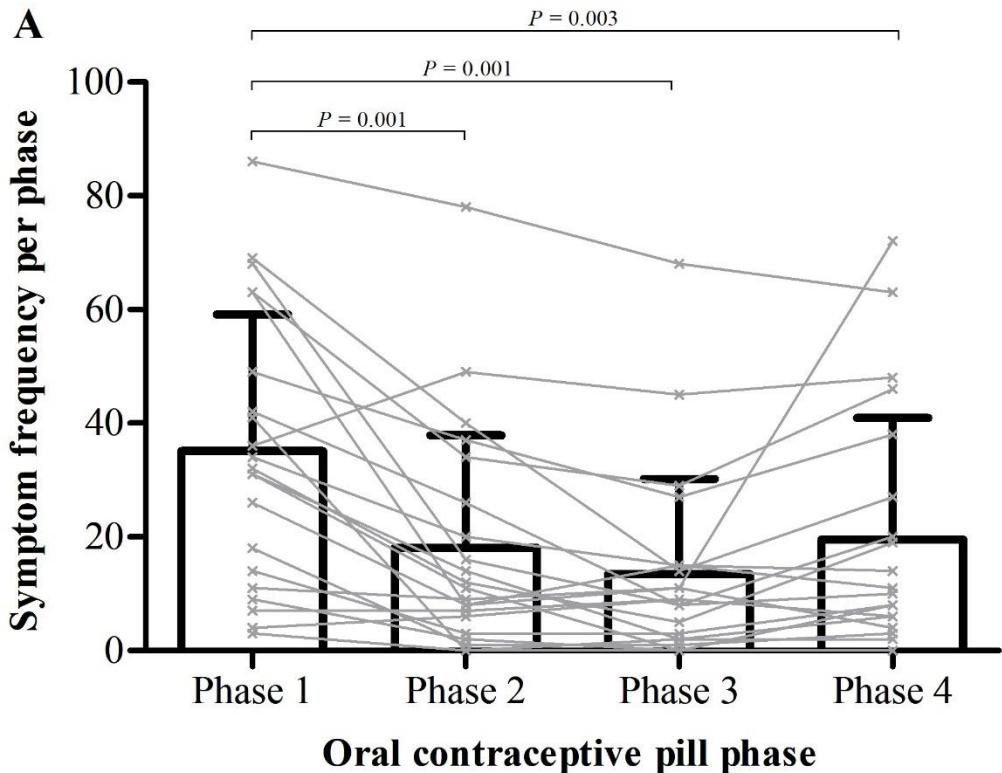


Figure 5-5 A) Symptom frequency per *phase*; and B) the ‘*phase* symptom frequency x severity score’ across the combined, monophasic, oral contraceptive pill (_mOCP) *phases* (*i.e.*, *phase* one: ‘_mOCP withdrawal’, days 1 to 7 of pill-free days; *phase* two: ‘_mOCP consumption, days 1 to 7’; *phase* three: ‘_mOCP consumption, days 8 to 14’; and *phase* four: ‘_mOCP consumption, days 15 to 21’) in pill users ($n = 21$). Values are individual means and bars with error lines represent the overall mean \pm standard deviation response.

5.3.4 Perceived effect of menstrual cycle and combined monophasic oral contraceptive pill phase on aspects of exercise performance and training from the initial 54-part online survey

The perceived effect of MC and _mOCP *phase* on aspects of exercise performance and training in naturally menstruating women and _mOCP users is shown in Table 5.3. Sixty-seven percent of naturally menstruating women reported a perceived improvement in their exercise performance during *phase* two of the MC, whilst 38% reported a perceived decrease in exercise performance during *phase* one of the MC. Most naturally menstruating women reported that their perceived recovery time following a training session took longer during *phase* one (48%), whereas the majority perceived their recovery time following a training session to be quicker in *phase* two (67%). Fifty-seven percent of _mOCP users reported a perceived improvement in their exercise performance during _mOCP taking days, whilst 57% reported a perceived decrement in exercise performance during _mOCP free days. Most _mOCP users reported no differences in perceived recovery time following a training session across _mOCP *phases* (57% and 71%, respectively).

Table 5-3 Perceived effect of menstrual cycle *phase* (*i.e.*, *phase* one: ‘early follicular phase’; *phase* two: ‘late follicular/ovulatory phase’; and *phase* three: ‘mid-luteal phase’) and combined, monophasic, oral contraceptive pill *phase* (*i.e.*, *phase* one: ‘_mOCP withdrawal’, days 1 to 7 of pill-free days; *phase* two: ‘_mOCP consumption, days 1 to 7’; *phase* three: ‘_mOCP consumption, days 8 to 14’; and *phase* four: ‘_mOCP consumption, days 15 to 21’) on aspects of exercise performance and training in naturally menstruating women (n = 21) and pill users (n = 21).

Outcome	Group	Not applicable		Phase 1		Phase 2		Phase 3		Phase 4	
		n	%	n	%	n	%	n	%	n	%
More likely to decrease the number of training sessions	Naturally menstruating	6	29	11	52	0	0	0	0	-	-
	_m OCP	8	38	12	57	1	5	1	5	1	5
More likely to increase the number of training sessions	Naturally menstruating	8	38	1	5	10	48	7	33	-	-
	_m OCP	9	43	0	0	12	57	12	57	12	57
More likely to miss a training session	Naturally menstruating	2	10	16	76	0	0	0	0	-	-
	_m OCP	10	48	11	52	0	0	0	0	0	0
More likely to miss competition	Naturally menstruating (n = 4)	2	50	2	50	0	0	0	0	-	-
	_m OCP (n = 4)	2	50	2	50	0	0	0	0	0	0
Perceive a training session to be harder	Naturally menstruating	3	14	12	57	1	5	5	24	-	-
	_m OCP	5	24	16	76	0	0	0	0	0	0
Perceive a training session to be easier	Naturally menstruating	6	29	3	14	11	52	8	38	-	-
	_m OCP	10	48	2	10	9	43	9	43	9	43
Perceive performance to be improved	Naturally menstruating	3	14	4	19	14	67	9	43	-	-
	_m OCP	8	38	1	5	12	57	12	57	12	57
Perceive performance to be reduced	Naturally menstruating	6	29	8	38	1	5	1	5	-	-
	_m OCP	9	43	12	57	0	0	0	0	0	0

Feel more fatigued prior to, during and post a training session	Naturally menstruating mOCP	17	533	114	5267	00	00	30	140	-0	-0
Feel more energised prior to, during and post a training session	Naturally menstruating mOCP	313	1462	32	1410	137	6233	77	3333	-7	-33
Experience reduced motivation towards training	Naturally menstruating mOCP	28	1038	1013	4862	00	00	30	140	-0	-0
Experience increased motivation towards training	Naturally menstruating mOCP	412	1957	20	100	129	5743	109	4843	-9	-43
Perceive recovery to take longer post a training session	Naturally menstruating mOCP	412	1957	109	4843	00	00	10	50	-0	-0
Perceive recovery to be quicker post a training session	Naturally menstruating mOCP	515	2471	11	55	145	6724	85	3824	-5	-24

mOCP, combined monophasic oral contraceptive pill.

5.3.5 Association between perceived exercise performance and recovery time post exercise across menstrual cycle and combined, monophasic, oral contraceptive pill phases and the symptoms experienced during these phases from both the initial 54-part online survey and daily tracking data

The effect of ‘*phase* symptom frequency × severity score’ on the probability of perceived reduced/improved exercise performance or longer/quicker recovery time post exercise across MC *phases* in naturally menstruating women and across _mOCP *phases* in pill users is shown in Table 5.4. The odds ratios for the ‘*phase* symptom frequency × severity score’ provide an estimate of the change in odds for the corresponding response variable per unit increase in ‘*phase* symptom frequency × severity score’. A higher ‘*phase* symptom frequency × severity score’ was associated with a perceived reduction in exercise performance and a longer recovery time post exercise during *phase* one of the MC in naturally menstruating women. Specifically, it is estimated that the odds of perceiving performance as reduced in *phase* one of the MC are multiplied by 1.07 per unit increase in ‘*phase* symptom frequency × severity score’. Likewise, it is estimated that the odds of perceiving recovery time to take longer post exercise during *phase* one of the MC are multiplied by 1.04 per unit increase in ‘*phase* symptom frequency × severity score’. Moreover, a higher ‘*phase* symptom frequency × severity score’ was associated with perceived reduced exercise performance and a longer recovery time post exercise during _mOCP-free days in pill users. Indeed, it is estimated that the odds of perceiving performance as reduced during _mOCP-free days are multiplied by 1.04 per unit increase in ‘*phase* symptom frequency × severity score’. Likewise, it is estimated that the odds of perceiving recovery time to take longer post exercise during _mOCP-free days are multiplied by 1.03 per unit increase in ‘*phase* symptom frequency × severity score’.

Table 5-4 Estimated odds ratios and 95% confidence intervals for the effect of the ‘*phase* symptom frequency × severity score’ on perceived exercise performance and recovery time post exercise across menstrual cycle *phases* (*i.e.*, *phase* one: ‘early follicular phase’; *phase* two: ‘late follicular/ovulatory phase’; and *phase* three: ‘mid-luteal phase’) and combined, monophasic, oral contraceptive pill _mOCP *phases* (*phase* one: ‘_mOCP withdrawal’, days 1 to 7 of pill-free days; *phase* two: ‘_mOCP consumption, days 1 to 7’; *phase* three: ‘_mOCP consumption, days 8 to 14’; and *phase* four: ‘_mOCP consumption, days 15 to 21’) in naturally menstruating women (n = 19) and pill users (n = 21).

Group	Reduced performance				Improved performance				Longer recovery				Quicker recovery				
	Phase 1	Phase 2	Phase 3	Phase 4	Phase 1	Phase 2	Phase 3	Phase 4	Phase 1	Phase 2	Phase 3	Phase 4	Phase 1	Phase 2	Phase 3	Phase 4	
‘ <i>Phase</i> symptom frequency × severity score’	Naturally menstruating	n = 8	n = 1	n = 1	-	n = 4	n = 14	n = 9	-	n = 10	n = 0	n = 1	-	n = 1	n = 14	n = 8	-
		1.07 (1.01 to 1.14)*	-	-	-	0.84 (0.66 to 1.08)	1.00 (0.97 to 1.05)	1.00 (0.97 to 1.04)	-	1.04 (1.00 to 1.08)	-	-	-	0.99 (0.96 to 1.03)	1.01 (0.97 to 1.05)	-	-
_m OCP		n = 12	n = 0	n = 0	n = 0	n = 1	n = 12	n = 12	n = 12	n = 9	n = 0	n = 0	n = 0	n = 5	n = 5	n = 5	
		1.04 (1.00 to 1.08)*	-	-	-	-	0.99 (0.97 to 1.01)	0.99 (0.96 to 1.01)	1.00 (0.98 to 1.02)	1.03 (1.00 to 1.05)*	-	-	-	1.01 (0.99 to 1.03)	1.00 (0.98 to 1.02)	1.00 (0.99 to 1.02)	

Values are odd ratios (95% CI). *denotes odd ratios deemed significant (P ≤ 0.05). -denotes data not available (*e.g.*, no participant/not enough participants reported specific variable in specific *phase*). _mOCP, combined monophasic oral contraceptive pill.

5.4 Discussion

The purpose of this Chapter was to examine the type, frequency, and severity of symptoms experienced by naturally menstruating women and _mOCP users, and their perceived effect on exercise performance and recovery time post exercise. Two approaches were used to answer these aims, firstly an initial retrospective 54-part online survey, and secondly a cycle and symptom form completed daily across one MC or _mOCP *cycle*. Data from the initial retrospective survey showed that cycle related symptoms were commonly reported by a group of active women, and there appears to be no differences in symptomology between naturally menstruating women and _mOCP users. As such, these results emphasise the need for active women, and those working with them, to consider regular and consistent monitoring of cycle related symptoms, to the same degree, irrespective of _mOCP use. Moreover, data from daily symptom tracking showed that the type of symptoms reported, as well as symptom frequency and severity, changed across MC and _mOCP *phases*, whereby participants experienced a greater frequency and severity of symptoms whilst bleeding (*i.e.*, during *phase* one of the MC in naturally menstruating women, and during the _mOCP-free days in pill users) compared to all other timepoints. Finally, experiencing a greater frequency and severity of symptoms, and therefore having higher '*phase* symptom frequency × severity score', was associated with a greater likelihood of perceived negative outcomes, including a perceived reduction in exercise performance and a perceived longer recovery time post exercise, whilst participants were bleeding. Taken together, these results highlight the importance of daily symptom mapping, as retrospective recall does not account for the potential effect of different *phases* on the frequency and severity of cycle related symptoms, which when elevated might translate to negative implications on perceived performance and recovery outcomes. These findings support the need for further research to establish whether the symptoms experienced and their perceived negative effects result in an actual reduction in performance and/or recovery in sportswomen.

Data from the present Chapter showed that cycle related symptoms are prevalent in _mOCP users, and that symptomology appears to be similar amongst naturally menstruating women and _mOCP users, even though OCPs are often prescribed to women with the intention of alleviating the negative symptoms associated with the MC (Elliott-Sale & Hicks, 2018; Ferries-Rowe *et al.*, 2020; Wong *et al.*, 2009). Indeed, this Chapter shows that the most reported symptoms in _mOCP users are 'Mood changes/ irritability/anxiety', which agrees with previous

findings by Heather *et al.* (2021) who reported that the majority (56%) of OCP users reported side effects of use, with the most common being mood disturbances. Interestingly, results from the current Chapter show no difference in the frequency and severity of cycle related symptoms between the naturally menstruating women and _mOCP users. This is despite 48% of pill users in the present Chapter reporting the use of _mOCPs to manage the symptoms experienced during the MC, although it is important to note that previous experience of symptoms prior to _mOCP use is unknown so this finding must be interpreted in context. In agreement with these findings, Clarke *et al.* (2021) showed similarities in the symptoms experienced between HC users and naturally menstruating women, although this Chapter extends these findings using a novel symptom monitoring tool. However, regardless of the prevalence of cycle related symptoms, they might not be seen as a deterrent from OCP use, with previous work highlighting that the reported benefits of HC use, such as its use as a birth control measure, outweigh the experience of negative symptoms (Martin *et al.*, 2018; Parker *et al.*, 2022). Thus, it is important that sportswomen do not solely make their decision to use, or not use, OCPs based on the cycle related symptom data reported herein and all relevant factors should be considered before individuals make this decision. Overall, these results indicate that with or without the intention of OCP use to reduce cycle related symptoms, there appears to be no difference in symptomology between naturally menstruating women and _mOCP users. Therefore, practitioners are recommended to monitor the magnitude of cycle related symptoms in all sportswomen irrespective of reproductive hormonal profile.

Few studies in active women have quantified the symptoms experienced across pre-defined MC and _mOCP *phases* in real-time, and instead have focused on collecting retrospective symptom data across the MC and HC *cycle* (Armour *et al.*, 2020; Brown *et al.*, 2021; Bruinvels *et al.*, 2021; Clarke *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022; Oxfeldt, Dalgaard, Jørgensen, & Hansen, 2020; Parker *et al.*, 2022; Read *et al.*, 2021; Solli *et al.*, 2020). However, considering the different potential factors driving symptoms, and the individual nature of the MC and responses to _mOCP use, key timepoints for symptoms are likely to vary across *phases* and between individuals. Indeed, the present Chapter shows that during *phase* one of the MC the frequency and severity of symptoms experienced was greater when compared to all other MC *phases*, in naturally menstruating women. This agrees with previous work in the general population showing that moderate-to-severe MC symptoms (physical and psychological) appear towards the end of the luteal phase, immediately preceding the onset of menstruation, peak during menstruation, and then reduce

by the end of menstruation (Taylor, 1979). Whilst the aetiology of cycle related symptoms remains unknown and is likely complex and multifactorial, the changes in symptoms across MC *phases* might be attributable to changes in endogenous sex hormones (oestrogen and progesterone) across the MC. For example, the ‘*phase* symptom frequency × severity score’ in this Chapter was greater when oestrogen and progesterone are at their lowest in the naturally menstruating group. Additionally, an overproduction of prostaglandins occurring during menstruation has been commonly cited to result in primary dysmenorrhea (Guo *et al.*, 2013), as well as the impact of changes in the release of inflammatory markers (Ma *et al.*, 2013; Puder *et al.*, 2006) and reactive oxygen species (Gaskins *et al.*, 2012) which together might have caused the ‘period pain’ and other physical symptoms experienced at this time in the present Chapter. Moreover, it is thought that changes in neurobiology across the MC, such as alterations in serotonergic and gamma-aminobutyric acid systems (Ans dell *et al.*, 2019), as well as dopaminergic signalling (Del Río *et al.*, 2018) could affect the prevalence and severity of psychological symptoms experienced by naturally menstruating women across MC *phases*. Results from the current Chapter also revealed that, like their naturally menstruating counterparts, _mOCP users also experienced changes in symptom frequency and severity across _mOCP *phases*, with a greater frequency and severity of symptoms reported during the _mOCP-free days when typically, a withdrawal bleed occurs, which agrees with previous literature (Sulak *et al.*, 2000). Therefore, it is plausible that the action of bleeding during the pill-free days might play a role in the aetiology of _mOCP symptoms during the pill-free days regardless of circulating sex hormone concentrations. In contrast, given that exogenous ethinyl oestradiol has a higher ER affinity and is more potent than endogenous oestradiol (Bennink, 2004), its sudden withdrawal during the pill-free days might remove any potential positive effects on symptomology, and thus contribute to the symptoms experienced during this time. Although, it is important to gain a better understanding of the aetiology of cycle related symptoms in both naturally menstruating and _mOCP users from future research.

Understanding the frequency and severity of symptoms is important as recent research has shown that an increased number of both physical and psychological cycle related symptoms is associated with changes in various aspects of exercise performance and training (Armour *et al.*, 2020; Brown *et al.*, 2021; Bruinvels *et al.*, 2021; Clarke *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022; Oxfeldt, Dalgaard, Jørgensen, & Hansen, 2020; Parker *et al.*, 2022; Read *et al.*, 2021; Solli *et al.*, 2020). Specifically, Bruinvels *et al.* (2021) reported that experiencing a greater number of MC symptoms was associated with

changing/missing training, missing a competition, as well as needing to use pain medication. Although agreeing with the work by Bruinvels *et al.* (2021), the current Chapter extends these findings to consider the *phase* effect of cycle related symptoms on exercise performance and recovery time post exercise. Indeed, the current Chapter highlights that having a higher ‘*phase* symptom frequency × severity score’ was associated with negative outcomes, such as a perceived reduction in exercise performance and a longer recovery time post exercise, whilst participants were bleeding (*i.e.*, *phase* one in both naturally menstruating women and _mOCP users). Whilst previous work investigating the effect of the MC and OCP use on performance and training has focussed on qualitative outcomes, few studies have examined the influence of symptoms on these outcomes. Indeed, *Chapter 3* showed that exercise performance might, on average, be reduced by a trivial amount during the early follicular phase of the MC, compared with all other MC phases, in some individuals. Whilst a mechanistic explanation was beyond the scope of this Chapter, it was indicated that performance changes could be attributable to the fluctuations in endogenous sex hormones across the MC. However, as established from the current results, the perceived reduction in performance during *phase* one of the MC, in some individuals, could be attributable to the greater magnitude of symptoms at this timepoint which was not considered within *Chapter 3*. Unfortunately, within the current Chapter it was not possible to compare time aligned phase symptomology between naturally menstruating women and _mOCP users, thus it is unknown if the previous trivial difference in exercise performance reported between naturally menstruating and OCP users in *Chapter 4* might also be explained by group differences in symptom type, frequency, and severity during *phase* one, when both groups were bleeding. As such, there is a need to adopt a multifaceted approach to investigating the effect of the MC and _mOCP use on performance and training, which considers not only the reproductive hormonal milieu, but also the symptoms experienced by the individual, irrespective of whether they are naturally menstruating or taking the _mOCP. Thus, *Chapter 6* will adopt this real-time, daily, data collection processes to investigate the potential relationship between cycle related symptoms and objective exercise performance and training outcomes. From a practical position, it is important for practitioners to track cycle related symptom data daily, rather than retrospectively, to identify key timepoints where an individual might experience a greater magnitude of symptoms which could potentially negatively impact their perception of performance and/or recovery.

5.4.1 Limitations and future directions

It is important to acknowledge that the current Chapter has several limitations. Indeed, data was collected from a group of recreationally active women, therefore the average response presented in this Chapter might not be specific and meaningful to all women. As such, further research investigating within different populations (*i.e.*, elite woman athletes) is warranted. Data from the initial 54-part online survey are self-reported, and therefore reliant on memory recall. Additionally, this Chapter used an adapted version of the MSi tool developed by Bruinvels *et al.* (2021) to evaluate the type, frequency, and severity of symptoms, however, quantifying symptoms in this way has not been formally validated. Moreover, although the current Chapter utilised two (*i.e.*, calendar-based counting and urinary ovulation detection kits) out of the possible three recommended methods to identify MC *phase* and confirm an ovulatory cycle for experimental designs within this field, the methods used do not provide any information regarding endogenous sex hormone concentrations (Thompson & Han, 2019). Since MC *phase* was not subsequently verified by serum for both oestrogen and progesterone (due to restrictions because of the COVID-19 pandemic) it slightly reduces our confidence in the accuracy of the sex hormone environment implied by the phase definitions used in the present Chapter (*i.e.*, if the actual sex hormone concentrations matched the predicted concentrations; [Elliott-Sale *et al.*, 2021]). Whilst we have a high degree of confidence in the determination of *phases* one and two, as oestrogen and progesterone need to be low to menstruate, and a positive urinary ovulation test result infers the pre-ovulatory peak in oestrogen, *phase* three is estimated and thus, where possible, future studies need to improve methodological quality (*e.g.*, appropriate biochemical outcomes to confirm MC *phase*). However, it is important to acknowledge the real-world application of the methods utilised in the present Chapter. For example, it can be impractical and expensive to take serum blood samples from all women to verify phase of cycle within an applied environment and instead the use of non-evasive, cost-effective, and immediate methods, such as BBT and urinary ovulation detection kits offer useful insights into potential sex hormone concentrations (Hicks *et al.*, 2022). Only naturally menstruating women and _mOCP users were included in the current Chapter, however previous research shows that negative symptoms are more common in progestin-only HC users (Martin *et al.*, 2018; Parker *et al.*, 2022). Therefore, future research should consider investigating symptoms and perceived performance and training effects in active women using different forms of HC. Previous education and experience with cycle tracking might also have affected the results in the present Chapter. Specifically, 81% of

naturally menstruating women reported previously tracking their cycle characteristics (*i.e.*, cycle length and number of days bleeding) and symptom type, severity, and timing, whereas only 25% of _mOCP users had experience tracking their pill *cycle*, which could have impacted self-awareness of symptoms and the subsequent reporting of them. It is also important to acknowledge that symptomology is complex, and it remains impossible to decipher whether the reported symptoms were directly related to the MC or _mOCP use. Further, it is important to consider the individual nature of the MC and responses to _mOCP use, and that physiology (McNulty *et al.*, 2021), symptoms (Brown *et al.*, 2021), and lifestyle factors (*i.e.*, those known to have a bi-directional relationship with sex hormones, such as diet, exercise, sleep, and stress) might not be the same across consecutive MCs or _mOCPs within the same individual. As such, it is possible that symptoms might differ largely between individuals, and between cycles within the same individual. Therefore, practically it is important to consider these effects on an individual level, as some women might be affected and others not, and future studies should explore variability in symptoms within individuals from one cycle to the next to facilitate a deeper understanding of individual responses. Finally, data were collected during the COVID-19 pandemic, thus it is unknown whether, and to what extent, this might have had an influence on the cycle related symptoms experienced during this time (Phelan *et al.*, 2021). Despite these limitations, our dataset provides a new insight into the symptoms experienced by some naturally menstruating women and _mOCP users, which should be considered by sportswomen and those working with them.

5.4.2 Practical implications

These findings emphasise the importance of continued awareness of cycle related symptoms, and their potential impact on exercise performance and recovery time post exercise to inform best practice. Given the similarities in symptomology between naturally menstruating and _mOCP users, regular screening of symptom profiles across all women (irrespective of reproductive hormonal profile) is advised based on these results, and the use of methods provided in the present Chapter to monitor symptoms might be considered as a suitable tool within a practical setting. Moreover, given the potential perceived negative effect of symptoms on exercise performance and training outcomes at different timepoints across the MC and _mOCP *cycle*, real-time, consistent, symptom mapping should be considered to identify and predict key windows of opportunity for symptom management strategies, and thus limit any potential negative effect of symptoms on performance or training outcomes. Additionally, the inter-individual variability in symptoms experienced and their association with perceived

performance and training outcomes in the present Chapter supports an individualised approach. For example, it is likely that individuals who experience a greater magnitude of symptoms and perceive these symptoms to influence performance and training will report the biggest benefit of symptom mapping alongside proactive symptom management.

5.5 Conclusion

This Chapter provides an in-depth insight into the type, frequency, and severity of symptoms experienced by a group of naturally menstruating women and _mOCP users, across pre-defined MC and _mOCP *phases*, relative to their perceived impact on exercise performance and recovery time post exercise. Results revealed that cycle related symptoms were common in these women, but there were no differences in symptomology between naturally menstruating women and _mOCP users. Additionally, the type, frequency, and severity of symptoms changed across MC and _mOCP *phases*, with a greater frequency and severity of symptoms reported whilst participants were bleeding in both groups. Finally, a higher '*phase* symptom frequency × severity score', was associated with perceived negative outcomes, such as reduced exercise performance and a longer recovery time post exercise whilst participants were bleeding. As such, from a practical perspective, these results emphasise the need for sportswomen, and those working with them, to consider regular and consistent monitoring of symptoms, and any associated impact on exercise performance and training, rather than relying on retrospective recall data. This recommendation is applicable regardless of _mOCP use. In turn, this should be accompanied, where needed, by individualised symptom management strategies to minimise any potential negative effects of cycle related symptoms on exercise performance and training, particularly around key phases where the magnitude of symptoms might be greater. From a research perspective, further investigation is needed to provide additional insights into cycle related symptoms in sportswomen, with a particular focus on understanding the influence of symptomology on objective markers of exercise performance and recovery time post exercise (see *Chapter 6*).

CHAPTER 6 – THE EFFECT OF THE MENSTRUAL CYCLE, ORAL CONTRACEPTIVE PILL USE, AND RELATED SYMPTOMS ON EXERCISE PERFORMANCE AND RECOVERY TIME POST AN EXERCISE SESSION IN RECREATIONALLY ACTIVE WOMEN.

This Chapter has been presented at the following conferences:

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). The menstrual cycle, oral contraceptive pill use, and associated symptoms on exercise performance and recovery. Pre-conference symposium at: Europhysiology 2022; 15th – 18th September; Copenhagen, Denmark.

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). Are performance and recovery time influenced by the menstrual cycle, oral contraceptives, and associated symptoms. 8-minute oral presentation at: Women in Sport Congress; 17th – 19th August; Melbourne, Australia.

McNulty, K.L., Ansdell, P., Goodall, S., Thomas, K., Elliott-Sale, K.J., Howatson, G., & Hicks, K.M. (2020). The menstrual cycle, oral contraceptive pill use, and associated symptoms on exercise performance and recovery. Symposium at: The Physiological Society Physiology Symposium 2022; 11th May; Derby, United Kingdom.

6.1 Introduction to Chapter 6

One unique consideration for sportswomen is the potential influence of fluctuations in endogenous and exogenous sex hormones on exercise performance (Burrows & Peters, 2007; Constantini *et al.*, 2005; Lebrun *et al.*, 2013; Rechichi *et al.*, 2009), as well as the responses to and recovery from exercise (Hackney *et al.*, 2019; Minahan *et al.*, 2015; Romero-Parra, Cupeiro, *et al.*, 2021; Romero-Parra, Rael, *et al.*, 2021). Specifically, as highlighted in *Chapters 3 and 4* the MC and OCP use might have subsequent implications for exercise performance, whereby both strength and endurance performance might be reduced, by a trivial amount, during the early follicular phase of the MC, and OCP use might potentially result in a slightly inferior exercise performance, on average, compared to naturally menstruating women. Moreover, longitudinal resistance training studies also support a possible effect (both enhanced and impaired) of fluctuations in sex hormones across the MC (Kissow *et al.*, 2022; Thompson *et al.*, 2020) and with OCP use (Dalgaard *et al.*, 2019; Myllyaho *et al.*, 2021; Riechman & Lee, 2021; Sung *et al.*, 2022) on adaptation outcomes. However, whilst most studies examining the MC and OCP use have focused on investigating what happens during exercise performance, or following a training programme, both the responses to, and recovery from an exercise session have been relatively overlooked in the literature (Hackney *et al.*, 2019; Mackay *et al.*, 2019; Romero-Parra, Alfaro-Magallanes, *et al.*, 2020; Romero-Parra, Barba-Moreno, *et al.*, 2020; Romero-Parra, Rael, *et al.*, 2021). As such, the potential role of endogenous and exogenous sex hormones on the responses to, and recovery process post exercise are not fully understood, despite being critical timepoints relative to the adaptation process associated with exercise.

As highlighted in *Chapter 2, Section 2.5.3*, there are a range of suggested mechanisms by which the cyclical fluctuations in oestrogen and progesterone across the MC might affect the responses to, and recovery from exercise. For example, research in animal models suggests that oestrogen might offer protection against EIMD and play a role in muscle repair and regeneration (Tiidus, 2005). Despite an oestrogenic effect on these mechanisms, few studies to date have investigated the role of changes in endogenous sex hormones across the MC on recovery outcomes following exercise in women. Of the literature available, Hackney *et al.* (2019) demonstrated that a longer recovery, following endurance-based exercise, was required during the mid-follicular phase compared to the mid-luteal phase. In contrast, Romero-Parra and colleagues found no differences across the MC in direct (Romero-Parra, Barba-Moreno, *et al.*, 2020) or indirect markers of recovery, except perceived muscle soreness (Romero-Parra, Alfaro-Magallanes, *et al.*, 2020), following an eccentric squat-based exercise. A recent

systematic review with meta-analysis concluded that longer recovery times might be required post exercise during the early follicular phase, when endogenous sex hormone concentrations are at their lowest, as women might be more vulnerable to EIMD (Romero-Parra, Cupeiro, *et al.*, 2021). Although, the authors noted that the lack of research in this area (*i.e.*, only seven studies have compared EIMD across MC phases), and large between-study variance limit the findings reported within the review. Therefore, it is apparent that further research investigating the effect of fluctuations in endogenous sex hormones across the MC on the recovery process post exercise is warranted.

As discussed in *Chapter 2, Section 2.3.5*, the different sex hormone profile experienced by _mOCP users, compared to naturally menstruating women, might have different implications for the responses to, and recovery from exercise. For instance, in the study by Hackney *et al.* (2019) the authors attributed their findings of a longer recovery during the mid-follicular phase to the antioxidant and/or stabilising role of oestrogen being mitigated at this timepoint. Thus, given the downregulated endogenous oestrogen profile in _mOCP users across the pill-taking days the findings by Hackney *et al.* (2019) in naturally menstruating women might not be replicated in _mOCP users. Indeed, previous studies have shown a reduced recovery after eccentric exercise in OCP users compared to naturally menstruating women (Hicks *et al.*, 2017; Mackay *et al.*, 2019; Minahan *et al.*, 2015; Roth *et al.*, 2001). In contrast, other studies have shown an improved recovery response in OCP users (Hayward *et al.*, 1998; Thompson *et al.*, 1997), as well as no differences between the groups (Savage & Clarkson, 2002). Although, discrepancies between studies could be attributed to the different potency of exogenous hormones found in OCPs, which could influence any effect (Elliott-Sale & Hicks, 2018). Moreover, given the changing hormonal profile between pill-taking and pill-free days it could be theorised that the recovery response to exercise might differ across the _mOCP cycle. For example, a study by Romero-Parra, Rael, *et al.* (2021) showed a greater biomarker (*i.e.*, CK) response during the recovery period post an eccentric squat-based exercise during the pill-free days, suggesting a longer recovery period was needed at this time, although no difference in jump performance and perceived muscle soreness were reported across the _mOCP cycle. Despite these initial findings, relatively few studies have addressed the potential influence of _mOCP use versus naturally menstruating women, and the different sex hormone environments across the _mOCP cycle, on the responses to, and recovery from an exercise session, and further research is required.

Whilst exercise performance and the recovery process post exercise might be susceptible to changes in exogenous and endogenous sex hormone concentrations, another plausible reason could be the influence of cycle related symptoms and their relationship with perceived outcomes. Indeed, previous studies have shown that cycle related physical and psychological symptoms are commonly reported in recreationally active women and have the potential to influence an individual's ability to perform and train (Bruinvels *et al.*, 2021; Martin *et al.*, 2018). Specifically, *Chapter 5* showed that experiencing a greater number and severity of symptoms was associated with a perceived reduction in exercise performance and a longer recovery time post exercise, in both naturally menstruating women and _mOCP users. As such, these findings highlight the importance of considering not only the reproductive hormonal milieu on objective exercise performance and training outcomes, but also cycle related symptoms and perceived responses. To date, however no study has adopted such a multifaceted approach when investigating the effects of endogenous and exogenous sex hormones on exercise performance and recovery outcomes. Furthermore, previous studies have used long-established research designs which align data analysis to predefined cycle phases whereby sex hormone concentrations significantly differ. Whilst this is an optimal design for investigating the impact of key hormone ratios on outcomes, it does not paint a full picture of the holistic impact of the MC and _mOCP *cycle*, as often cycle related symptoms and their perceived impact are reported to be highest during the shifts between cycle phases (Bruinvels *et al.*, 2022). Thus, by using this type of design, the impact of any residual effects of cycle related symptoms on exercise performance and the recovery process post exercise are potentially missed. Establishing whether there is a residual effect of cycle related symptom frequency and severity, irrespective of cycle phase is important as sportswomen need to be able to perform and train regardless of sex hormone concentration.

Overall, understanding the effect of the MC, _mOCP use, and related symptoms on exercise performance, as well as the responses to and recovery from exercise is essential to optimise the support provided to sportswomen. Therefore, the purpose of this Chapter was to: 1) determine whether MC and _mOCP *phase* influence physical and perceptual measures of exercise performance and recovery time following an exercise session; and 2) evaluate whether the symptoms experienced in the days before and after exercise are associated with exercise performance and recovery time post exercise.

6.2 Method

6.2.1 Participants

To ensure a power of 0.85 with an alpha level of 0.05, a sample size of 28 participants (14 naturally menstruating women and 14 _mOCP users) was necessary, as calculated from the anticipated change in CMJ height prior to and post exercise across the MC using G* power (Thompson *et al.*, 2019). To protect against drop out, and the potential large percentage of exclusions in this research area (Thompson & Han, 2019), the same 42 women (21 naturally menstruating women and 21 _mOCP users) included in *Chapter 5* also participated in this Chapter. Full details of participant inclusion and exclusion criteria, as assessed using the retrospective online 54-part survey, are reported in *Chapter 5*. In brief, all naturally menstruating participants self-reported having a regular MC, were not taking any form of HC, and were free from any other medication, MC related irregularity, or condition known to affect the HPO axis. Participants in the _mOCP group reported taking the _mOCP for a minimum of three-months prior to the study. All participants were deemed at least recreationally active, with a small percentage (19%) classified as trained (McKay *et al.*, 2022). Furthermore, all participants reported regularly exercising at home and all self-reported as being highly familiar, confident, and proficient in basic movement patterns, such as squat and lunge. All participants were free from any injury in the past six months. Full ethical approval was granted from the Northumbria University, Health and Life Sciences ethics committee (HLSKM29409) and the study was conducted in accordance with the Declaration of Helsinki. Written, informed consent was obtained from all participants prior to participation. This Chapter uses the terms ‘woman’ for people who self-report identifying with the sex they were assigned with at birth (Robinson *et al.*, 2022).

6.2.2 Research design

This Chapter utilised a mixed design with a between-subjects factor of group (naturally menstruating women and _mOCP users), and a within-subjects factor of time (pre, post, and 24, 48, and 72 h post exercise). A schematic of the research design is shown in Figure 6.1. Participants were given a verbal explanation of the study during an online pre-testing session and to habituate participants to all experimental protocols, and negate any potential learning effect, participants attended a virtual familiarisation session a minimum of two-weeks prior to any experimental sessions. During this familiarisation session participants practiced all physical and perceptual measures used in the present Chapter. Additionally, to ensure that the

exercise session was not an unaccustomed bout of exercise (to avoid any potential repeated bout effect), and to ensure that exercise techniques were correct, participants completed the exercise session in full during the familiarisation session. Exercise sheets were provided (see *Appendix L*) which detailed how to perform each exercise, and each exercise was coached during the familiarisation session to ensure the exercise session was performed correctly. Following familiarisation each participant performed the exercise session (see *Section 6.3.3*) at three different timepoints across their MC or m OCP cycle (see *Section 6.3.2*). For all participants, starting MC or m OCP phase was counterbalanced, and trials were conducted over one or the following consecutive MC or m OCP cycle. Pre, post, and 24, 48, and 72 h post the exercise session participants completed physical (see *Section 6.3.4*) and perceptual (see *Section 6.3.5*) measures. All sessions were completed at the same time each day (± 2 h), across each testing phase, to minimise the effects of diurnal variation. Additionally, all participants tracked cycle related data and their symptoms daily (see *Section 6.3.1*) across the study duration to quantity symptom frequency, and severity in the days before and after the exercise session in each testing phase. Participants completed daily cycle and symptom tracking at the same time each day (± 2 h), and a daily text reminder from the leading researcher was sent to all participants to ensure compliance.

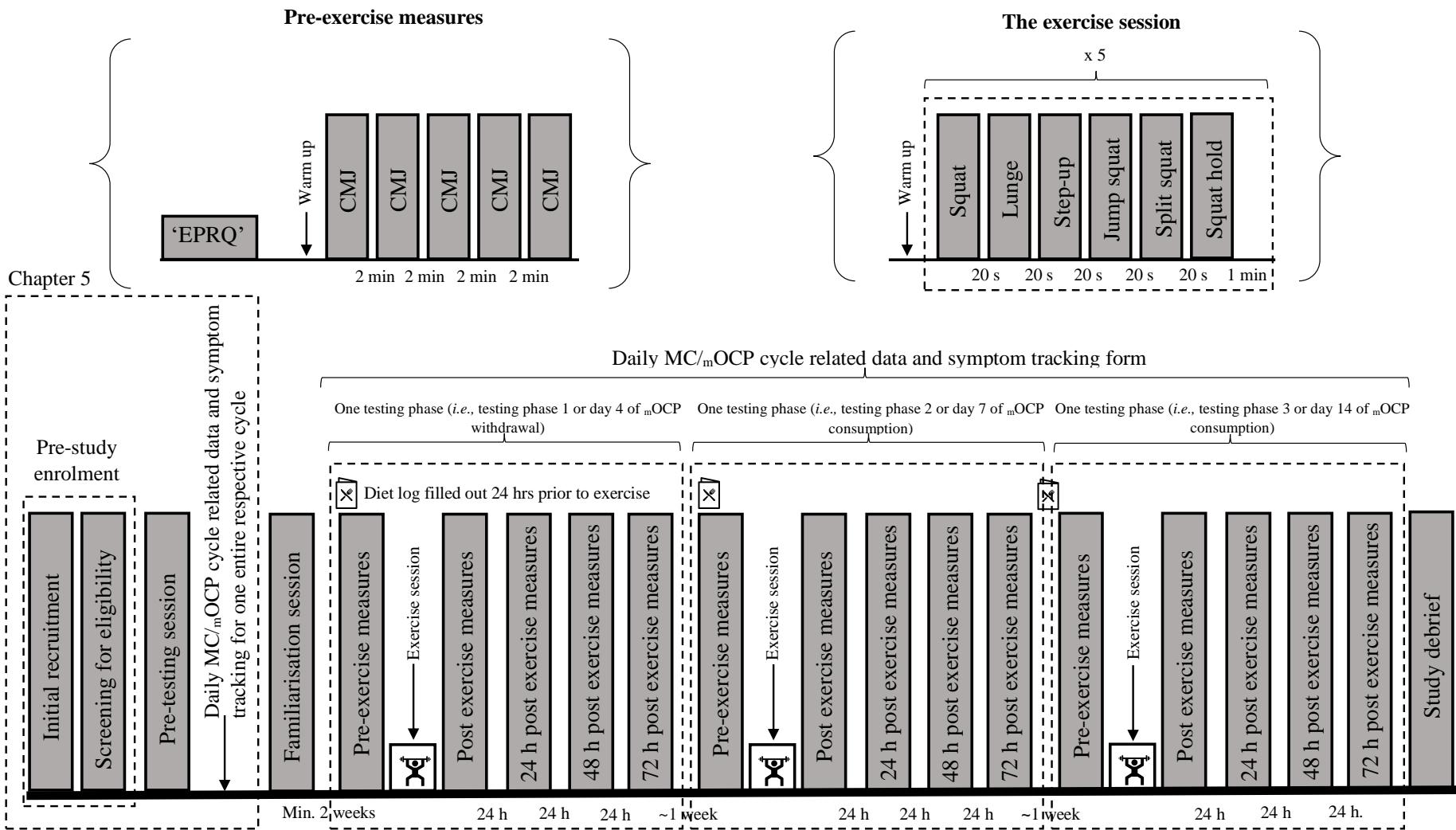


Figure 6-1 Schematic showing the research design. CMJ, countermovement jump; ‘EPRQ’, ‘Elite Performance Readiness Questionnaire’; MC, menstrual cycle; _mOCP, combined monophasic oral contraceptive pill.

6.2.2.1 Experimental controls

Participants were instructed to complete the exercise session in a rested state having refrained from strenuous, unaccustomed exercise (72 h) and any form of strenuous physical activity (48 h) prior to the exercise session. To ensure that training activities between testing *phases* were similar, participants recorded their training session data daily in an online form (Google Forms, Google, United Kingdom). As it is not common practice for individuals to compete in a fasted state (*i.e.*, more than 3 h post absorptive), participants followed their normal dietary routine, and completed the exercise session in a ‘normal’ fed state. Participants were asked to avoid consuming both alcohol and caffeine (24 h) prior to the exercise session, and to avoid any recovery enhancing supplements and any anti-inflammatories during each testing *phase*. Participants recorded their dietary intakes during the 24 h prior to each exercise session in an online food diary (Google Forms, Google, United Kingdom) and were asked to replicate this diet as closely as possible in the 24 h preceding each subsequent exercise session. To avoid the transient acute peak in exogenous ethinyl oestradiol concentration (Sneader, 2005), participants in the pill group completed the exercise session and outcome measures post a minimum of 2 h after taking their _mOCP.

6.2.3 Procedures

6.2.3.1 Cycle related data and symptom tracking

Cycle related and symptom data for all participants was collected as in *Chapter 5*, where each participant received a daily unique link to an online form (Google Forms, Google, United Kingdom), which gathered data including: 1) *phase* of MC or _mOCP cycle; 2) blood flow during menses in naturally menstruating women or the withdrawal bleed in _mOCP users; 3) symptom type, presence, and severity; and 4) training session data (*i.e.*, type of training performed, duration, and session RPE). Additionally, to identify MC *phases* participants in the naturally menstruating group were asked to track ovulation using the same method as in *Chapter 5*. In brief, urinary ovulation detection kits (Advanced Digital Ovulation Test, Clearblue, Switzerland), and BBT from a digital thermometer (One Step Digital Basal Thermometer, Home Health UK Ltd, United Kingdom) were used. Recording of daily cycle related data and symptom tracking began on day one of menses in naturally menstruating women, or day one of _mOCP withdrawal in pill users and continued until completion of the study.

6.2.3.2 Menstrual cycle and combined, monophasic, oral contraceptive pill phase classification

The MC and _mOCP cycle, were separated into key *phases*. To ensure the exercise session occurred at timepoints where there were key differences in the sex hormone profile across the MC in naturally menstruating women, the exercise session occurred, and recovery was tracked during the following *phases*: ‘early follicular’ *phase* (*i.e.*, testing *phase* one = low oestrogen and progesterone); the ‘late follicular’ to ‘ovulatory’ *phases* (*i.e.*, testing *phase* two = rising/high oestrogen and low progesterone); and the ‘mid-luteal’ to ‘late luteal’ *phases* (*i.e.*, testing *phase* three = high oestrogen and progesterone). Specifically, during testing *phase* one the exercise session occurred within two-days (day one of menses: n = 1; day two of menses: n = 19) of the onset of self-reported menstruation. To help determine when the exercise session would occur during testing *phase* two, cycle related data from the month prior (*i.e.*, average cycle length and the day of ovulation) were used to predict day of ovulation. Subsequently, for participants in the naturally menstruating group the exercise session in testing *phase* two occurred either on the day of a positive ovulation test (n = 2), or within 24 (n = 8), 48 (n = 3), or 72 h (n = 7) prior to a positive ovulation test. Although, it is acknowledged that this gives a broad range of oestrogen status. For example, it is likely that for those tested on the day of a positive ovulation test, a declining oestrogen profile (*i.e.*, moderate oestrogen concentration) would have been captured, whereas for those tested within 24 h of a positive ovulation test, oestrogen concentration was likely at its highest (Elliott-Sale *et al.*, 2021). During testing *phase* three participants in the naturally menstruating group performed the exercise session between six to eight days (day six: n = 2; day seven: n = 12; and day eight: n = 6) following a positive ovulation test, which was supported by BBT measurement (*i.e.*, a rise in BBT [approximately 0.25 to 0.50 of a degree] that remains relatively constant for 10 to 16 days). Participants that did not report a positive ovulation test within 72 h following the exercise session in testing *phase* two or a positive ovulation test alongside a rise in BBT post ovulation in testing *phase* three were subsequently excluded from the analysis (n = 1). For the pill group, the testing *phases* in the _mOCP cycle were defined using counting from either the first day of the pill withdrawal *phase* or the first day of the pill consumption *phase*. During testing *phase* one, the exercise session occurred on day 4 of the _mOCP withdrawal *phase* (\pm 1 day). During testing *phases* two and three, the exercise session occurred on day 7 (\pm 1 day) and day 14 (\pm 1 day) of the _mOCP consumption *phase*, respectively. These time points were chosen because they are aligned to the testing timepoints of the naturally menstruating group. It is important to

acknowledge that these profiles, reflecting m OCP consumption and withdrawal, are pseudo-phases as they are ‘artificial’ *phases* in comparison with the *phases* of the natural MC, but for the purposes of this Chapter will be referred to as *phases*. Further, it is important to note that herein this Chapter will use the umbrella terms ‘testing *phase* one, two, and three’ which relate to the above respective timepoints in the MC and m OCP cycle.

6.2.3.3 The exercise session

Following assessment of pre-exercise outcome measures and prior to the exercise session, a standardised warm-up, designed to progressively prepare participants for the subsequent activity, was completed. The warm-up consisted of eight exercises (*i.e.*, 60 s jogging on the spot, 30 s high knees, 30 s heel flicks, inch worm [10 repetitions], standing hurdle stretch [5 repetitions each leg], side lunge [5 repetitions each leg], squat [5 repetitions], and forward lunge [5 repetitions each leg]), performed once through, with 10 s rest between each exercise. The exercise session was completed at each participant’s home and all participants were supervised by a member of the research team virtually on Zoom (Zoom, Zoom Video Communications, United States of America). The exercise session protocol was an amended version of the ‘Gambetta Leg Circuit’ (Gambetta, 2007). This protocol has been shown to elicit strength-based adaptations when used as a typical, regular, training stimulus (Gambetta, 2007), and due to the restrictions of the COVID-19 pandemic, the protocol was easy to implement outside of a lab environment, thus providing a rationale for the use of the ‘Gambetta Leg Circuit’ in the present Chapter. The exercise session consisted of six lower body focused exercises performed five times, with 20 s rest between each exercise, and one minute’s rest between each circuit. The six lower-body exercises consisted of: 1) bodyweight squat (20 repetitions); 2) bodyweight lunge (10 repetitions each leg); 3) bodyweight step-up (10 repetitions on each leg ensuring a knee angle of roughly 90°); 4) bodyweight jump squat (10 repetitions); 5) bodyweight split squat (10 repetitions on each leg); and 6) bodyweight squat hold (30 s). Participants aimed to complete each exercise at a standardised tempo, whereby the goal was to complete one repetition per second for the bodyweight squat, step-ups, and split squats, and as close to one repetition per second as possible on the jump squat and lunge exercises. The entire protocol lasted approximately 30 minutes in duration and all participants were verbally encouraged during each session to ensure that the entire protocol was completed. During the exercise session participants were required, where available, to record HR ($n = 37$) using a commercially available HR monitor (*i.e.*, Apple Watch, Garmin, and Fitbit) immediately pre and post the warm-up, and after each completed set during the one-minute rest period. Likewise, RPE was

recorded immediately pre and post the warm-up and after each completed set during the one-minute rest period using Borg's CR10 scale.

6.2.3.4 Physical measures of exercise performance and recovery time

Participants completed two practice CMJs which acted as a warm-up. Following this, participants performed five CMJs, with two-minutes passive rest between each jump. To perform the CMJ participants began in an erect position with hands akimbo. On verbal command, participants performed a downward countermovement before jumping vertically (with their legs straight during the flight phase) for maximum height. Jump height (cm) and flight time (s) were then assessed using the 'My Jump 2' app. The app has been shown to be an accurate and reliable measure of CMJ performance (Balsalobre-Fernández *et al.*, 2015). With the lead investigator virtually present each participant self-recorded their own jump using a mobile device capable of recording in 240 FPS and sent this recording to the lead investigator for analysis. Participants were instructed to record each CMJ by laying their phone on the ground, with the camera facing them (in the frontal plane), at a distance approximately 1.5 m away. In addition to a marker of performance, changes in CMJ height were used as a marker of fatigue and recovery in the present Chapter (Brownstein *et al.*, 2017; Cormie *et al.*, 2009; Halson, 2014; Twist & Highton, 2013; Watkins *et al.*, 2017).

6.2.3.5 Perceptual measures of exercise performance and recovery time

The 'Elite Performance Readiness Questionnaire' ('EPRQ'; see *Appendix M*) has been used in previous work assessing readiness to train (Brownstein *et al.*, 2017) and was adapted for use in this Chapter to include measures of self-reported recovery (Laurent *et al.*, 2011). The data collected from the 'EPRQ' included subjective measures of sleep, anger, confusion, depression, confidence, alertness, tension, fatigue, passive and active muscle soreness, recovery, and motivation to train. Participants marked on a 10-point Likert scale in response to 12 questions, such as "how fatigued do you feel?", "how sore do your muscles feel?", "how recovered do you feel?", and "how motivated to train do you feel?". Each scale was anchored with verbal descriptors "not at all" to "extremely".

6.2.4 Data analysis

6.2.4.1 Cycle related data and symptom tracking

The raw data from the daily cycle and symptom tracking form were exported from Google Forms directly to Microsoft Excel software for Windows. The frequency and severity of

symptoms reported in the days before (-72 , -48 , -24 h, and pre) and after (post, $+24$, $+48$, and $+72$ h) the exercise session was quantified in each testing *phase*. Specifically, the number of symptoms experienced in the days before and after the exercise session in each testing *phase* were summed to create the ‘symptom frequency prior to the exercise session’ and the ‘symptom frequency post the exercise session’. The mode severity of all the symptoms experienced (*i.e.*, “absent” = 1, “mild” = 2, “moderate” = 3 and “severe” = 4) in the days before and after the exercise session in each testing *phase* was then calculated to create the ‘symptom severity prior to the exercise session’ and the ‘symptom severity post the exercise session’. Finally, the ‘symptom frequency prior to the exercise session’ and the ‘symptom frequency post the exercise session’ were multiplied by the ‘symptom severity prior to the exercise session’ and the ‘symptom severity post the exercise session’, respectively, to give an overall ‘symptom frequency \times severity score’ in the days before and after the exercise session at each testing *phase*.

6.2.5 Statistical analysis

The statistical software package IBM SPSS Statistics (Version 24, SPSS Inc., USA) for Windows was used to conduct the statistical analysis. Data are presented as mean \pm SD. Normal distribution of data was confirmed using the Shapiro-Wilk test. Sphericity was assessed using Mauchly’s test of sphericity. Where sphericity was violated, a Greenhouse-Geisser correction was used. To compare HR and RPE during the exercise protocol (averages calculated from sets one to five) across phases and between groups a 3×2 (*phase* \times group) mixed-model ANOVA was used. To examine the effect of *phase* on physical performance (*i.e.*, pre-exercise CMJ height) and perceptual (*i.e.*, the ‘EPRQ’) data, 3×2 (*phase* \times group) mixed-model ANOVAs were employed. To compare the recovery profile in physical and perceptual data, $3 \times 5 \times 2$ (*phase* \times time \times group) way mixed-model ANOVAs were used. Where appropriate, least significant *post hoc* tests were applied to examine pairwise comparisons of each significant main effect and interaction effect. Where participants were missing CMJ data for only one timepoint (naturally menstruating group: $n = 2$ at 24 h post the exercise session in testing *phase* two; and 72 h post the exercise session in testing *phase* two) multiple imputation was used. To assess for differences in the ‘symptom frequency \times severity score’ in the days before and after the exercise session across testing *phases* in naturally menstruating women and _mOCP users, 3×2 (*phase* \times group) repeated measures ANOVAs were used. To investigate the effect of the exercise session on the ‘symptom frequency \times severity score’ across testing *phases* in naturally menstruating women and _mOCP users, a $3 \times 2 \times 2$ (*phase* \times time \times group) mixed-model

ANOVA was used. A linear correlation (Pearson r) was used to investigate whether any relationship was present between the change in CMJ height pre-exercise (calculated from CMJ height in testing *phase* one – best CMJ height across all testing *phases*) and the change in cycle related symptoms experienced pre-exercise (calculated from the ‘symptom frequency x severity score’ pre-exercise in testing *phase* one – the ‘symptom frequency x severity score’ pre-exercise in the testing *phase* which had the best CMJ height). The α for all statistical tests was set at $P \leq 0.05$.

6.3 Results

6.3.1 Participant menstrual cycle and combined, monophasic, oral contraceptive pill characteristics

Self-reported, descriptive, MC and _mOCP characteristics data for the participants included in this Chapter are presented in *Chapter 5, Table 5.2*.

6.3.2 Data from the exercise session

Heart rate and RPE data during the exercise session at each testing *phase* is shown in Figure 6.2 and Figure 6.3, respectively. Five participants were excluded from the HR data analysis (naturally menstruating group: n = 4; and _mOCP group: n = 1) because of unavailable data. There was no difference in the average HR response to exercise across *phases* and between groups ($P = 0.129$ and $P = 0.329$, respectively) and no *phase* \times group interaction ($P = 0.089$). No *phase* \times group interaction was observed for average RPE during the exercise session ($P = 0.326$). Based on a main effect of *phase* ($P < 0.001$), RPE was greater at testing *phase* one (5 ± 0 Au) compared to testing *phases* two (4 ± 0 Au, $P < 0.001$) and three (4 ± 0 Au, $P = 0.003$); but there was no difference between testing *phases* two and three ($P = 0.230$). There was no main effect of group ($P = 0.998$).

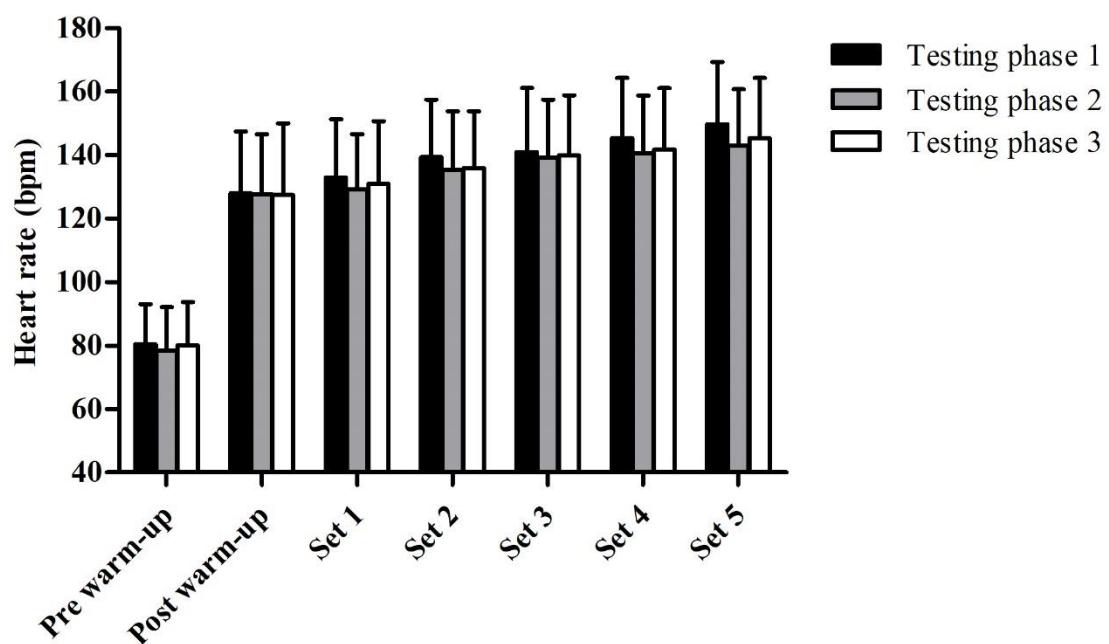


Figure 6-2 Heart rate response during the exercise session at each testing phase in naturally menstruating women ($n = 16$) and combined, monophasic, oral contraceptive pill ($_mOCP$) users ($n = 20$). Bars with error lines represent the combined groups mean \pm SD response.

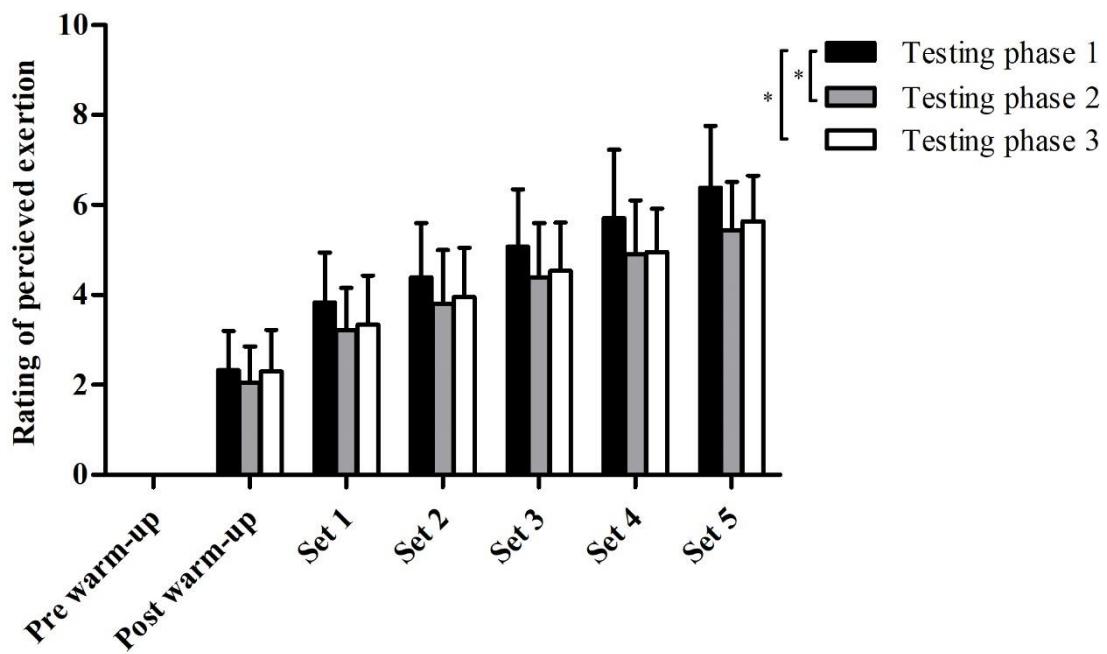


Figure 6-3 Perceived exertion during the exercise session at each testing phase in naturally menstruating women ($n = 20$) and combined, monophasic, oral contraceptive pill (_mOCP) users ($n = 21$). *greater average RPE during the exercise session at testing *phase one* ($P \leq 0.05$) compared to *phases two and three*. Bars with error lines represent the combined groups mean \pm SD response.

6.3.3 Physical measures of exercise performance and recovery time

Three participants were excluded from the CMJ data analysis because of missing data at more than one time point (naturally menstruating group: $n = 1$; and _mOCP group: $n = 2$).

6.3.3.1 Countermovement jump performance pre-exercise

No *phase* \times group interaction was observed for pre-exercise CMJ height ($P = 0.532$). No main effect of group ($P = 0.387$) was observed, but a main effect of *phase* was shown ($P = 0.007$), whereby CMJ height was lower at testing *phase one* (19.9 ± 0.6 cm) compared to testing *phases two* (21.1 ± 0.6 cm; $P = 0.005$) and *three* (20.5 ± 0.5 cm; $P = 0.017$); but there was no difference between *phases two and three* ($P = 0.121$, Figure 6.4).

6.3.3.2 Countermovement jump recovery profile

No *phase* \times time \times group interaction was observed for the recovery profile (pre, immediately post, and 24, 48 and 72 h post) of CMJ performance ($P = 0.265$). Countermovement jump

performance changed across time ($P < 0.001$); CMJ height was 20.5 ± 0.6 cm pre-exercise and was reduced immediately post exercise (18.4 ± 0.6 cm, $P < 0.001$), 24 h (18.4 ± 0.6 cm, $P < 0.001$), and 48 h (19.6 ± 0.6 cm, $P < 0.001$) post exercise, but had recovered by 72 h (20.6 ± 0.6 cm, $P = 0.694$, Figure 6.4). The recovery of CMJ height in the days post-training was similar across *phase* and group ($P \geq 0.158$ for all other main and interaction effects; Figure 6.4).

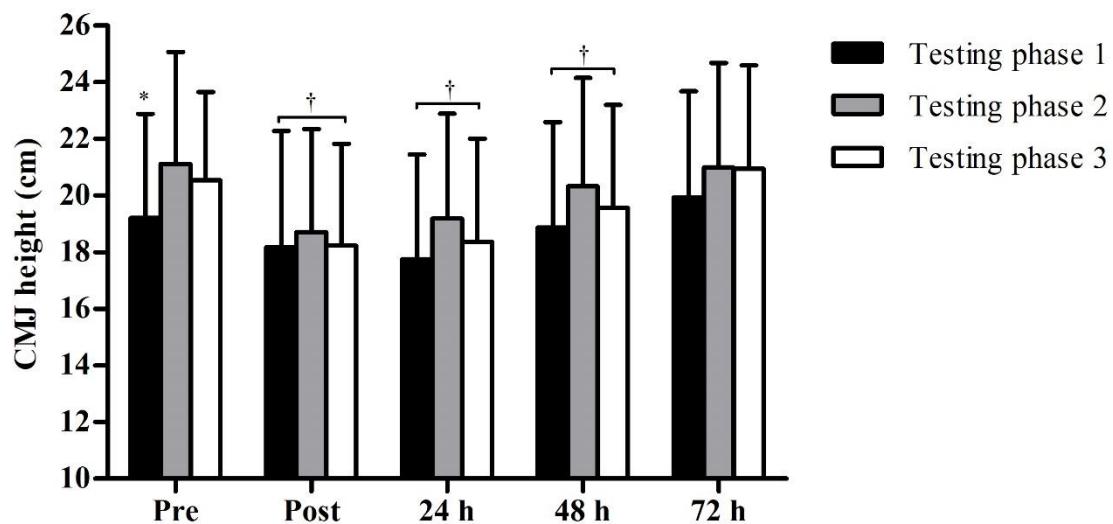


Figure 6.4 Bar chart showing countermovement jump (CMJ) height data pre-exercise, immediately post, and 24, 48, and 72 h post-exercise across the different testing phases in both naturally menstruating women ($n = 19$) and combined, monophasic, oral contraceptive pill (_mOCP) users ($n = 19$). *lower at testing *phase* one ($P \leq 0.05$). †reduced in comparison with pre-exercise value ($P \leq 0.05$). Bars with error lines represent the combined groups mean \pm SD response.

6.3.4 Perceptual measures of exercise performance and recovery time

Perceptual measures data from the ‘EPRQ’ are displayed in Table 6.1.

Table 6-1 Perceptual measures data from the ‘Elite Performance Readiness Questionnaire’ (EPRQ) pre, post, and 24, 48, and 72 h post the exercise session across all testing *phases* in naturally menstruating women (n = 20) and combined, monophasic, oral contraceptive pill (_mOCP) users (n = 21).

Measure	Group	Phase 1					Phase 2					Phase 3					Pre-exercise (2 × 3 ANOVA)		Recovery profile (2 × 3 × 5 ANOVA)			
		Pre	Post	24 h	48 h	72 h	Pre	Post	24 h	48 h	72 h	Pre	Post	24 h	48 h	72 h	Phase effect	Phase × Group	Time effect	Group × Time	Phase × Time	Phase × Time × Group
Sleep	Naturally menstruating	6 ± 2	6 ± 2	7 ± 2	7 ± 2	7 ± 2	6 ± 2	6 ± 2	7 ± 2	7 ± 2	8 ± 2	7 ± 2	7 ± 2	7 ± 2	7 ± 2	7 ± 2	0.568	0.428	0.039	0.103	0.307	0.643
	_m OCP users	7 ± 2	7 ± 2	6 ± 2	6 ± 2	7 ± 2	6 ± 2	7 ± 2	7 ± 2	7 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	7 ± 2						
Anger	Naturally menstruating	3 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	< 0.001	0.526	< 0.001	0.155	< 0.001	0.766
	_m OCP users	3 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1						
Confusion	Naturally menstruating	3 ± 2	2 ± 2	2 ± 2	2 ± 2	2 ± 2	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 2	2 ± 2	2 ± 2	2 ± 2	2 ± 2	0.012	0.158	< 0.001	0.028	0.173	0.198
	_m OCP users	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	1 ± 1	2 ± 1						
Depression	Naturally menstruating	3 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	1 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1	< 0.001	0.277	< 0.001	0.235	< 0.001	0.081
	_m OCP users	3 ± 2	2 ± 2	2 ± 2	3 ± 2	2 ± 2	2 ± 1	1 ± 1	3 ± 1	2 ± 1	2 ± 1	2 ± 1	1 ± 1	2 ± 1	2 ± 1	2 ± 1						
Confidence	Naturally menstruating	5 ± 2	7 ± 2	7 ± 2	6 ± 2	7 ± 2	7 ± 2	8 ± 2	7 ± 2	7 ± 2	7 ± 2	7 ± 2	8 ± 2	7 ± 2	6 ± 2	6 ± 2	< 0.001	0.216	< 0.001	0.713	< 0.001	0.194
	_m OCP users	5 ± 2	6 ± 2	6 ± 2	5 ± 2	6 ± 2	6 ± 2	7 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	7 ± 2	6 ± 2	6 ± 2	6 ± 2						
Alertness	Naturally menstruating	5 ± 2	8 ± 2	6 ± 2	7 ± 2	7 ± 2	7 ± 2	8 ± 2	7 ± 2	7 ± 2	7 ± 2	7 ± 2	8 ± 2	7 ± 2	7 ± 2	6 ± 2	< 0.001	0.395	< 0.001	0.581	0.008	0.246
	_m OCP users	5 ± 2	7 ± 2	7 ± 2	6 ± 2	6 ± 2	7 ± 2	7 ± 2	6 ± 2	6 ± 2	6 ± 2	6 ± 2	8 ± 2	7 ± 2	7 ± 2	6 ± 2						
Tension	Naturally menstruating	4 ± 2	2 ± 2	3 ± 2	3 ± 2	2 ± 2	3 ± 1	2 ± 1	3 ± 1	2 ± 1	3 ± 1	3 ± 2	2 ± 2	3 ± 2	3 ± 2	3 ± 2	0.105	0.476	< 0.001	0.284	0.017	0.468
	_m OCP users	3 ± 2	3 ± 2	3 ± 2	3 ± 2	2 ± 2	3 ± 1	2 ± 1	3 ± 1	2 ± 1	3 ± 1	3 ± 2	2 ± 2	3 ± 2	3 ± 2	3 ± 2						
Fatigue	Naturally menstruating	5 ± 2	4 ± 2	5 ± 2 *	4 ± 2	3 ± 2	3 ± 2	5 ± 2 †	4 ± 2 †	4 ± 2 #	4 ± 2	3 ± 2	4 ± 2	5 ± 2 †	4 ± 2	4 ± 2	< 0.001	0.127	< 0.001	0.547	0.019	0.048
	_m OCP users	5 ± 2	5 ± 2	5 ± 2	5 ± 2	4 ± 2	4 ± 2	5 ± 2 †	5 ± 2 †	5 ± 2	4 ± 2	4 ± 2	5 ± 2 †	5 ± 2 †	4 ± 2	4 ± 2						
Passive muscle soreness	Naturally menstruating	2 ± 2	5 ± 2	4 ± 2	3 ± 2	3 ± 2	1 ± 1	3 ± 1	3 ± 1	2 ± 1	1 ± 1	2 ± 1	4 ± 1	4 ± 1	3 ± 1	2 ± 1	< 0.001	0.812	< 0.001	0.002	0.178	0.412
	_m OCP users	2 ± 2	5 ± 2	5 ± 2	4 ± 2	3 ± 2	2 ± 2	4 ± 2	5 ± 2	5 ± 2	4 ± 2	4 ± 2	5 ± 2	5 ± 2	4 ± 2	4 ± 2						
Active muscle soreness	Naturally menstruating	4 ± 2	7 ± 2	7 ± 2	5 ± 2	4 ± 2	1 ± 1	4 ± 1	4 ± 1	2 ± 1	1 ± 1	2 ± 2	4 ± 2	5 ± 2	3 ± 2	2 ± 2	< 0.001	0.212	< 0.001	< 0.001	0.096	0.094
	_m OCP users	4 ± 2	7 ± 2	7 ± 2	5 ± 2	4 ± 2	1 ± 1	4 ± 1	4 ± 1	2 ± 1	1 ± 1	2 ± 2	4 ± 2	5 ± 2	3 ± 2	2 ± 2						
Recovery	Naturally menstruating	6 ± 2	4 ± 2 *†	2 ± 2 *‡	2 ± 2 *‡	6 ± 2 *	6 ± 2 *	8 ± 2	6 ± 2 †	7 ± 2 †	8 ± 2 #	9 ± 2 #	7 ± 2	6 ± 2 †	6 ± 2 †	8 ± 2 #	< 0.001	0.131	< 0.001	< 0.001	< 0.001	< 0.001
	_m OCP users	6 ± 2	4 ± 2 †	3 ± 2 †	3 ± 2 *†	6 ± 2	7 ± 2	5 ± 2 †	3 ± 2 †	4 ± 2 †	4 ± 2 †	6 ± 2	7 ± 2	5 ± 2 †	4 ± 2 †	4 ± 2 †						
Motivation to train	Naturally menstruating	6 ± 2	4 ± 2 †	3 ± 2 †	3 ± 2 *†	6 ± 2	7 ± 2	5 ± 2 †	3 ± 2 †	4 ± 2 †	4 ± 2 †	6 ± 2	7 ± 2	5 ± 2 †	4 ± 2 †	4 ± 2 †	< 0.001	0.064	< 0.001	0.268	0.031	0.012
	_m OCP users	5 ± 2	5 ± 2	5 ± 2	5 ± 2	6 ± 2	6 ± 2	5 ± 2 †	5 ± 2	6 ± 2	6 ± 2	7 ± 2	6 ± 2	5 ± 2	5 ± 2	7 ± 2						

Symbols apply to the phase × time × group interaction for the recovery profile (2 × 3 × 5 ANOVA). [†]difference in comparison with pre value (P ≤ 0.05). ^{*}difference at testing phase 1 (P ≤ 0.05). [#]difference between groups (P ≤ 0.05). Bold face text indicates significant change.

6.3.4.1 Readiness to perform pre-training

There was no *phase* × group interaction for any ‘EPRQ’ variable pre-exercise (all $P \geq 0.064$), whilst a main effect of *phase* was shown for several variables (all $P \leq 0.012$, Table 6.1). Specifically, at testing *phase* one anger, confusion, depression, fatigue, passive, and active muscle soreness were perceived to be greater, and confidence, alertness, recovery, and motivation to train were perceived to be lower compared to testing *phases* two and three (all $P \leq 0.019$). Additionally, at testing *phase* two recovery and motivation to train were perceived to be greater ($P \leq 0.041$), whereas fatigue and active muscle soreness were perceived to be lower ($P \leq 0.035$) compared to testing *phase* three; however, there was no difference in anger, confusion, depression, confidence, alertness, and passive muscle soreness between testing *phases* two and three (all $P \geq 0.145$).

6.3.4.2 Readiness to perform recovery profile

A *phase* × time × group interaction was observed for the recovery profile (pre, immediately post, and 24, 48 and 72 h post) of perceived fatigue ($P = 0.048$, Table 6.1), recovery ($P < 0.001$, Table 6.1), and motivation to train ($P = 0.012$, Table 6.1). Specifically, focusing on perceptions of recovery, in testing *phase* one naturally menstruating women perceived full recovery at the 72 h timepoint ($P = 0.649$ compared to pre-exercise), but in testing *phases* two and three perceived full recovery at the 48 h timepoint (both $P \geq 0.494$ compared to pre-exercise). In contrast, _mOCP users perceived full recovery at the 72 h time point across all testing *phases* (all $P \geq 0.066$ compared to pre-exercise).

6.3.5 The frequency and severity of cycle related symptoms experienced in the days before and after the exercise session at each testing phase

The ‘symptom frequency × severity score’ in the days before (−72, −48, −24 h, and pre) and after (immediately post, +24, +48, and +72 h) the exercise session for naturally menstruating women and _mOCP users is shown in Figure 6.5. No *phase* × group interaction was observed in the days before ($P = 0.051$) or after ($P = 0.516$) the exercise session. Based on a main effect of *phase* (both $P < 0.001$), participants experienced a greater frequency and severity of cycle related symptoms in the days before (53 ± 6 Au) and after (38 ± 4 Au) the exercise session in testing *phase* one compared to testing *phases* two (before: 22 ± 4 Au, $P < 0.001$; after: 20 ± 3 Au, $P < 0.001$) and three (before: 22 ± 3 Au, $P = < 0.001$; after: 25 ± 4 Au, $P = 0.004$); however there was no difference between testing *phases* two and three (before: $P = 0.961$; after: $P = 0.099$). No main effect of group was observed (both $P \geq 0.155$).

6.3.5.1 The effect of exercise on the experience of cycle related symptoms

No *phase* \times time \times group interaction was observed on the ‘symptom frequency \times severity score’ immediately pre and post the exercise session ($P = 0.380$). There was no time \times group interaction ($P = 0.055$), whilst there was a *phase* \times time ($P < 0.001$, Figure 6.5). Specifically, at testing *phase* one the ‘symptom frequency \times severity score’ immediately pre- and post-exercise were greater (pre: 16 ± 2 Au; post: 9 ± 1 Au) compared to testing *phases* two (pre: 6 ± 1 Au; post: 3 ± 1 Au, both $P < 0.001$) and three (pre: 6 ± 1 Au; post: 3 ± 1 Au. both $P < 0.001$), but there was no difference between testing *phases* two and three (both $P \geq 0.632$). A main effect of time was shown ($P < 0.001$, Figure 6.5), whereby the ‘symptom frequency \times severity score’ was greater immediately pre (9 ± 1 Au) compared to post (5 ± 1 Au, $P < 0.001$) the exercise session. No main effect of group was observed ($P = 0.143$).

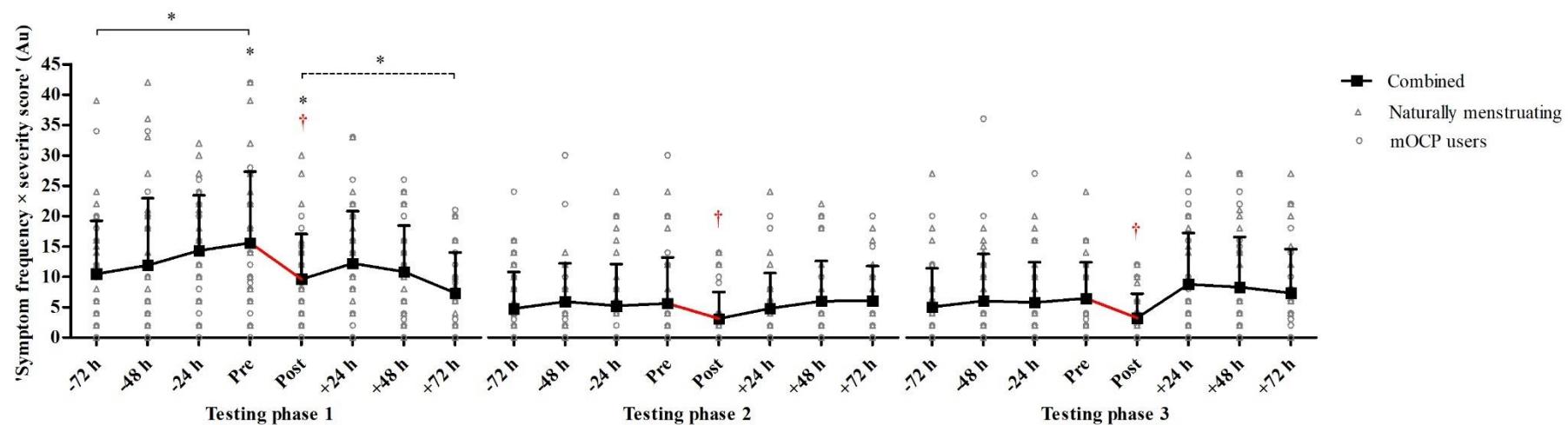


Figure 6-5 The 'symptom frequency \times severity score' experienced in the days before (-72 , -48 , -24 h pre, and pre) and after (post, $+24$, $+48$, and $+72$ h post) the exercise session across testing phases in naturally menstruating women ($n = 20$) and combined, monophasic, oral contraceptive pill ($_m$ OCP) users ($n = 21$). *greater at testing phase one ($P \leq 0.05$). †reduction from pre-exercise value ($P \leq 0.05$). Triangles represent individual data points for naturally menstruating women and circles represent individual data points for $_m$ OCP users, with combined mean \pm SD data overlaid as filled square symbols and connecting line.

6.3.6 The relationship between the change in countermovement jump height pre-exercise and the change in cycle related symptoms experienced pre-exercise

Data from naturally menstruating women and _mOCP users were pooled as no evidence was obtained that indicated a differential effect between groups. There was a moderate negative correlation between the change in CMJ height pre-exercise (calculated from CMJ height in testing *phase* one – best CMJ height across all testing *phases*) and the change in cycle related symptoms experienced pre-exercise (calculated from the ‘symptom frequency x severity score’ pre-exercise in testing *phase* one – the ‘symptom frequency x severity score’ pre-exercise in the testing *phase* which had the best CMJ height; Figure 6.6, $r = -0.316$, $P = 0.05$).

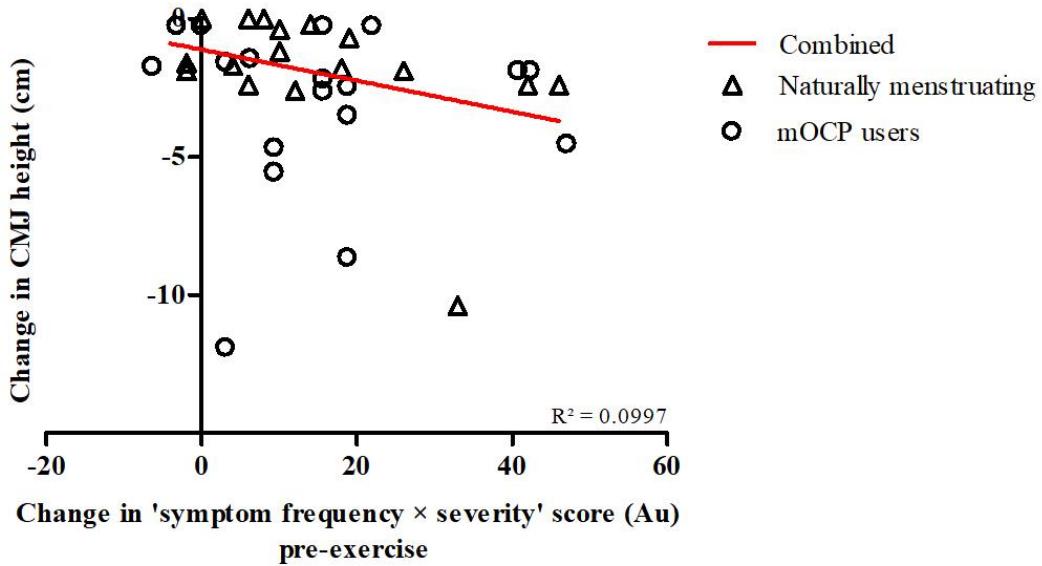


Figure 6-6 Correlation between the change in CMJ height (calculated from CMJ height in testing *phase* one – best CMJ height across all testing *phases*) and cycle related symptoms experienced pre-exercise (calculated from the ‘symptom frequency x severity score’ pre-exercise in testing *phase* one – the ‘symptom frequency x severity score’ pre-exercise in the testing *phase* which had the best CMJ height) in both naturally menstruating women ($n = 19$) and combined, monophasic, oral contraceptive pill (_mOCP) users ($n = 19$). Triangles represent individual data points for naturally menstruating women and circles represent individual data points for _mOCP users. The red line denotes the regression line for combined data.

6.4 Discussion

The purpose of this Chapter was to investigate the effect of the MC, _mOCP use, and related symptoms on exercise performance and recovery time post an exercise session, in recreationally active women. Data from physical measures demonstrated that CMJ height was lowest when participants were bleeding in both naturally menstruating women and _mOCP users compared to all other testing *phases*. The exercise session reduced CMJ height immediately post-training which recovered by 72 h across all *phases* in both groups. In contrast to physical indicators of recovery, perceptual data revealed that naturally menstruating women did not perceive full recovery until 72 h post the exercise session in testing *phase* one (*i.e.*, early follicular phase/while bleeding) compared to 48 h post in all other testing *phases*, whereas _mOCP users perceived full recovery at 72 h across all testing *phases*. Results from daily symptom tracking showed that symptom frequency and severity was greater in the accumulative days before and after the exercise session in testing *phase* one compared to all other testing *phases*, although exercise reduced the experience of symptoms pre to post exercise, across all *phases* and groups. Finally, the change in CMJ height pre-exercise was correlated with the change in cycle related symptoms experienced pre-exercise in both naturally menstruating women and _mOCP users. Collectively these findings highlight the importance of considering the indirect effects of endogenous and exogenous sex hormones and their interaction with performance and recovery outcomes. Practically, these findings support the inclusion of monitoring both physical and perceptual outcome measures, as well as cycle related symptoms to provide a more comprehensive understanding of the effect of the MC and _mOCP use on exercise performance and recovery in sportswomen.

Pre-exercise CMJ height was reduced in both groups whilst participants were bleeding compared to all other testing *phases*. This finding contradicts that of previous studies which show no effect of MC phase (Julian *et al.*, 2017; Tounsi *et al.*, 2017) or OCP phase (Rechichi & Dawson, 2009) on CMJ performance. For instance, Julian *et al.* (2017) demonstrated no difference in CMJ performance between the early follicular and mid-luteal phases of the MC in naturally menstruating women, concluding that changes in endogenous sex hormones across the MC do not affect CMJ performance. Similarly, Rechichi and Dawson (2009) assessed jump performance in _mOCP users across the _mOCP *cycle* and found no differences in CMJ performance, suggesting that the exogenous ethinyl oestrogen and progestin do not influence CMJ performance. However, in the present Chapter, pre-exercise CMJ height followed the same *phase* pattern independent of group, despite the different reproductive hormone

environments experienced. Therefore, it is plausible that endogenous and exogenous sex hormones might not be having a direct impact on performance *per se*, and instead influence performance via indirect pathways. Indeed, the findings herein highlight the multifaceted way in which performance might be altered. Firstly, it is well accepted that negative changes to an individual's wellness can subsequently affect their performance (McGuinness *et al.*, 2020). As such, the reduced performance in testing *phase* one of the current Chapter might be attributed to the residual effect of cycle related symptoms experienced going into performance. For example, in the present Chapter, the change in CMJ height pre-exercise was correlated with the change in cycle related symptoms experienced pre-exercise in both naturally menstruating women and _mOCP users. Secondly, perceptions of readiness could have influenced an individual's ability to perform. For example, perceived fatigue and muscle soreness were greater whilst perceived confidence, alertness, and readiness to perform were reduced pre-exercise, when participants were bleeding, compared to all other *phases*. As potential confounding variables on psychometric measures were controlled (*e.g.*, training, caffeine etc.), it is plausible that a residual effect of elevated symptom frequency and severity in the days preceding the exercise session in testing *phase* one, could also explain the differences in psychometric measures pre-exercise during this *phase* compared to other *phases*. This agrees with previous findings in *Chapter 5* which showed that experiencing a greater frequency and severity of symptoms influenced the extent to which an individual perceived their performance to be affected by the MC or _mOCP use. Overall, the findings from this Chapter show that performance was reduced at a time when symptom magnitude was greater (particularly across the preceding days) and perceptions of readiness to perform were reduced. Therefore, it is suggested that the residual accumulation of cycle related symptoms in combination with perceived effects of the MC and _mOCP use, might impair a sportswomen's ability to perform, although this is speculation. Practically, these results highlight the importance of considering not only the reproductive hormonal milieu, but also the symptoms experienced and perceived effects, in tandem, when it comes to managing exercise performance, particularly in sportswomen who experience a greater magnitude of cycle related symptoms, and when symptoms are perceived to impact performance.

Recovery is an essential aspect when it comes to the optimal management of training plans, and it is possible that the changes in endogenous and exogenous sex hormones might influence the recovery process following exercise (Hackney *et al.*, 2019; Mackay *et al.*, 2019; Romero-Parra, Alfaro-Magallanes, *et al.*, 2020; Romero-Parra, Barba-Moreno, *et al.*, 2020; Romero-

Parra, Rael, *et al.*, 2021). Results from the present Chapter demonstrate that CMJ height was reduced immediately post, and at 24 h and 48 h post an exercise session, before recovering by 72 h. These findings indicate that whilst the exercise session induced prolonged decrements in function, the magnitude of this decrement and the time-course of recovery in CMJ height was not different across testing *phases*, or between groups. Although research investigating the effect of endogenous and exogenous sex hormones on recovery is minimal, the findings from the current Chapter agree with previous work by Romero-Parra, Alfaro-Magallanes, *et al.* (2020) which showed no differences across MC phases in indirect markers of recovery (*i.e.*, CMJ), except perceived muscle soreness, following an eccentric squat-based exercise. In contrast, Hackney *et al.* (2019) demonstrated that the recovery time from an acute bout of strenuous endurance exercise took longer during the mid-follicular phase of the MC, in eumenorrheic women. Several possible explanations could account for the discrepancies between the study by Hackney *et al.* (2019) and the present Chapter. For instance, this Chapter utilised a performance measure of recovery whilst Hackney *et al.* (2019) utilised biochemical (*i.e.*, CK and IL-6) measures of recovery. It is possible that endogenous and exogenous sex hormones could impair recovery at a cellular level, but participants were able to maintain their jumping performance by modifying jump strategy (Cormack *et al.*, 2008; Gathercole *et al.*, 2015). Moreover, the type of exercise might have influenced any response. For instance, Hackney *et al.* (2019) utilised an endurance-based protocol whilst the current Chapter used a strength-based stimulus. Furthermore, recovery is not just a restorative process of physical measures relative to time, an individual's perception of recovery is also a critical determinant of the recovery time course (Kellmann *et al.*, 2018), and if altered can have subsequent effects on performance and training (Laurent *et al.*, 2011). Interestingly, results from the present Chapter show that despite physical measures of recovery returning to baseline by 72 h post, naturally menstruating women perceived a quicker recovery in testing *phases* two and three (48 h) compared to testing *phase* one (72 h). Additionally, perceived recovery was reduced across testing *phases* two and three in _mOCP users compared to naturally menstruating women but was consistent across the _mOCP cycle (72 h). It is plausible that the greater magnitude of cycle related symptoms experienced in the days post exercise, whilst bleeding, could explain the differences between physical and perceived recovery. For instance, experiencing cycle related symptoms could theoretically increase perceptions of reduced recovery (*see Chapter 5*). Although, given that there were no differences in symptomology between the groups, a similar perceived response might be expected across all testing *phases* in both groups, which was not observed. Collectively, these findings provide support for the inclusion of both

physical and perceptual measures when monitoring the recovery process following an exercise session, to provide a more comprehensive understanding of an individual's recovery profile, especially across the MC and _mOCP cycle.

In the present Chapter, the exercise session reduced the experience of cycle related symptoms, pre to post, across all testing *phases* and in both groups. This agrees with previous literature reporting that regular exercise can help reduce cycle related symptoms (Armour *et al.*, 2019; Daley, 2009; Matthewman *et al.*, 2018), but expands upon these findings to suggest that an acute bout of exercise can have a similar effect. Whilst a mechanistic explanation has yet to be elucidated, and is likely to be multifactorial, one plausible reason for this effect of exercise on cycle related symptoms could be the exercise-induced release of endorphins which could subsequently improve psychological outcomes (Harber & Sutton, 1984). This speculation is supported by the finding presented here that exercise reduced perceived anger, confusion, depression, and tension, whilst increasing perceived confidence and alertness. Although, as anticipated, the exercise session did also result in greater perceptions of passive muscle soreness and reduced recovery from pre to post. Overall, whilst the current Chapter cannot identify the mechanisms responsible, it does indicate that exercise might help in alleviating cycle related symptoms. Thus, from a practical perspective, exercise could be a potential strategy to adopt by some sportswomen to help manage cycle related symptoms that could negatively impact performance and training. However, it is acknowledged that further intervention-based, randomised controlled trials, are needed before guidelines on exercise as an effective symptom mitigation strategy in recreationally active women can be made.

6.4.1 Limitations and future directions

The current Chapter has several limitations. Firstly, data was collected from a group of recreationally active women, therefore the average response presented in this Chapter might not be specific and meaningful to all women. As such, further research investigating within different populations (*i.e.*, elite woman athletes) and cohorts of women with different hormonal profiles (*i.e.*, progestin-only HC users) is warranted. Moreover, whilst the methods used to identify MC *phase* and confirm an ovulatory cycle in naturally menstruating women (*i.e.*, calendar-based counting and urinary ovulation detection kits) are useful in an applied environment (Hicks *et al.*, 2022), MC *phase* was not subsequently verified by serum measurement for both oestrogen and progesterone which limits the reliability of the *phases* used in the present Chapter (Elliott-Sale *et al.*, 2021). Specifically, whilst our confidence in the

determination of *phase* one (oestrogen and progesterone need to be low to menstruate) and two (a positive urinary ovulation test result infers the pre-ovulatory peak in oestrogen) are high, *phase* three is estimated. As such, where available, the use of appropriate biochemical outcomes to confirm MC phase in future studies would improve methodological quality. However, it is important to acknowledge the real-world application of the methods utilised in the current Chapter. For example, whilst using pre-defined cycle phases and verifying sex hormone concentrations should be priority when the goal of a study is to investigate the effect of a particular reproductive hormonal profile on physiology, and subsequent performance and training outcomes, it is evident that in real-world practice sportswomen must perform and train optimally and consistently throughout the entirety of their respective cycle. Thus, as the current Chapter implies, there is a need for sportswomen, and those working with them, to think outside predefined cycle phases when monitoring the holistic impact of the MC and ^mOCP cycle. Furthermore, this Chapter focused on indirect (*i.e.*, performance) markers of recovery, due to restrictions of the COVID-19 pandemic, thus whilst these markers are attainable in a real-world setting and offer insight into the recovery process in an applied environment, further research into biochemical and physiological responses would be of interest to quantify the magnitude and time-course of recovery post exercise in sportswomen. It is also important to acknowledge that both the perceptual measures recorded (*i.e.*, sleep, depression, anger, confidence etc.) and cycle related symptomology are complex, and it remains impossible to decipher whether the reported perceptual outcomes and cycle related symptoms were directly related to the MC or ^mOCP use or other external influences (*i.e.*, lifestyle factors). Moreover, it is likely that physical and perceptual measures of exercise performance and recovery, as well as cycle related symptoms will differ between individuals and between cycles within the same individual (McNulty *et al.*, 2021), which is supported by the inter-individual variability in symptoms experienced in the present Chapter. Therefore, practically it is necessary to consider these effects on an individual level, as some women might be affected and others not, and future studies should explore intra-individual variability in responses to facilitate a deeper understanding. Finally, it is important to consider that factors, such as the method for assessing jump performance, as well as jump technique might also explain some of the variation within the physical responses measured.

6.4.2 Practical implications

The current findings highlight the importance of considering not only the reproductive hormonal milieu, but rather the holistic impact (*i.e.*, cycle related symptoms and perceived

effects) of the MC and m OCP cycle on performance and recovery outcomes in some sportswomen. It is advised that cycle related symptoms and perceived effects should be individually considered concurrent to physical outcomes, where possible, to facilitate performance and/or training achievement in each individual sportswoman accordingly. Specifically, real-time, consistent, symptom mapping (*i.e.*, rolling average ‘symptom frequency \times severity score’), alongside psychological readiness monitoring, should be considered particularly during the shifts between cycle phases (*i.e.*, not to be restricted solely to phases defined by sex hormone concentrations; [Bruinvels *et al.*, 2022]). Adopting such an approach will allow sportswomen, and those working with them, to see the full picture (*e.g.*, account for the residual accumulation of symptoms in the days pre performance and training and perceived readiness). This appears to be particularly important in individuals who experience magnitude of cycle related symptoms and perceive their respective cycle to influence performance and recovery outcomes. Ultimately, this will allow sportswomen, and those working with them, to proactively identify and predict key windows of opportunity for management strategies, which will help to limit any negative changes in performance and recovery outcomes due to cycle related symptoms and perceived readiness.

6.5 Conclusion

This Chapter provides the first multifaceted insight into the effect of the MC, m OCP use, and related symptoms on exercise performance and recovery time post exercise in a group of recreationally active women. Results from physical measures revealed that CMJ height was reduced when participants were bleeding, compared to all other testing *phases*, with no difference between groups. Results from physical data also showed that the exercise session resulted in an immediate decline in CMJ height that persisted for 72 h, but there was no difference in recovery time post exercise across testing *phases* or between groups. In contrast, there was a difference in perceived recovery, with naturally menstruating women reporting not feeling fully recovered post exercise until 72 h in testing *phase* one compared to 48 h in testing *phases* two and three, whereas m OCP users perceived full recovery at 72 h post exercise across all testing *phases*. Finally, the change in CMJ height pre-exercise was correlated with the change in cycle related symptoms experienced pre-exercise in both naturally menstruating women and m OCP users. Practically, these results highlight the importance of considering and monitoring the potential indirect effects of changes in sex hormones (*i.e.*, cycle related

symptoms and perceived effects), rather than solely focusing on the sex hormones themselves, as this will provide a more comprehensive understanding of the effect of the MC and _mOCP use on performance and recovery outcomes in sportswomen.

CHAPTER 7 – GENERAL DISCUSSION

7.1 Introduction to general discussion

The overall aim of this thesis was to investigate the effect of the MC, OCP use, and related symptoms on exercise performance and recovery time post exercise in sportswomen. The present Chapter will provide an overarching discussion of the thesis and is separated into five major sections. Firstly, *Section 7.2* will outline the main aims, findings, and implications of this thesis. Following this, *Sections 7.3 and 7.4*, will explore the findings from this thesis in greater detail, including discussion of the identified and proposed mechanisms of the MC and OCP use on exercise performance and the recovery process post exercise, within the context of existing literature. Then, in *Section 7.5*, the practical implications for sportswomen, and those working with them, based on the findings within this thesis, are provided. Finally, recommendations for future research conclude this Chapter (*Section 7.6*).

7.2 Summary of thesis aims, main findings, and implications

A summary of the main aims, findings, and implications of this thesis is provided in Table 7.1.

Table 7-1 Summary of thesis aims, main findings, and implications.

Chapter number	Aim	Finding	Implications
<i>Chapter 3</i>	Examine the effect of the MC on exercise performance and appraise the quality of previous studies.	Exercise performance might be reduced, by a trivial amount, during the early follicular phase of the MC, when compared with other phases. The quality of evidence was mostly classified as poor.	The current evidence does not warrant general guidance on exercise performance across the MC; rather, a personalised approach should be taken. Further high-quality research is required.
<i>Chapter 4</i>	Explore the effect of OCPs on exercise performance and appraise the quality of previous studies.	OCP use might result in slightly inferior exercise performance when compared to non-use, although any group-level effect is most likely to be trivial. Exercise performance appeared relatively consistent across the OCP cycle. The quality of evidence was mostly classified as moderate.	The current evidence does not warrant general guidance on OCP use compared with non-use for exercise performance. Thus, an individualised approach might be more appropriate. Different guidance is not warranted for pill-free versus pill-taking days. Further high-quality research is required.
<i>Chapter 5</i>	Examine the type, frequency, and severity of cycle related symptoms experienced by naturally menstruating women and _m OCP users, and their	Symptoms were commonly reported with no difference in symptomology between groups. The magnitude of symptoms was greater whilst bleeding, which was associated	Monitoring of symptoms should be considered, to the same degree, irrespective of sex hormone profile. Real-time symptom mapping is recommended to account for the phase

	<p>perceived effects on exercise performance and recovery time post exercise.</p>	<p>with perceived reductions in exercise performance and a longer recovery time post exercise.</p>	<p>effect on the magnitude of symptoms, which, when elevated, might have negative implications.</p> <p>Further research examining the influence of symptomology on objective markers of performance and recovery is needed.</p>
<i>Chapter 6</i>	<p>Determine whether the MC, _mOCP use, and related symptoms influence physical and perceptual measures of exercise performance and recovery time post an exercise session.</p>	<p>Performance was reduced, in both groups, whilst bleeding, compared to all other <i>phases</i>. This difference was correlated with experiencing a greater magnitude of symptoms at this time. Physical recovery time post exercise was not directly affected by <i>phase</i> or group, but dichotomy existed between physical and perceptual markers of recovery. Accumulative symptom frequency and severity were greater in the days before and after exercise, whilst bleeding.</p>	<p>It is important to consider the holistic impact of the MC and _mOCP <i>cycle</i> on performance and recovery outcomes, rather than solely focusing on the reproductive hormonal milieu.</p> <p>Real-time, consistent, monitoring of psychological readiness and symptoms is recommended to proactively identify and predict key windows of opportunity for strategies to limit any negative effects.</p> <p>Further high-quality research is required.</p>

MC, menstrual cycle; _mOCP, combined monophasic oral contraceptive pill; OPC, oral contraceptive pill.

7.3 The influence of the menstrual cycle and oral contraceptive pill use on exercise performance

Chapters 3 and 4 both reported a slightly impaired, group-level, exercise performance when endogenous oestrogen and progesterone concentrations are low. This finding can potentially be explained by a range of sex hormone mechanisms. Firstly, oestrogen, at the mechanistic level, has been shown to have several positive effects on aspects of physiology. For example, its known for its anabolic (Baltgalvis *et al.*, 2010; Lowe *et al.*, 2010a), and neuroexcitatory effects (Ans dell *et al.*, 2019), as well as its role in regulating substrate metabolism by increasing glycogen uptake and sparing glycogen stores (Boisseau & Isacco, 2022). Thus, when oestrogen concentrations are higher (*i.e.*, the late follicular/ovulatory phases, respectively, and the mid-luteal phase) this might positively affect strength and endurance performance, compared to when oestrogen concentrations are lower (*i.e.*, the early follicular phase), hence the findings in *Chapter 3*. Moreover, it is recognised that progesterone can have anti-oestrogenic effects; therefore, the beneficial performance effects of oestrogen are likely to be greater when the oestrogen to progesterone ratio is high: low (*i.e.*, late follicular/ovulatory phase) compared to high: high (*i.e.*, mid-luteal phase). This speculation was supported in *Chapter 3* whereby the biggest difference in exercise performance was shown between the early follicular and late follicular phases. Moreover, *Chapter 4* strengthens these findings demonstrating that OCP use (*i.e.*, a chronically downregulated endogenous sex hormone profile) might reduce exercise performance when compared to the MC, but there were no differences in exercise performance across the OCP cycle (consistently low concentrations of endogenous sex hormones). Overall, taken together, the findings from *Chapters 3 and 4* agree with the assumption that both strength and endurance performance might be mediated by the concentration of endogenous sex hormones in some sportswomen (Constantini *et al.*, 2005; de Jonge, 2003; Lebrun *et al.*, 2013).

Whilst there are known effects of endogenous and exogenous sex hormones on mechanisms pertaining to exercise performance (see *Chapter 2* for a full discussion), these might not translate to an actual measurable influence on exercise performance across the MC or with OCP use. Indeed, this is demonstrated by the small effect size and the large between-study variance in exercise performance observed in *Chapters 3 and 4*. Whilst the effect size and study variance might be partly attributed to the multifaceted nature of exercise performance, the individual lived experiences (*i.e.*, cycle related symptoms and perceived effects) of the MC and OCP use might also play a role in mediating exercise performance in sportswomen (Armour *et*

al., 2020; Brown *et al.*, 2021; Findlay *et al.*, 2020; Heather *et al.*, 2021; Martin *et al.*, 2018; Nolan *et al.*, 2022; Oxfeldt, Dalgaard, Jørgensen, & Hansen, 2020; Parker *et al.*, 2022; Read *et al.*, 2021; Solli *et al.*, 2020). For instance, both *Chapters 3* and *4* solely focused on elucidating the effect of fluctuations in sex hormones on exercise performance, without consideration of the potential effect of an individual's lived experiences. By expanding beyond solely focusing on the impact of the reproductive hormonal milieu, *Chapter 5* showed that cycle related symptoms are common in sportswomen, irrespective of sex hormone profile, and experiencing a greater frequency and severity of cycle related symptoms influenced the extent an individual perceives their exercise performance to be affected by their MC or _mOCP use. For example, experiencing a greater magnitude of symptoms resulted in a greater perception of reduced exercise performance whilst participants were bleeding. This finding agrees with previous work by Bruinvels *et al.* (2021) who reported that experiencing a greater number of MC symptoms was associated with changing/missing training, missing a competition, as well as needing to use pain medication. The findings from *Chapter 5* also extend Bruinvels *et al.* (2021) work to consider the phase effect of cycle related symptoms on exercise performance. Particularly, this Chapter highlights that the current practice of assessing symptoms retrospectively across the entity of the MC or OCP *cycle* overlooks the potential for clusters of negative symptoms, which could affect exercise performance across phases. Furthermore, and interesting to note, symptomology and perceived effects were the same in both groups in *Chapter 5*, which strengthens the notion that factors beyond the reproductive hormone profile might play a role in influencing exercise performance, as well as highlighting that symptom monitoring in applied environments must be considered irrespective of _mOCP use (as it is often assumed that HC users do not have to contend with the experience of symptoms unlike their naturally menstruating counterparts). Finally, the results in *Chapter 5* demonstrate that the reduced performance during the early follicular phase of the MC reported in *Chapter 3* might be partly attributable to the potential impact of cycle related symptoms and perceived effects when sportswomen are bleeding, rather than solely the effects of low endogenous oestrogen and progesterone concentrations.

From an applied perspective, it is important to consider that sportswomen need to be able to perform optimally and consistently every day, and not just within predefined cycle phases. For example, if a sportswoman is required to perform on day one of her period, there is potential for the symptoms experienced in the days prior to menstruation (*i.e.*, the time between the mid-luteal and early follicular phases, commonly referred to as the late luteal phase), to impact

performance. As demonstrated in *Chapter 3* (see Figure 3.5), most studies have compared exercise performance across the early follicular, late follicular, and the mid-luteal phases, whereas very few studies have compared the ovulatory, early luteal, and late luteal phases. Whilst this three-phase design is necessary to assess the effect of key ratios in endogenous and exogenous sex hormones on performance, it overlooks the other MC phases (and the shifts between them) sportswomen contend with. To combat this conventional phase-based research approach, *Chapter 6* monitored the day-to-day variation in cycle related symptoms and their potential impact on exercise performance by adopting a more fluid research design (*i.e.*, monitoring symptoms in the days before and after exercise during the shifts between key cycle phases, such as the late luteal phase). The findings within *Chapter 6* build upon the findings in *Chapter 5*, showing that actual exercise performance (CMJ height) was reduced whilst participants were bleeding, a timepoint when participants experienced a greater symptom frequency and severity in the preceding days. Moreover, *Chapter 6* also demonstrated how perceptions of readiness could also influence an individual's ability to perform. For example, when participants were bleeding, perceived fatigue and muscle soreness were greater, whilst perceived confidence, alertness, and readiness to perform were reduced pre-exercise, compared to all other *phases*. As such, it is likely that a residual effect of elevated symptoms in the days preceding the exercise session at this time, could also explain the differences in psychological readiness pre-exercise, in this *phase* compared to all other *phases*.

It is interesting to note that in *Chapter 6* reduced exercise performance was reported during the pill-free days in _mOCP users, and no difference was shown between the groups, which contradicts with the findings presented in *Chapter 4*. This discrepancy between Chapters could be attributed to the fact that in *Chapter 4* none of the included studies detailed the impact of cycle related symptoms experienced by OCP users. Without this information, it is unclear if the difference in exercise performance between groups, in *Chapter 4*, was due to greater differences in the symptoms experienced. For example, the OCP users included in the analysis might have experienced a greater magnitude of symptoms, or, alternatively, the naturally menstruating women included might have experienced less symptoms. Moreover, it is also unclear if the lack of difference in exercise performance across the OCP *cycle*, in *Chapter 4*, was a result of a reduced experience of symptoms in the OCP users included in the analysis, compared to those included in *Chapter 6*. Thus, it could be theorised that, to isolate the impact of endogenous and exogenous sex hormones on exercise performance, symptomology must be controlled for, although this is speculation, and more research is required. Furthermore, unlike

the participants included within the studies assessed in *Chapter 4* (*i.e.*, a mixture of monophasic and triphasic OCP users), *Chapter 6* used a more homogeneous participant group (*i.e.*, _mOCP users), which could also explain the differences between results. Overall, despite these discrepancies, the findings in *Chapters 5* and *6* highlight that it might not be solely the changes in sex hormone concentrations across the MC and with OCP use that alter exercise performance, but instead it is likely to be a combination of effects (*i.e.*, cycle related symptoms and perceived effects) that are responsible for any of the potential changes in exercise performance reported in some sportswomen. The practical implications of the above findings are discussed in *Section 7.5*.

7.4 The influence of the menstrual cycle and oral contraceptive pill use on the responses to and recovery from exercise

Chapters 5 and *6* considered the potential impact of the MC and OCP use on the recovery process post exercise. Indeed, *Chapter 6* demonstrated that changes in endogenous and exogenous sex hormones across the MC and with _mOCP use do not appear to influence the physical recovery process following exercise. Specifically, in this Chapter, CMJ height was reduced at several timepoints (*i.e.*, immediately post and at 24 h and 48 h) post exercise, before recovering by 72 h post. Whilst this indicates that the exercise session utilised in this Chapter induced prolonged decrements in physical function, the magnitude of decrement and the time-course of recovery in CMJ height was not different across testing *phases*, or between groups. Research, predominately in animal models, suggests that oestrogen might offer protection against EIMD and play a role in muscle repair and regeneration (Enns & Tiidus, 2010; Kendall & Eston, 2002; Tiidus, 2005; Tiidus, 2003). However, despite differences in endogenous oestrogen concentrations across the MC in naturally menstruating women, *Chapter 6* showed no differences in physical recovery across MC *phases*. Moreover, regardless of the difference in endogenous oestrogen concentrations between naturally menstruating women and _mOCP users, this Chapter also demonstrated no differences in physical recovery between groups. Of note, although representative of an applied setting, this Chapter did not verify the respective cycle phases using the recommended bloods analysis. Whilst research investigating the effect of endogenous and exogenous sex hormones on the recovery process post exercise is lacking, the findings in *Chapter 6* agree with previous work by Romero-Parra, Alfaro-Magallanes, *et al.* (2020) who showed no difference across MC phases in CMJ recovery following an eccentric

squat-based exercise. The results in *Chapter 6* also agree partly with Savage and Clarkson (2002) who reported no differences in most physical markers of recovery following eccentric exercise between OCP users and non-users. Similarly, these findings agree with Romero-Parra, Rael, *et al.* (2021) who showed a lack of difference in physical measures of EIMD across the OCP cycle. Overall, whilst previous studies in animal models demonstrate distinct mechanistic effects of sex hormones on the recovery process post exercise, this does not appear to translate into clear changes in actual enhanced/impaired physical recovery post-exercise across the MC or with OCP use in sportswomen.

It is important to acknowledge that recovery is not limited to the restoration of physical measures relative to time, and instead an individual's perception of recovery can determine the recovery time course (Kellmann *et al.*, 2018). Consequently, perceived effects can influence overall recovery. For instance, in *Chapter 6*, despite physical performance measures of recovery returning to baseline by 72 h post exercise, naturally menstruating women perceived a quicker recovery (48 h) in testing phases two (rising/high oestrogen and low progesterone) and three (high oestrogen and progesterone) compared to testing phase one (72 h; low oestrogen and progesterone). This agrees with findings from both Romero-Parra, Alfaro-Magallanes, *et al.* (2020) and Oosthuysen and Bosch (2017) who showed no difference in physiological markers of recovery in response to exercise across MC phases but did report a difference in perceived effects (*i.e.*, perceived muscle soreness). Specifically, in these previous studies perceived recovery of muscle soreness was delayed during the early follicular phase of the MC in naturally menstruating women. Additionally, in *Chapter 6* perceived recovery was reduced across testing phases two and three (*i.e.*, downregulated endogenous sex hormone profile) in _mOCP users compared to naturally menstruating women but was consistent across the _mOCP cycle (72 h). Indeed, this agrees with the only previous study to assess recovery responses between OCP phases, demonstrating a lack of differences in most muscle damage variables (*i.e.*, muscle soreness, CMJ, and blood markers of muscle damage and inflammation) post an eccentric squat-based exercise across OCP phases (Romero-Parra, Rael, *et al.*, 2021). One plausible reason for this perceived response could be the influence of cycle related symptoms. Specifically, *Chapter 6* indicates that the greater magnitude cycle related symptoms experienced in the days post exercise whilst bleeding could explain the differences in perceived recovery. For example, as demonstrated in *Chapter 5*, experiencing cycle related symptoms can increase perceptions of reduced recovery. Although, given that there were no differences in symptomology between the groups, a similar perceived response might be expected across

all testing phases in both groups, which was not observed, indicating that other factors might be involved. For instance, sex hormones are known to influence lifestyle factors, such as sleep (Baker & Lee, 2018), nutrition (Holtzman & Ackerman, 2021), and psychological factors (Garcia *et al.*, 2022; Prado *et al.*, 2021) which could indirectly affect the recovery process post exercise, and thus influence an individual's perceptions of recovery. Therefore, it is possible that the effect of changes in endogenous and exogenous sex hormones on indirect pillars of recovery could explain the differences in perceived recovery between groups. Overall, these findings, again, suggest the importance of considering the indirect effects of endogenous and exogenous sex hormones, for example cycle related symptoms and perceived effects, and their interaction with recovery outcomes post exercise in sportswomen. The practical implications of the above findings are discussed in *Section 7.5*.

7.5 Practical implications arising from this thesis

The results from this thesis could have several important practical implications for sportswomen, and those working with them, which can be considered as part of a three-zone model (Figure 7.1). Firstly, the findings within this thesis emphasise the need for creating an environment whereby, holistically, woman's physiology (*i.e.*, the MC and OCP use) is openly acknowledged and considered by sportswomen, and those working with them (*i.e.*, the 'inquisitive zone'). This might be best achieved through sportswomen and practitioner education to raise awareness and facilitate conversation.

Secondly, whilst understanding the effects of different reproductive hormone milieus is essential for those working with sportswomen (*i.e.*, not only for performance and training outcomes, but also for identifying dysfunctions and irregularities), the findings within this thesis suggest that practitioners need to move beyond solely focusing on sex hormone concentrations. Specifically, insights gathered from sex hormones alone might be limited and not truly reflect an individual's lived experience of the MC and OCP use. For example, as described in *Chapters 5 and 6*, cycle related symptoms, which are related to the changes in endogenous and exogenous sex hormones, are common in sportswomen and have the potential to influence both physical and perceptual measures of performance and recovery. Thus, respective cycle tracking that includes both symptom mapping and psychological readiness monitoring, across all women, irrespective of reproductive hormone profile, is advised based

on the findings within this thesis (*i.e.*, the ‘learning zone’). Notably, as highlighted in *Chapter 5*, symptom mapping should be consistent and performed in real-time, rather than retrospectively (as recall does not account for the phase effect on the magnitude of symptoms, which when elevated might have negative implications) to achieve the best results. Another novel practical recommendation arising from this thesis is the concept of a rolling average symptom score. Specifically, rather than solely using daily scores, a rolling score allows sportswomen, and those working with them, to account for the residual accumulation of symptoms in the days before and after exercise, as identified in *Chapter 6*. To add to symptom mapping, *Chapter 6* also highlights the importance of concurrently monitoring psychological readiness. Indeed, whilst individual wellness/readiness is frequently monitored within applied settings, rarely is it considered with a woman-centric focus (*i.e.*, information indirectly pertaining to reproductive hormonal profiles). Of note, is that real-time cycle tracking via symptom and psychological readiness mapping might present as a tool to overcome the regular need for sex hormone analysis, which is often inconvenient, expensive, and impractical within applied settings. Although importantly this tool should not replace the use of these gold standard assessments altogether, which are still recommended (where available), and it should be recognised that at present a consensus on respective cycle monitoring in applied environments is yet to be established, and further research is needed.

Thirdly, implementing the above real-time monitoring of symptoms and psychological readiness will help sportswomen and those working with them, to identify and predict key windows of opportunity for management strategies, and thus limit any potential negative effect of symptoms and perceived influences on performance and/or recovery outcomes (*i.e.*, the ‘growth zone’). Indeed, it is known that negative cycle related symptoms can often be mitigated using appropriate interventions. However, like many strategies adopted presently in practice, the evidence base that currently exists for the management of certain symptoms is based on data from men. Thus, where needed, it is advised that practitioners use the current data, alongside creative thinking to develop and implement bespoke symptom management strategies. However, practitioners need to be aware of the potential pros and cons of such an approach until more woman-specific research is available. For example, as recognised in *Chapter 6*, the use of exercise might be considered as a suitable strategy for managing symptoms in some sportswomen within a practical setting.

Importantly, in *Chapters 3* and *4* general guidelines on exercise performance across the MC and with OCP use could not be formed and instead it was recommended that a personalised approach should be taken. Indeed, sportswomen, and those working with them, should be aware of the MC and OCP use, and their potential effects, but this approach should be tailored to, and informed by, the individual, on a case-by-case basis. Building upon these findings, the inter-individual variability in cycle related symptoms and perceived effects of the MC and OCP use on performance and recovery outcomes reported in *Chapters 5* and *6* continue to support the need for an individualised approach. For instance, individuals who experience a greater magnitude of symptoms concurrent with negative changes in readiness to perform will likely report the biggest benefit of symptom mapping/ psychological readiness monitoring alongside proactive management strategies. Therefore, it is recommended that sportswomen become their own scientist, and any adjustments to their performance and/or training should be based on high-quality research (where available) and their own individual data through ‘me-search’ (*i.e.*, cycle tracking). Ultimately, as every woman’s response to their MC or OCP use is different, and likely changes across their lifespan, as well as possible cycle-to-cycle variations, there might never be universal guidelines to direct performance and training in all sportswomen. However, the goal for practitioners is to be able to work with, and react to, any changes in sportswomen using the information that is available. In particular, the findings from this thesis highlight the importance of considering the holistic impact of the MC and _mOCP *cycle* on performance and recovery outcomes in sportswomen, where needed. The above recommendations are intended to inform practice and ensure sportswomen can perform and train optimally, and consistently, on any given day, irrespective of their reproductive hormonal milieu.

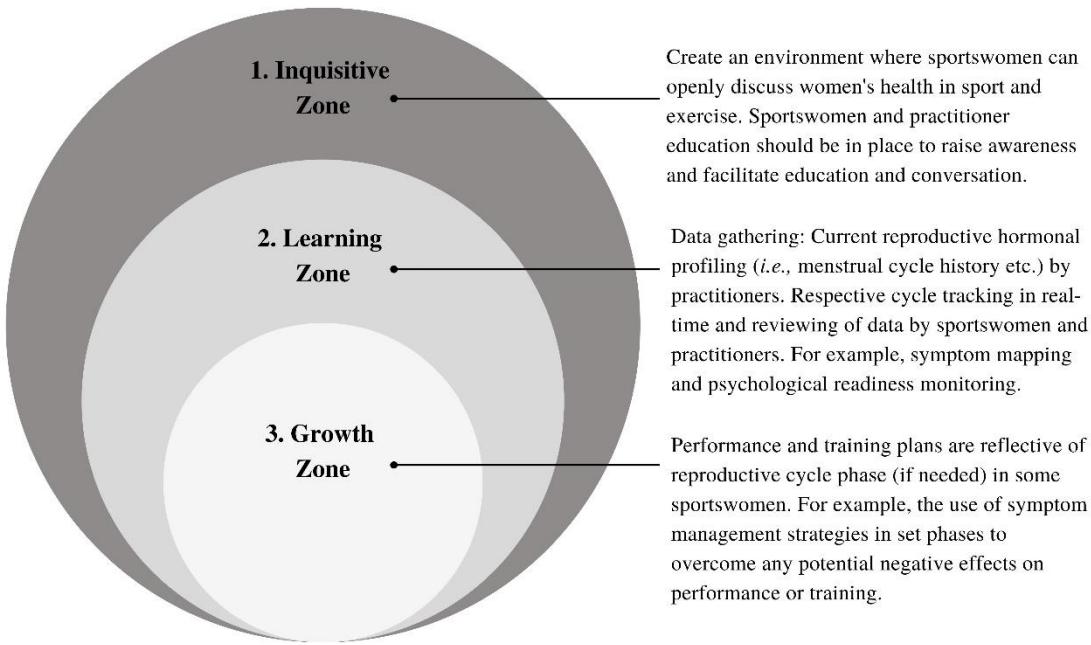


Figure 7-1 A conceptual model demonstrating sportswoman-specific monitoring zones for practice. Relative size of the circles gives an indication of probable impact.

7.6 Recommendations for future research

Alongside the previous recommendations for future research within *Chapters 3 to 6*, three main recommendations arose from this penultimate Chapter. Firstly, one issue that researchers need to consider moving forward is that the MC and responses to OCP use are likely to be highly individual, in both the underpinning physiology and individual lived experiences between different women. Consequently, this means that the broad-brush generalisations taken from average group responses within research might not be reflective of the individual response in practice. Indeed, future research should consider capturing this individual response within the research. For instance, this could be achieved through presenting data within results sections which showcase individual data points rather than solely presenting mean data, conducting case studies on individual sportswomen, and exploring intra-individual variability in responses across consecutive MC and OCP cycles. Furthermore, it is likely that there are both 'responders' (*i.e.*, sportswomen who are sensitive to sex hormone changes and/or perceive that their performance and training are affected by sex hormones) and 'non-responders' (*i.e.*, sportswomen who are less sensitive to sex hormone changes and/or do not perceive their performance and training to be affected by sex hormones). Thus, by merging both types of

individuals within study designs any potential effect of the MC and OCP use on performance and training outcomes might be reduced and/or diminished entirely. As such, future research investigating ‘responders’ and ‘non-responders’ would appear beneficial in this area. For example, it could be theorised that a specific ‘threshold’ of reproductive hormone concentrations and/or ratio exists whereby sportswomen over the ‘threshold’ are more likely to experience changes in their performance and training across the MC or with OCP use compared to those under the ‘threshold’. Additionally, it might be that the cycle related symptoms experienced by individuals (or a set threshold of symptoms) could indicate those who are more likely to experience changes in their performance and training across the MC or with OCP use, compared to those who are unaffected. Therefore, these types of metrics might provide information to distinguish between participants who are considered ‘responders’ and ‘non-responders’ in future studies. Moreover, it is recognised that the underpinning physiology and individual responses can vary from cycle-to-cycle within the same woman, and across a woman’s lifespan. As such, the above suggestions could also be relevant in helping to identify within woman variability. Whilst this is an interesting concept worth exploring it is noted that this theory is speculative, and further research is warranted.

Secondly, within the literature date, most studies have investigated the effects of the MC and OCP use on outcome measures assessed within pre-defined cycle phases, such as: 1) the early follicular phase/ OCP-free days; 2) the late follicular and ovulatory phases/ early OCP-taking days; and 3) the mid-luteal phase/ late OCP-taking days. Whilst this type of study design is optimal for assessing the effect of key ratios in endogenous and exogenous sex hormones on performance and training outcomes, it ignores the fluidity in changes in sex hormones across the MC or OCP use, and any associated impact of these fluctuations (*i.e.*, cycle related symptoms and perceived effects) outside these well-established timepoints. For example, the shift between the abovementioned phases (*e.g.*, the late luteal phase) can be swift and substantial in their magnitude creating sudden changes to a woman’s reproductive hormonal milieu. Consequently, these sudden ratio changes in sex hormone concentrations, alongside the potential indirect effects of these fluctuations, such as symptoms and perceived effects, could theoretically have a greater influence on performance and training outcomes. Moreover, it is important to recognise that women do not experience the MC, or OCP use, solely within set phases, and instead experience these reproductive hormonal profiles continuously. Therefore, the ability to translate the current research (measuring performance and recovery outcomes solely in two or three timepoints across the MC or OCP use) into real-life practice is reduced.

Future studies should therefore consider adopting a more fluid research design that allows for the investigation of multiple timepoints across the MC or OCP use, as this will help provide a complete picture of potential effects, allowing sportswomen to perform and train consistently across their entire respective cycle.

Finally, *Chapters 5* and *6* highlight the importance of considering both the reproductive hormonal milieu in tandem with the individual impact (*i.e.*, cycle related symptoms and perceived effects) of the MC and _mOCP *cycle* on performance and recovery outcomes in some sportswomen. Indeed, combining both the techniques used within *Chapters 5* and *6* with more traditional models of assessing endogenous and exogenous sex hormones and their potential effect on measures of exercise performance and training provides the opportunity to characterise the complex, interactive, and individual nature of the MC and OCP in sportswomen. Thus, to advance the knowledge within this area, and ultimately improve practice, future studies should consider utilising and building upon this hybrid study design.

CHAPTER 8 – CONCLUSION

8.1 Concluding remarks

This thesis has studied the effects of the MC, OCP use, and related symptoms on both physical and perceptual measures of performance and recovery in sportswomen. The summaries of each Chapter are presented in *Chapter 7, Section 7.2*; however, the overarching theme of the individual Chapters' conclusions is that sportswomen, and those working with them, should also consider any individual lived experiences (namely, cycle related symptoms and perceived effects) of the MC and OCP use on exercise performance and recovery post exercise, rather than solely focusing on the effects of reproductive hormonal milieus alone. Indeed, this will provide a more comprehensive understanding of the influence of the MC and OCP use on performance and recovery outcomes in sportswomen. Moreover, it appears that moving beyond a 'one-size-fits-all' approach to working with sportswomen and instead determining 'what size fits the individual sportswoman' will help to maximise any benefits and minimise any potential barriers of both the direct and/or indirect effects of endogenous and exogenous sex hormones on performance and recovery outcomes. Overall, the findings within the present thesis contribute to advancing scientific knowledge on woman-specific physiology, in the context of sport and exercise science, which will ultimately allow sportswomen to unlock their full health and performance potential.

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APPENDICES

Appendix A: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 Checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	51-52
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	52
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (<i>e.g.</i> , Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (<i>e.g.</i> , PICOS, length of follow-up) and report characteristics (<i>e.g.</i> , years considered, language, publication status) used as criteria for eligibility, giving rationale.	52-54
Information sources	7	Describe all information sources (<i>e.g.</i> , databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	54-55
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	<i>Appendix C</i>
Study selection	9	State the process for selecting studies (<i>i.e.</i> , screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	61
Data collection process	10	Describe method of data extraction from reports (<i>e.g.</i> , piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	61

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	52-61
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	61-62
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	53-54 <i>Appendix B</i>
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	62-64
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	62-64
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	62-64
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	64-65
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	65-66 and <i>Appendix B</i>
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	66-67
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	67-72
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	67-72
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	67-72
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	67-72
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	72-76
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	72-76
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	76-77
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix B: Full List of Considered Outcomes from the Included Studies.

Considered outcome(s)
Strength
Hamstring: quadricep strength ratio at 60 and 180° s ⁻¹
Maximum voluntary contraction (N) with motor nerve stimulation
Time to task failure (s) during fatiguing task involving sets of intermittent isometric contractions performed in the lower body
Peak isokinetic torque of the knee flexors and extensors at 1.05 and 3.14 rad.s ⁻¹ through 90° range of motion on an isokinetic dynamometer (Nm)
Maximal voluntary isometric contraction of the knee flexors and extensors measured at 0 rad.s ⁻¹ and 60° of knee flexion with and without electrical stimulation (Nm)
Rate of force production during a maximal voluntary isometric hamstring contraction (N.s ⁻¹)
Time to 50% peak force during a maximal voluntary isometric hamstring contraction (ms)
Maximal isometric lifting strength (MILS) performed at both knee and waist height (N)
Time to volitional fatigue at 45% MILS performed at both knee and waist height (s)
Maximal acceptable load (kg)
Handgrip strength (N)
Standing long jump performance x body mass (kg.m)
Mean peak torque of knee flexors and extensors at 60, 180, 240°.s (Nm)
Muscular endurance and work ratios of knee flexors and extensors at 240°.s
Maximal torque produced during an isometric muscle action (Nm)
Torque produced at a sub-maximal (20, 50 and 75%) isometric muscle action (Nm)
Peak isokinetic muscle torque of knee extensors at 120°.s (Nm)
Handgrip strength (kg)
Peak length of hop during a one-leg hop test (cm)
Maximum voluntary isometric force of the first dorsal interosseous (N)
Maximal jump power from a multi-jump test (W.kg)
Maximal jump height from a squat jump test (cm)
Torque production (Nm) of the knee extensors and flexors at 60, 80, 120 and 240°.s
Torque ratios (peak and total work) during concentric and eccentric hamstring and quadriceps testing at 60 and 180°.s
Peak torque of quadricep and hamstring flexors and extensors at 120°.s (Nm)

Hamstring: quadricep strength ratio

Time to task failure during a sustained isometric fatiguing contraction at 25% of MVC (s) performed in the upper body

Back lift strength (kg)

Isometric quadricep strength (N) at 60° with electrical stimulation

Isokinetic strength of the quadricep flexors and extensors at 60°.s⁻¹ and 140°.s⁻¹ (Nm)

Time to fatigue during static handgrip at 40% of maximum (s)

Counter movement jump height (cm)

Maximal voluntary isometric strength of knee extensors and plantar flexors (Nm) with electrical stimulation

Peak isokinetic torque of quadriceps and hamstrings at 30°.s (Nm)

Force to flex the knee from 90° to 125° (N)

Maximal voluntary isometric strength of the quadriceps and hamstrings (Nm.kg)

Isometric hip strength (Nm)

Work done during Mosso's Ergograph test (J)

Endurance time at 20, 40 and 60% handgrip maximum strength (s)

Bench press mean weight lifted (pounds)

Leg press mean weight lifted (pounds)

MVC (kg) during leg press exercise

Mean and peak force at 20, 40, 60 and 80% of one-repetition maximum performed on a Smith Machine

Maximum voluntary isometric strength of the quadriceps (N)

Jump height (cm) from a drop jump

Maximum isometric torque of knee extensor muscles (Nm) with electrical stimulation

Maximum voluntary contraction (Nm)

Mean time to task failure (s) during an endurance task

Absolute performance during a five-jump test (m)

Standing broad jump performance distance (inches)

Maximum hip flexion and extension strength (pounds)

Endurance

Cycling TTE at 70% $\dot{V}O_{2\text{peak}}$ (min)

Queens College Step Test to predict $\dot{V}O_{2\text{max}}$ (ml.kg⁻¹.min⁻¹)

Treadmill running TTE at a heart rate of 135–140 b.min⁻¹ (min)

$\dot{V}O_{2\text{peak}}$ (ml.kg⁻¹.min⁻¹) during a progressive-intensity, continuous, treadmill running test to exhaustion

Treadmill running TTE at 70% $\dot{V}O_{2\text{peak}}$ (min)

$\dot{V}O_{2\text{max}}$ (ml.kg⁻¹.min⁻¹) during a progressive incremental exercise test on a treadmill until exhaustion

TTE during a progressive incremental exercise test on a treadmill (min)

$\dot{V}V_{O_{2\text{max}}}$ (km.h) during an incremental maximal test to exhaustion performed on a treadmill

Peak treadmill velocity (km.h) during an incremental maximal test to exhaustion

Anaerobic capacity (W) from a Wingate Test

Peak power (W) from a Wingate Test

Power decline (W) from a Wingate Test

Margaria-Kalamen (kgm.s)

Cycled for 2 hrs at 70% $\dot{V}O_{2\text{peak}}$ and then completed a 4 kJ/kg body weight TT on a cycle ergometer (min)

Power output (W) during a continuously graded incremental test until exhaustion on a cycle ergometer

TTE (min) during a continuously graded incremental test until exhaustion on a cycle ergometer

$\dot{V}O_{2\text{peak}}$ (l.min) from a continuously graded incremental test until exhaustion on a cycle ergometer

$\dot{V}O_{2\text{max}}$ (ml.kg⁻¹.min⁻¹) from an incremental graded-exercise test until volitional exhaustion on a cycle ergometer

TTE (min) from an incremental graded-exercise test until volitional exhaustion on a cycle ergometer

$\dot{V}O_{2\text{max}}$ (l.min⁻¹) from a progressively increasing protocol for nine minutes on a cycle ergometer

Working capacity at a heart rate of 170 b.min (W) from a progressively increasing protocol for nine minutes on a cycle ergometer

Maximal pedalling time (s) from a progressively increasing protocol for nine minutes on a cycle ergometer

$\dot{V}O_{2\text{max}}$ (ml.kg⁻¹.min⁻¹) from a maximal incremental exercise treadmill protocol until exhaustion

TTE (min) from a maximal incremental exercise treadmill protocol until exhaustion

$\dot{V}O_{2\max}$ (ml.kg⁻¹.min⁻¹) from an incremental test on a cycle ergometer until exhaustion
TTE (s) during a progressive maximal exercise test performed on a cycle ergometer
 $\dot{V}O_{2\max}$ (ml.kg⁻¹.min⁻¹)
TTE during a 1.5-mile run-walk (s)
TTE during a 600-yard run-walk (s)
Distance covered during a 12-minute run-walk (miles)
 $\dot{V}O_{2\max}$ (ml.kg⁻¹.min⁻¹) during a graded exercise test on a cycle ergometer until exhaustion
Maximal cycling power (W) during a force-velocity test
Optimal velocity (rpm) during a force-velocity test
Optimal force (kg) during a force-velocity test
Physical working capacity (kg.m.min)
 $\dot{V}O_{2\max}$ (l.min⁻¹) from an incremental stress test until exhaustion on a cycle ergometer
TTE (s) from an incremental stress test until exhaustion on a cycle ergometer
Maximum power output (W) from an incremental stress test until exhaustion on a cycle ergometer
 $\dot{V}O_{2\max}$ (ml.kg⁻¹.min⁻¹) from a maximal progressive incremental test until exhaustion on a cycle ergometer
TTE (min) during a prolonged exercise performance test on a cycle ergometer at 60%
 $\dot{V}O_{2\max}$ followed by an incremental exercise test until exhaustion
Sprint time (s) at 5, 10 and 30 m
Distance covered during Yo-Yo Intermittent Endurance Test (m)
Maximum power output (kpm.min) during a progressive incremental exercise test to exhaustion on a cycle ergometer
Cycling TTE at 90% W_{\max} (min)
Peak power (W.kg), from a Wingate test
Mean power (W.kg) from a Wingate test
Fatigue index (%) from a Wingate test
Peak cycling power (W.kg) during a ramp test on a cycle ergometer until exhaustion
 $\dot{V}O_{2\max}$ (l.min⁻¹) from a continuous progressive test until exhaustion on a treadmill
Anaerobic speed test (s)
TTE during an endurance run at 90% $\dot{V}O_{2\max}$ (s)
TTE (s) during a 20 s repeat sprint continuous incremental protocol until exhaustion on a treadmill

TTE (min) during a continuous incremental exercise protocol on a treadmill
16 km TT performance (min) on a cycle ergometer
15 km TT performance (min) on a cycle ergometer
30 km TT performance (min) on a cycle ergometer
Tennis serve performance accuracy
Tennis serve performance velocity (mph)
100-m freestyle time (s)
200-m freestyle time (s)
Peak power output (W) from an incremental exercise test on a cycle ergometer
Total work done (kJ) from an incremental exercise test on a cycle ergometer
Sprint duration until exhaustion throughout maximum accumulated oxygen deficit tests on a cycle ergometer
Power relative (W.kg) from an incremental test until voluntary exhaustion on a cycle ergometer
 $\dot{V}O_{2\max}$ (ml.min) from an incremental test until voluntary exhaustion on a cycle ergometer
Distance ran during Loughborough Intermittent Shuttle Test (m)
15 m sprint time (s)
Mean and peak power outputs during an all-out 30 second sprint (W)
TTE (min) from an incremental maximal exercise test on a cycle ergometer
Repeated shuttle-sprint ability test mean time (s)
Peak and mean power output during repeat sprint tests (W)
Fatigue index for power during repeat sprint tests (%)
Peak and mean speed during repeat sprint tests (m.s)
Fatigue index for speed during repeat sprint tests (m.s)
Incremental rowing ergometer test to determine $\dot{V}O_{2\max}$ (l.min)
Incremental rowing ergometer test to determine maximal power output (W)
Time of attaining anaerobic peak power during maximal cycling sprint test (s)
Time of maintaining anaerobic peak power during maximal cycling sprint test (s)
Power decrease during maximal cycling sprint test (W.kg.s)
Peak cycling power during an incremental test on a cycle ergometer until exhaustion (W.kg)

TTE, time to exhaustion; MILS, maximal isometric lifting strength; $\dot{V}O_{2\max}$ maximal oxygen uptake; $\dot{V}O_{2\text{peak}}$ peak oxygen uptake; $v\dot{V}O_{2\max}$, velocity at maximal oxygen uptake.

Please note that exact duplicate outcomes were deleted.

Appendix C: Example of a Search Strategy Conducted in PubMed (14/01/2019).

Limits applied	
Search terms	Number of results
Humans	
Females	
English language	
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and athletic performance	221
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and sports performance	277
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and strength	197
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and torque	16
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and force	144
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and max* voluntary contraction	24
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and isometric	55
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and isokinetic	16
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and neuromuscular	46
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and skeletal muscle	184
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and muscular performance	14
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and power	285
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and anaerobic	65

Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and anaerobic capacity	9
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and anaerobic power	12
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and aerobic	119
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and endurance	158
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and aerobic capacity	27
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and aerobic power	19
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and endurance capacity	26
Menstrual cycle OR menstrual phase OR follicular phase OR luteal phase and endurance power	13

Total: 1927 (with duplicates)

Appendix D: Study Quality Assessment.

Downs and Black checklist (maximum score attainable = 16). Study quality was categorised as follows: “high”: 14 – 16; “moderate”: 10 – 13; “low”: 6 – 9; “very low”: 0 - 5).

Reporting

Q1. Is the hypothesis/aim/objective of the study clearly described?

Yes = 1

No = 0

Q2. Are the main outcomes to be measured clearly described in the introduction or methods section? If the main outcomes are first mentioned in the results section, answer no.

Yes = 1

No = 0

Q3. Are the characteristics of the participants included in the study clearly described? In observational studies, inclusion and/or exclusion criteria should be given. In case-control studies, inclusion and/or exclusion and the source of controls should be given.

Yes = 1

No = 0

Q4. Were the tested menstrual cycle phases clearly described? Answer yes if the precise criteria used to define phase were provided, answer no if the exact phase tested cannot be ascertained (*e.g.*, vague language such as “early” or “late” were used, without defining the criteria)

Yes = 1

No = 0

Q5. Are the main findings of the study clearly described? Simple outcome data should be reported for all major findings so the reader can check the major analyses and conclusions. This does not cover statistical tests which are addressed in other questions.

Yes = 1

No = 0

Q6. Does the study provide estimates of the random variability in the data for the main outcomes? In non-normal data, inter-quartile range should be reported. In normal data, standard deviation, standard error, or confidence intervals should be reported.

Yes = 1

No = 0

External validity

Q7. Were the participants confirmed as non-hormonal contraceptive users, for at least three months prior to participation?

Yes = 1

No = 0

Unable to determine = 0

Internal validity – bias

Q8. Was at least one familiarisation trial conducted prior to exercise testing?

Yes = 1

No = 0

Unable to determine = 0

Q9. Were the exercise test conditions adequately standardised (taking into consideration factors including time of day, prior nutritional intake [including caffeine] and prior exercise).

Yes (all relevant factors standardised) = 2

Yes (some relevant factors standardised) = 1

Exercise testing unstandardized = 0

Unable to determine = 0

Q.10 If any of the results of the study were based on ‘data dredging’ was this made clear? Any analyses that had not been planned at the outset should be clearly indicated. If no retrospective subgroup analyses were reported, then answer yes.

Yes = 1

No = 0

Unable to determine = 0

Q11. Were statistical tests used to assess the main outcomes appropriate? The statistical techniques used must be appropriate to the data and the research question.

Yes = 1

No = 0

Unable to determine = 0

- Q12. Were the main outcome measures used accurate (*i.e.*, valid, and reproducible)? For studies where the validity and reproducibility of outcome measures are clearly described, the question should be answered yes. For studies which refer to other work that demonstrates the outcome measures are accurate, answer yes.

Yes = 1

No = 0

Unable to determine = 0

Internal validity – confounding (selection bias)

- Q.13 Was the order of phase testing randomised?

Yes = 1

No = 0

Unable to determine = 0

Power

- Q.14 Did the study have sufficient power to detect an *a priori* specified scientifically important effect at a pre-determined probability threshold? Answer yes if they included a power calculation, and no if not.

Yes = 1

No = 0

- Q15. Was study retention > 85%?

Yes = 1

No = 0

Unable to determine = 0

GRADE (assign an *a-priori* study quality rating based on the modified Downs and Black checklist, so all studies will start out as being of “high”, “moderate”, “low”, “very low”).

- Q1. Identify if menstrual cycle phase was confirmed using blood samples. If yes, the *a priori* rating is maintained, and this is the final study quality rating. If not, the study is downgraded a level (*e.g.*, a study that started out as high, drops to moderate).
- Q2. Identify if menstrual cycle phase was confirmed using ovulation kits. If yes, the Q1. rating is maintained. If not, the study is downgraded another level (*e.g.*, a study that started out high, drops to low). This means that the maximum rating that any study that does not use blood analysis or ovulation kits is “low” or “very low”.
-

Appendix E: Table of Included Studies.

Author and date	Aim	Population (participant health, training status and sample size)	MC phases tested	Methods of determining MC phase	Outcome measure(s)	Study conclusion	Quality rating
Abt <i>et al.</i> (2007)	To determine whether MC phase affects fine motor coordination, postural stability, knee strength and knee joint kinematics and kinetics	Physically active women (n = 10)	EF, ovulation, and ML	Counting of days, MC history, urinary ovulation detection test and serum oestrogen and progesterone	Hamstring: quadricep strength ratio at 60 and 180 s ⁻¹	No differences existed between phases of the MC for hamstring: quadriceps strength ratio at 60 and 180 s ⁻¹	Moderate
Ansdell <i>et al.</i> (2019)	To investigate knee extensor neuromuscular function and fatigability across the MC	Eumenorrheic women (n = 13)	EF, ovulation, and ML	Counting of days, MC history, and serum oestrogen and progesterone	MVC with motor nerve stimulation (N) Time to task failure during fatiguing task	MVC was not affected by MC phase. Time to task failure was longer in the ML phase compared	Moderate

Bailey <i>et al.</i> (2000)	To determine whether MC phase influences the effect of carbohydrate supplementation on substrate metabolism and fatigue during prolonged exercise	Moderately trained women cyclists (n = 9)	EF and ML	Counting of days and serum oestrogen and progesterone	Cycling TTE at 70% $\dot{V}O_{2\text{peak}}$ (min)	No differences in TTE were observed between MC phases	Low
Bambaeichi <i>et al.</i> (2004)	To determine whether the isolated and combined effects of circamensal variation and diurnal changes affect muscle strength	Sedentary women (n = 8)	EF, LF, ovulation, ML and LL	Counting of days, MC history, BBT (one month prior) and urinary ovulation detection test	Peak isokinetic torques of the knee flexors and extensors at 1.05 and 3.14 rad.s ⁻¹ (Nm) through 90° range of motion	MC phase variation was observed for peak torque of knee flexors at 1.05 and 3.14 rad.s (Nm) and also isometric	Low

Bandyopadhyay and Dalui (2012)	To determine whether MC phase influences endurance capacity and cardiorespiratory responses	Sedentary women (n = 45)	EF, LF and ML	Counting of days and BBT	Queens College Step Test to predict $\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹)	$\dot{V}O_{2\max}$ and running TTE were lower in the EF phase	Very low
Beidleman <i>et al.</i> (1999)	To determine whether MC phase affects	Physically active women (n = 8)	EF and ML	MC history, counting of	$\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹ or l.min ⁻¹)	Neither $\dot{V}O_{2\max}$ nor running TTE	High

	maximal and submaximal exercise performance at sea level and acute altitude	days, urinary ovulation detection test and serum oestrogen and progesterone	during a progressive- intensity, continuous, treadmill running test to exhaustion Running TTE at 70% $\dot{V}O_{2\text{peak}}$ (min)	was affected by MC phase		
Bell <i>et al.</i> (2011)	To determine whether MC phase affects hamstring neuro- mechanics and leg stiffness	Physically active women (n = 15)	EF and ovulation Counting of days, MC history, urinary ovulation detection test and serum oestrogen and progesterone	Rate of force production during a maximal voluntary isometric hamstring contraction ($N.s^{-1}$) Time to 50% peak force during a maximal voluntary isometric hamstring contraction (ms)	No changes were observed across the MC for both variables	Moderate

Bemben <i>et al.</i> (1995)	To determine whether MC phase affects ventilatory and blood lactate responses to maximal treadmill exercise	Moderately active women (n = 5)	EF, ovulation, and ML	Counting of days, BBT and serum oestrogen and progesterone	$\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹) and running TTE during a progressive incremental exercise test (min)	There were no differences in $\dot{V}O_{2\max}$ and running TTE between MC phases	Low
^a Birch and Reilly (1999)	To determine whether MC phase affects the physical, physiological, and subjective responses to both isometric and dynamic lifting performance	Healthy women (n = 17)	EF, LF, ovulation, ML and LL	Counting of days, MC history, BBT (two months prior and during), and assessment of symptoms and alterations in cervical mucus	MILS performed at both knee and waist height (N) Time to volitional fatigue at 45% MILS performed at both knee and waist height (s) Maximal acceptable load (kg)	No differences between MC phases were identified for any of the lifting performances variables	Very low
^b Birch and Reilly (2002)	To determine whether the circamensal and diurnal rhythms in	Moderately active women (n = 10)	LF and ML	Counting of days, MC history, BBT	MILS at knee height (N)	MILS and time to fatigue did not	Very low

	temperature affect the production of maximal voluntary muscle force			and assessment of symptoms and alterations in cervical mucus	Time to volitional fatigue at 45% MILS at knee height (min)	differ between either MC phase
Burrows and Bird (2005)	To determine whether MC phase affects $\dot{V}O_{2\text{max}}$ and peak treadmill velocity in a homogenous group of highly trained female endurance runners	Highly trained endurance women (n = 10)	EF, LF, EL and LL	MC history, counting of days and salivary progesterone	$\dot{V}O_{2\text{max}}$ (km.h) and peak treadmill velocity (km.h) during an incremental maximal test to exhaustion performed on a treadmill	No differences in $\dot{V}O_{2\text{max}}$ or peak treadmill velocity were found between the phases of the MC
Bushman <i>et al.</i> (2006)	To determine whether MC phase affects short term, high intensity (power) performance in moderately active women	Active women (n = 7)	EF and EL	MC history, counting of days, BBT and urinary ovulation detection test	Anaerobic capacity, peak power, and power decline from a Wingate Test (W) Margaria-Kalamen performance	There were no differences in Wingate or Margaria-Kalamen (kgm.s)

						between MC phases	
Campbell <i>et al.</i> (2001)	To determine whether MC phase and carbohydrate ingestion affects glucose kinetics and exercise performance	Healthy, moderately endurance-trained women (n = 8)	EF and ML	MC history, urinary ovulation detection test and serum oestrogen and progesterone	Cycled for 2 hrs at 70% $\dot{V}O_{2\text{max}}$ and then completed a 4 kJ/kg body weight TT performance on a cycle ergometer (min)	TT performance was longer in the EF phase, compared to the ML phase of the MC	Moderate
Casazza <i>et al.</i> (2002)	To determine whether MC phase affects peak exercise capacity, as measured by $\dot{V}O_{2\text{peak}}$	Healthy, habitually exercised women (n = 6)	LF and ML	MC history, counting of days, urinary ovulation detection test and serum oestrogen and progesterone	Power output (W), TTE (min) and $\dot{V}O_{2\text{peak}}$ (l.min) from a continuously graded test on a cycle ergometer	MC phase does not affect peak exercise capacity, with no changes in power output, TTE and $\dot{V}O_{2\text{peak}}$	Moderate
Davis <i>et al.</i> (1991)	To determine whether MC phase affects muscle performance	Healthy women (n = 12)	EF, ovulation, and ML	No information	Handgrip strength (N) Standing long jump performance	Handgrip strength and performance was superior during	Very low

				x body mass (kg.m)	the EF than both the ovulatory and ML phases of the MC. Standing long jump performance was again superior during the EF phase, although not with respect to the ML phase of the MC
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Dean <i>et al.</i> (2003)	To determine whether MC phase affects lactate threshold	Habitually active women (n = 8)	EF, LF and ML	MC history, counting of days, BBT and serum oestrogen and progesterone	$\dot{V}O_{2\max}$ and TTE (min) from an incremental graded-exercise test until volitional exhaustion on a cycle ergometer	There were no differences in MC phase $\dot{V}O_{2\max}$ and TTE	Low
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De Bruyn- Prevost <i>et al.</i> (1984)	To determine whether MC phase affects the physiological response to aerobic and anaerobic tests by young women	Healthy women (n = 7)	EF, ovulation, and LL	BBT	Progressively increasing protocol for nine minutes on a cycle ergometer to determine $\dot{V}O_{2\max}$ (l.min ⁻¹), working capacity (W) and maximal pedalling time (s)	There were no differences in any performance variables	measures across the MC	Very low
De Souza <i>et al.</i> (1990)	To determine whether MC phase affects the physiological and metabolic responses to maximal and submaximal exercise in eumenorrheic runners	Well-conditioned woman athletes (n = 8)	EF and ML	MC history, counting of days, urinary ovulation detection test (one month prior, during and one month post) and serum oestrogen and progesterone	Maximal exercise treadmill protocol to determine $\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹) and TTE (min)	No differences were observed for $\dot{V}O_{2\max}$ and TTE between MC phases		High

Dibrezzo <i>et al.</i> (1988)	To determine whether MC phase affects dynamic strength and work performance of the knee flexors and extensors	Healthy women (n = 21)	EF, ovulation, and LL	MC history, counting of days	Mean peak torque of knee flexors and extensors at 60, 180, 240°.s (Nm) Muscular endurance and work ratios of knee flexors and extensors	There were no differences in mean peak torque or work ratios among the three MC phases	Very low
Dombovy <i>et al.</i> (1987)	To determine whether MC phase affects the ventilatory response and exercise performance in normally menstruating, non-athletic women	Women not currently in active physical training (n = 8)	LF and ML	MC history, counting of days and serum oestrogen and progesterone	Incremental test on a cycle ergometer to determine $\dot{V}O_{2\text{max}}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$)	There were no differences in $\dot{V}O_{2\text{max}}$ across the MC	Moderate
Doolittle and Engebretsen (1972)	To determine whether MC phase affects variations in performance	Healthy women (n = 16)	LF, ovulation, EL and LL	Counting of days	$\dot{V}O_{2\text{max}}$ ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) TTE during a 1.5-mile run-walk (s)	There were no differences in any performance variable	Very low

					TTE during a 600-yard run-walk (s)	measured across the MC
					Distance covered during a 12-minute run-walk (miles)	
Drake <i>et al.</i> (2003)	To determine whether MC phase affects electromyography and mechanomyography during isometric muscle actions of the rectus femoris	Women not involved in any exercise program (n = 7)	EF, LF, ovulation, and EL	MC history, counting of days, urinary ovulation detection test	Maximal torque during an isometric muscle action (Nm) Torque at a sub-maximal (20, 50, 75%) isometric muscle action (Nm)	There were no differences in maximal and sub-maximal torque variables between MC phases
Ekenros <i>et al.</i> (2013)	To determine whether MC phase affects muscle strength in the upper and lower limb, as well as hop performance	Women involved in recreational physical activity (n = 9)	EF, ovulation, and ML	Counting of days, urinary ovulation detection test and serum	Peak isokinetic muscle torque of knee extensors at 120°.s (Nm) Handgrip strength (kg)	No differences in handgrip strength and hop performance were reported between MC

	strength and sex hormone bioavailability		ovulation detection test and serum oestrogen and progesterone	the first dorsal interosseous (N)	muscle strength during the MC	
Ettinger <i>et al.</i> (1998)	To determine whether MC phase affects reflex responses to static handgrip at 30% maximal voluntary contraction in women	Healthy women (n = 10)	EF and LF	Serum oestrogen and progesterone	Handgrip strength (kg)	There were no differences in handgrip MVC strength between MC phases
Frandsen <i>et al.</i> (2020)	To determine the influence of the MC on whole body peak fat oxidation rate during a graded exercise test	Recreationally active women (n = 19)	LF, ovulation, and ML	MC history and serum oestrogen and progesterone	$\dot{V}O_{2\text{max}}$ (ml.kg ⁻¹ .min ⁻¹) during a graded exercise test on a cycle ergometer until exhaustion	There were no differences in $\dot{V}O_{2\text{max}}$ between MC phases
Friden <i>et al.</i> (2003)	To determine whether MC phase affects muscle strength and muscle endurance	Physically active women (n = 10)	EF, ovulation, and ML	Counting of days, urinary ovulation detection test	Peak handgrip strength (kg)	No variation in any performance variable was detected during

				and serum oestrogen and progesterone	Best jump during a one-leg hop test (cm)	the different phases of the MC	
Giacomoni <i>et al.</i> (2000)	To determine whether MC phase affects maximal anaerobic performance during short-term anaerobic tests	Healthy women (n = 7)	EF, LF and ML	MC history, counting of days and serum progesterone	Maximal cycling power (W), optimal velocity (rpm) and optimal force (kg) during a force-velocity test Maximal jump power during a multi-jump test (W.kg) Maximal jump height from a squat jump test (cm)	No differences were observed in the force- velocity test or jump test performance among the three phases of the MC	Moderate

Girija and Veeraiah (2011)	To determine whether MC phase affects physical working capacity in an Indian population	Healthy women (n = 40)	EF, LF and ML	Counting of days, serial follicular scanning	PWC (kg.m.min) performed on a cycle ergometer	PWC decreased in the ML and EF phases of the MC when compared to the LF phase	Very low
^a Gordon <i>et al.</i> (2012)	To determine the effects of MC phase on the development of peak torque across a range of isokinetic speeds	Well trained woman participants (n = 11)	EF, LF, ML and LL	MC history, counting of days, salivary oestrogen, and progesterone	Torque production (Nm) of the knee extensors and flexors at 60, 80, 120 and 240°.s	There are fluctuations in peak torque of the knee extensors in response to phases of the MC	Very low
^b Gordon <i>et al.</i> (2017)	To determine whether MC phase affects maximal oxygen uptake and associated cardio dynamic response	Physically active women (n = 10)	EF, LF, ML and LL	MC history, counting of days and salivary	Incremental stress test on a cycle ergometer to determine $\dot{V}O_{2\text{max}}$ (l.min ⁻¹), TTE (s)	There were no differences in $\dot{V}O_{2\text{max}}$, TTE and maximum power	Very low

				oestrogen and progesterone	and maximum power output (W)	output across the MC phases
^a Grucza <i>et al.</i> (1993)	To determine whether MC phase affects changes in the thermo- sensitivity of the thermoregulatory system in exercising women	Physically active women (n = 10)	LF and ML	MC history and BBT (one month prior and during)	A maximal test on a cycle ergometer to determine $\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹)	$\dot{V}O_{2\max}$ did not differ between the phases of the MC
^b Grucza <i>et al.</i> (2002)	To determine whether MC phase affects cardiorespiratory responses to exercise	Physically active women (n = 10)	LF and ML	MC history and BBT (one month prior and during)	A maximal test on a cycle ergometer to determine $\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹)	$\dot{V}O_{2\max}$ was greater in the LF phase compared with the ML phase of the MC
Gur (1997)	To determine whether MC phase affects reliability of concentric and eccentric isokinetic measurements and reciprocal moment ratios in knee muscles	Sedentary women (n = 16)	EF, LF and ML	MC history, counting of days and serum oestrogen and progesterone	Torque ratios (peak and total) during concentric and eccentric hamstring and quadriceps testing at 60 and 180°.s	Concentric and eccentric peak torques, and total works, and their reciprocal ratio was not different among the MC phases

Hertel <i>et al.</i> (2006)	To determine whether MC phase affects hamstring and quadriceps strength, knee joint position sense, postural control and knee joint laxity	Competitive soccer or stunt cheerleading woman athletes (n = 14)	LF, ovulation, and ML	MC history, counting of days, urinary ovulation detection test (one month prior) and urinary oestrogen and progesterone	Peak torque of quadricep and hamstring flexors and extensors at 120°.s (Nm) Hamstring: quadricep strength ratio	There were no differences in the measures of strength (peak torque of hamstrings and hamstring: quadricep ratio) across the MC	Low
Hoeger-Bement <i>et al.</i> (2009)	To determine whether MC phase affects exercise-induced analgesia in young women after a fatiguing isometric contraction	Healthy women (n = 20)	LF and ML	MC history, counting of days and urinary ovulation detection test	Time to task failure during a sustained isometric fatiguing contraction at 25% of MVC (s) performed in the upper body	There was no difference in time to task failure of the sustained 25% MVC between the phases of the upper body	Low
Hoshi (1997)	To determine whether MC phase affects muscular strength, grip	Healthy women (n = 14)	EF, LF, ovulation and ML	Counting of days and serum	Handgrip strength (kg)	Handgrip strength was lower in the EF	Low

	strength and back lift strength	oestrogen and progesterone	Back lift strength (kg)	phase compared with all other MC phases.
				Back lift strength was lower in the EF phase compared with all other MC phases and was higher in the LF compared with ovulation and the ML phases of the MC
^a Janse de Jonge et al. (2001)	To determine whether MC phase affects skeletal muscle strength, fatigue, and contractile properties	Healthy women (n = 15)	EF, LF and ML	Counting of days, BBT, assessment of symptoms and serum oestrogen and progesterone
				Isometric quadricep strength (N) with electrical stimulation
				Isokinetic strength of the quadriceps flexors and
				No changes were found in any of the muscle function parameters throughout the MC

						extensors at 60°.s ⁻¹ (Nm)	
^b Janse de Jonge <i>et al.</i> (2012)	To determine whether MC phase affects prolonged exercise performance in both temperate and hot, humid conditions	Recreationally active women (n = 8)	EF and ML	Counting of days, BBT and serum oestrogen and progesterone	TTE (min) during a prolonged exercise performance test on a cycle ergometer at 60% $\dot{V}O_{2\text{max}}$ followed by an incremental exercise test until exhaustion	In temperate conditions, no changes in prolonged exercise performance were found over the MC	Moderate
Jarvis <i>et al.</i> (2011)	To determine whether MC phase affects the cardiovascular and vasomotor sympathetic response during static handgrip to fatigue and	Healthy women (n = 11)	EF and ML	Counting of days, urinary ovulation detection test and serum oestrogen and progesterone	Handgrip strength (kg) Time to fatigue during static handgrip at 40% of MVC (s)	MC phase did not influence MVC or time to fatigue	Moderate

post exercise circulatory arrest							
Julian <i>et al.</i> (2017)	To determine whether MC phase affects performance in soccer specific tests	High-level woman soccer players (n = 9)	EF and ML	MC history, counting of days and serum oestrogen and progesterone	Sprint time (s) at 5, 10 and 30 m CMJ height (cm) Distance covered during Yo-Yo IET (m)	Yo-Yo IET performance was considerably lower during the ML phase as compared to the EF phase of the MC. There were no differences across the MC in all other performance variables	Low
Jurkowski <i>et al.</i> (1981)	To determine whether MC phase affects exercise performance and the responses of oxygen transport, cardiac output, and lactate	Healthy women (n = 9)	LF and ML	Counting of days, BBT and serum progesterone	Maximum power output (kpm.min) during a progressive incremental	There was no difference in maximum power output across the MC. TTE was greater during	Low

	production at several work rates				exercise test to exhaustion on a cycle ergometer	the ML phase compared to the LF phase of the MC	
					Cycling TTE at 90% W _{max} (minutes)		
Kaygisiz <i>et al.</i> (2003)	To determine whether MC phase affects cardiorespiratory responses to exercise	Untrained women (n = 9)	LF and ML	MC history, counting of days and serum oestrogen and progesterone	Exercise test to exhaustion on a cycle ergometer determine $\dot{V}O_{2\max}$ (ml.kg ⁻¹ .min ⁻¹)	MC phase did not affect $\dot{V}O_{2\max}$	Low
Kraemer <i>et al.</i> (2006)	To determine whether MC phase affects plasma proenkephalin peptide F responses to high intensity exercise in young untrained eumenorrheic women	Active women not participating in a regular training program (n = 8)	EF and ML	MC history, BBT and serum oestrogen and progesterone	TTE (s) during a progressive maximal exercise test performed on a cycle ergometer	There were no differences in exercise duration between follicular and luteal phases	Low

Kubo <i>et al.</i> (2009)	To determine whether MC phase affects changes in the mechanical properties of human muscle and tendon during the MC <i>in vivo</i>	Sedentary, or mildly to moderately active women (n = 8)	EF, ovulation, and ML	MC history, BBT (two and ML months prior and during) and serum oestrogen and progesterone	Maximal voluntary isometric strength of knee extensors and plantar flexors (Nm) with electrical stimulation	No change in muscle strength was found during the MC	Moderate
^a Lara <i>et al.</i> (2019)	To determine the effects of caffeine intake on Wingate anaerobic test performance during three phases of the MC	Woman triathletes (n = 13)	EF, ovulation, and ML	MC history, BBT and urinary ovulation detection test	Peak power (W.kg), mean power (W.kg) and fatigue index (%) from a Wingate Test	There was no difference in Wingate test performance between MC phases	Low
^b Lara <i>et al.</i> (2019)	To determine the ergogenic effects of caffeine in three phases of the MC	Woman triathletes (n = 13)	EF, ovulation, and ML	MC history, BBT and urinary ovulation detection test	Peak cycling power (W.kg) during a ramp test on a cycle ergometer until exhaustion	There was no difference in peak cycling power between MC phases	Low

Lebrun <i>et al.</i> (1995)	To determine whether MC phase affects four selected induces of athletic performance: aerobic capacity, anaerobic capacity, isokinetic strength, and high intensity endurance	Trained woman athletes (n = 16)	EF and ML	MC history, ovulatory and menstrual symptoms, BBT and serum oestrogen and progesterone	$\dot{V}O_{2\max}$ (l.min) from a continuous progressive test until exhaustion on a treadmill	A higher $\dot{V}O_{2\max}$ was reported in the EF phase compared to the ML phase.	Low
Lee <i>et al.</i> (2014)	To determine whether MC phase affects anterior cruciate ligament elasticity, force to flex the knee, and knee flexion-extension	Nonathletic women (n = 10)	EF, LF, ovulation, and ML	MC history, counting of days and serum oestrogen and progesterone	Force to flex the knee from 90 to 125° (N)	Force to flex the knee was less at ovulation compared to the EF phase of the MC	Low

Lynch and Nimmo (1998)	To determine whether MC phase affects intermittent exercise performance, and some commonly used metabolic markers	Recreationally active women (n = 10)	LF and LL	MC history, counting of days and serum progesterone	TTE (s) during a 20 s repeat sprint continuous incremental protocol on a treadmill	There was no difference in performance between the LF and the LL phases of the MC	Moderate
Materson (1999)	To determine whether MC phase affects anaerobic power performance	Fairly active women (n = 32)	EF and ML	MC history and counting of days	Anaerobic capacity (W), anaerobic power (W) and fatigue index (%) from a Wingate Test	Wingate performance improved in the ML phase compared with the EF phase of the MC	Very low
Mattu <i>et al.</i> (2019)	To determine whether MC phase affects submaximal and maximal responses to exercise	Active women (n = 15)	LF and ML	MC history and urinary ovulation detection test	TTE on a cycle ergometer (s) $\dot{V}O_{2\text{max}}$ (l.min) and peak power output (W) from an incremental	MC phase did not affect the submaximal and maximal exercise responses	Low

						exercise test on a cycle ergometer	
McCracken <i>et al.</i> (1994)	To determine whether MC phase affects the blood lactate levels in response to intensive running	Physically active women (n = 9)	LF and ML	MC history, BBT (two months prior) and urinary oestrogen and progesterone	TTE (min) during an incremental and continuous exercise protocol on a treadmill	Running TTE was not different between the LF and ML phases of the MC	Low
McLay <i>et al.</i> (2007)	To determine whether MC phase affects muscle-glycogen storage, exercise performance, and substrate metabolism at varying exercise intensities	Moderately trained women (n = 8)	LF and LL	BBT and serum oestrogen and progesterone	16 km TT performance (min) on a cycle ergometer	TT performance was not affected by MC phase	Moderate
Montgomery and Shultz (2010)	To determine whether MC phase affects maximal voluntary isometric contraction	Recreationally active women (n = 29)	EF and EL	MC history, urinary ovulation detection kit and serum	Maximal voluntary isometric strength of the quadriceps	There was no difference in muscle strength between MC phases	Moderate

	torque of the knee flexors and extensors			oestrogen and progesterone	and hamstrings (Nm.kg)		
Okudan <i>et al.</i> (2005)	To determine whether MC phase affects anaerobic performance	Sedentary women (n = 15)	LF, ovulation, and ML	Serum oestrogen and progesterone	Anaerobic capacity (W), anaerobic power (W) and fatigue index (%) from a Wingate Test	There was no difference between the peak power, mean power and fatigue index calculated in three different phases of the MC	Low
Oosthuysse <i>et al.</i> (2005)	To determine whether MC phase affects exercise performance by means of a cycling time trial	Trained (n = 5) and untrained (n = 8) woman cyclists	EF, LF and ML	Counting of days, BBT, urinary ovulation detection test and serum oestrogen and progesterone	15 km TT performance (min) on a cycle ergometer 30 km TT performance (min) on a cycle ergometer	There was no difference in TT performance between MC phases in either the trained and untrained groups. Analysis of the combined trained	High

and untrained group data revealed a trend for a faster TT time in the LF phase compared to the EF phase of the MC

Otaka <i>et al.</i> (2018)	To determine whether MC phase affects tennis performance with and without dehydroepiandrosterone sulphate supplementation	Division 1 collegiate woman tennis players (n = 10)	EF, LF, ovulation, and ML	Counting of days	Isometric hip strength (Nm) Tennis serve performance accuracy Tennis serve performance velocity (mph)	The lowest tennis serve performance score (attributed to a change in accuracy and not velocity) occurred at ovulation. Isometric hip strength decreased at ovulation	Very low
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Pallavi <i>et al.</i> (2017)	To determine whether MC phase affects muscle strength variations and the rate of fatigue	Untrained or moderately trained woman students (n = 100)	EF, LF and ML	MC history	Work done (J) during Mosso's Ergograph test Handgrip strength (kg)	The amount of work done, and handgrip strength was higher in the LF phase and reduced in the EF and ML phases of the MC	Very low
Petrofsky <i>et al.</i> (2007)	To determine whether MC phase affects isometric endurance and skin and muscle blood flow during isometric exercise for contractions at low, medium, and high isometric tensions	Women not engaged in ovulation, athletic programs (n = 8)	EF, LF, ovulation, EL, ML and LL	MC history	Endurance time at 20, 40 and 60% handgrip MVC (s)	There was small variation in endurance time across the MC for contractions at 60% handgrip MVC. This effect increased at 40% and was greatest at 20% handgrip MVC	Very low

Quadagno <i>et al.</i> (1991)	To determine whether MC phase affects athletic performance as measured by weightlifting and swimming	Recreational woman weightlifters (n = 12) and highly trained woman swimmers (n = 15)	EF, LF and LL	MC history and counting of days	Bench and leg press mean weight lifted (pounds) 100-m freestyle swim time (s) 200-m freestyle swim time (s)	There were no differences in strength and swimming performance during the three MC phases	Very low
Redman <i>et al.</i> (2003)	To determine whether MC phase affects the metabolic response to exercise	Sedentary women (n = 14)	LF and ML	MC history, counting of days, urinary ovulation detection test and serum oestrogen and progesterone	Peak power output (W), TTE (min), total work done (kJ) and $\dot{V}O_{2\max}$ (l.min) from an incremental exercise test on a cycle ergometer	Incremental exercise test performance	High
Rodrigues <i>et al.</i> (2019)	To determine whether MC affects MVC of lower limbs	Recreationally trained women (n = 12)	LL, EF and LF	Counting of days	MVC (kg) during leg press exercise	MVC was greater in the EF phase than the LL phase. MVC	Low

was greater in
the LF phase
then both the EF
and LL phases.

Romero-Moraleda <i>et al.</i> (2019)	To determine whether MC phase affects muscle performance during half-squat exercise	Woman triathletes (n = 13)	EF, ovulation, and ML	MC history, BBT and urinary ovulation detection test	Mean and peak force at 20, 40, 60 and 80% of one-repetition maximum performed on a Smith Machine	Power outputs were very similar in all MC phases	Moderate
Sarwar <i>et al.</i> (1996)	To determine whether MC phase affects skeletal muscle strength, contractile properties and fatigability in young, healthy females	Relatively sedentary women (n = 10)	EF, LF, ovulation, ML and LL	Counting of days	Maximum voluntary isometric strength of the quadriceps (N) Handgrip strength (N)	There was an increase in quadriceps and handgrip strength at ovulation compared with other MC phases	Very low

Shaharudin <i>et al.</i> (2011)	To determine whether MC phase affects anaerobic capacity in repeated sprint cycling bouts	Moderately physically active women (n = 12)	LF and ML	BBT (three months prior and during), MC history and serum progesterone	Sprint duration until exhaustion throughout maximum accumulated oxygen deficit tests on a cycle ergometer	There were no differences between MC phases in sprint duration until exhaustion throughout maximum accumulated oxygen deficit tests	Low
Sipaviciene <i>et al.</i> (2013)	To determine whether MC phase affects susceptibility to exercise-induced muscle damage after stretch-shortening cycle exercise	Physically active women (n = 18)	EF and ovulation	BBT and serum oestrogen and progesterone	Jump height (cm) from a drop jump Maximum isometric torque of knee extensor muscles (Nm) with electrical stimulation	Jump height and MVC did not differ between MC phases	Low

Smekal <i>et al.</i> (2007)	To determine whether MC phase affects the metabolic and cardiorespiratory responses to exercise	Active women (n = 19)	LF and LL	MC history, BBT and serum oestrogen	Power relative (W.kg) and $\dot{V}O_{2\max}$ (ml.min) from an incremental test until voluntary exhaustion on a cycle ergometer	There were no differences in power relative and $\dot{V}O_{2\max}$ across the MC	Low
^a Sunderland and Nevill (2003)	To determine whether MC phase affects performance of high intensity intermittent running in the heat	Well trained woman game players (n = 7)	LF and ML	Counting of days and serum oestrogen and progesterone	Distance ran during Loughborough Intermittent Shuttle Test (m) 15 m sprint time (s)	There were no differences in distance run or 15 m sprint time between MC phases	Low
^b Sunderland <i>et al.</i> (2011)	To determine whether MC phase affects the growth hormone response to sprint exercise among normally menstruating women	Physically active women (n = 8)	LF and ML	Urinary ovulation detection test and serum oestrogen and progesterone	Mean and peak power outputs during an all-out 30 second sprint (W) on a treadmill	Mean and peak power outputs during an all-out 30 second sprint did not differ across the MC	Moderate

Takase <i>et al.</i> (2002)	To determine whether MC phase affects induced modulations in the cardiorespiratory response to exercise with and without acute exposure to altitude	Moderately trained woman athletes (n = 9)	LF and ML	MC history, BBT and serum oestrogen and progesterone	TTE (min) from an incremental maximal exercise test on a cycle ergometer	MC phase did not affect exercise TTE	Moderate
Tenan <i>et al.</i> (2016)	To determine whether MC phase affects maximal isometric force and tremor during an endurance task	Recreationally active women (n = 9)	EF, LF, ovulation, ML and LL	MC history and BBT (one month prior)	MVC (Nm) Mean time to task failure (s) during an endurance task	MVC in the ML phase was lower than LF, ovulatory, and LL phases. There was no effect of MC phase on mean time to task failure	Very low
Tounsi <i>et al.</i> (2018)	To determine whether MC phase affects soccer-related physical performance	Tunisian high-level woman soccer players (n = 11)	EF, LF and ML	Counting of days and serum progesterone	Distance covered during Yo-Yo IET (m)	None of the measured variables were altered due to MC phase	Low

Tsampoukos <i>et al.</i> (2010)	To determine whether MC phase affects sprinting, recovery from sprinting and metabolic responses to sprinting	Highly active women (n = 8)	EF, ovulation, and ML	MC history, urinary ovulation detection test and serum oestrogen and progesterone	Repeated shuttle-sprint ability test mean time (s) Absolute performance during five-jump test (m)	Peak and mean power output during repeat sprint tests (W) Fatigue index for power during repeat sprint tests (%) Peak and mean speed during repeat sprint tests (m.s) Fatigue index for speed during	All performance variables were unaltered due to MC phase.	High

					repeat sprint tests (m.s)		
Vaiksaar <i>et al.</i> (2011)	To determine whether MC phase affects endurance performance in trained rowers	Competitive woman rowers (n = 8)	LF and ML	MC history, counting of days and serum oestrogen and progesterone	Incremental rowing ergometer test to determine $\dot{V}O_{2\text{max}}$ (l.min) and maximal power output (W)	There were no differences in $\dot{V}O_{2\text{max}}$ and power output between the two MC phases	Moderate
Wearing <i>et al.</i> (1972)	To determine whether MC phase affects selected tests of physical fitness.	Woman intercollegiate basketball or volleyball players	EF, LF, EL and LL	No information	Standing broad jump distance (inches) Maximum hip flexion and extension strength (pounds)	Both standing broad jump and strength performance was reduced in the EF phase greatest in the LL phase of the MC	Very low
Wiecek <i>et al.</i> (2016)	To determine whether MC phase affects the values of starting speed and anaerobic endurance	Physically active women (n = 16)	LF and ML	Counting of days, BBT and serum	Peak and mean power (W), time of attaining anaerobic peak	There were no differences between MC phases in the	Low

oestrogen and power (s), time of measured
progesterone maintaining performance
anaerobic peak variables
power (s) and
power decrease
(W.kg.s) during a
maximal cycling
sprint test

BBT, basal body temperature; CMJ, countermovement jump; EF, early follicular; EL, early luteal; IET, intermittent endurance test; LF, late follicular; LL, late luteal; MC, menstrual cycle; MILS, maximal isometric lifting strength; ML, mid-luteal; MVC, maximal voluntary contraction; PWC, physical working capacity; TTE, time to exhaustion; TT, time trial; $\dot{V}O_{2\text{max}}$, maximal oxygen uptake; $\dot{V}O_{2\text{peak}}$, peak oxygen uptake; $v\dot{V}O_{2\text{max}}$, velocity at maximal oxygen uptake.

Appendix F: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2009 Checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	78
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	N/A
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	79-80
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	80
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	80-81
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	81-82
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	<i>Appendix G</i>
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	91-92
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	91-92

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	80-81
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	91-92
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	92-93 and <i>Appendix I</i>
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	92-93
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	92-93
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	92-93
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	93-94
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	95-95 and <i>Appendix I</i>
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	95-105
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	95-105
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	95-105
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	95-105
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	95-105
DISCUSSION			

Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	105-109
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	105-109
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	109-110
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix G: Example of a Search Strategy Conducted in PubMed (09/01/2019).

Limits applied	
Humans	
Randomised controlled trials	
Observational	
Clinical trials	
Clinical controlled trials	
English language	
Females	
Search terms	Number of results
Oral contraceptives and athletic performance	19
Oral contraceptives and sports performance	20
Oral contraceptives and muscle	38
Oral contraceptives and strength	22
Oral contraceptives and force	69
Oral contraceptives and skeletal muscle	12
Oral contraceptives and muscular strength	0
Oral contraceptives and power	47
Oral contraceptives and anaerobic	2
Oral contraceptives and anaerobic power	0
Oral contraceptives and anaerobic performance	1
Oral contraceptives and anaerobic capacity	1
Oral contraceptives and aerobic	8
Oral contraceptives and endurance	11
Oral contraceptives and endurance capacity	3
Oral contraceptives and endurance power	1
Oral contraceptives and aerobic capacity	2
Oral contraceptives and aerobic power	2
Oral contraceptives and aerobic performance	1
Oral contraceptives and endurance performance	4
Oral contraceptives and fatigue	42
Total: 336 (with duplicates)	

Appendix H: Study Quality Assessment.

Downs and Black checklist (maximum score attainable = 16). Study quality was categorised as follows: “high”: 14 – 16; “moderate”: 10 – 13; “low”: 6 – 9; “very low”: 0 - 5).

Note: For single-measure observational trials (*e.g.*, those that compared OCP users and naturally menstruating women at a single phase) questions 13 and 15 were deemed irrelevant and so were removed. The maximum attainable score for these studies was 14 and the categories were: High (12 – 14); Moderate (8 – 11); Low (4 – 7); Very Low (< 4).

Reporting

Q1. Is the hypothesis/aim/objective of the study clearly described?

Yes = 1

No = 0

Q2. Are the main outcomes to be measured clearly described in the introduction or methods section? If the main outcomes are first mentioned in the results section, answer no.

Yes = 1

No = 0

Q3. Are the characteristics of the participants included in the study clearly described? In observational studies, inclusion and/or exclusion criteria should be given. In case-control studies, inclusion and/or exclusion and the source of controls should be given.

Yes = 1

No = 0

Q4. Was the tested pill phase (and, if relevant, menstrual cycle phase) clearly described? Answer yes if the precise criteria used to define phase were provided, answer no if the exact phase tested cannot be ascertained.

Yes = 1

No = 0

Q5. Are the main findings of the study clearly described? Simple outcome data should be reported for all major findings so the reader can check the major analyses and conclusions. This does not cover statistical tests which are addressed in other questions.

Yes = 1

No = 0

- Q6. Does the study provide estimates of the random variability in the data for the main outcomes? In non-normal data, inter-quartile range should be reported. In normal data, standard deviation, standard error, or confidence intervals should be reported.

Yes = 1

No = 0

External validity

- Q7. Were the participants confirmed to be habitual pill users, or in the case of naturally menstruating controls, habitual non-users, for at least 3 months prior to the study?

Yes = 1

No = 0

Unable to determine = 0

Internal validity – bias

- Q8. Was at least one familiarisation trial conducted prior to exercise testing?

Yes = 1

No = 0

Unable to determine = 0

- Q9. Were the exercise test conditions adequately standardised (taking into consideration factors including time of day, prior nutritional intake [including caffeine] and prior exercise).

Yes (all relevant factors standardised) = 2

Yes (some relevant factors standardised) = 1

Exercise testing unstandardized = 0

Unable to determine = 0

- Q.10 If any of the results of the study were based on ‘data dredging’ was this made clear? Any analyses that had not been planned at the outset should be clearly indicated. If no retrospective subgroup analyses were reported, then answer yes.

Yes = 1

No = 0

Unable to determine = 0

- Q11. Were statistical tests used to assess the main outcomes appropriate? The statistical techniques used must be appropriate to the data and the research question.

Yes = 1

No = 0

Unable to determine = 0

- Q12. Were the main outcome measures used accurate (*i.e.*, valid, and reproducible)? For studies where the validity and reproducibility of outcome measures are clearly described, the question should be answered yes. For studies which refer to other work that demonstrates the outcome measures are accurate, answer yes.

Yes = 1

No = 0

Unable to determine = 0

Internal validity – confounding (selection bias)

- Q13 Was the order of phase testing randomised?

Yes = 1

No = 0

Unable to determine = 0

Power

- Q14 Did the study have sufficient power to detect an *a priori* specified scientifically important effect at a pre-determined probability threshold? Answer yes if they included a power calculation, and no if not.

Yes = 1

No = 0

- Q15. Was study retention > 85%?

Yes = 1

No = 0

Unable to determine = 0

GRADE (assign an *a-priori* study quality rating based on the modified Downs and Black checklist, so all studies will start out as being of “high”, “moderate”, “low”, “very low”).

- Q1. Was the natural MC phase confirmed using appropriate biochemical outcomes? If yes, the *a priori* rating is maintained, and this is the final study quality rating. If not, the study is downgraded a level.
- Q2. Was the type of OCP described to the level of detail required for categorisation or replication? If not, the study is downgraded another level.
-

Appendix I: Table of Included Studies.

Author (date)	Aim	Participant health and training status	Study design	Oral contraceptive pill type	Eumenorrheic group description	Exercise outcomes	Quality rating
Anderson <i>et al.</i> (2017)	To measure the influence of exogenous, endogenous, and low oestrogen conditions, on contraction-induced muscle damage in young women	Healthy women (24.8 ± 2.3 y) who were not involved in a structured resistance program, or progressive and intense aerobic program during, or within the six months prior, to the study	Parallel group, observational, single measure	Monthly ethinyl oestradiol containing OCP	Women with a self-reported natural monthly MC, tested at the EF and ML phases, verified using MC history, counting of days, and serum oestrogen levels	Maximal voluntary isometric contraction of the leg extensor (N) - S	Low
Armstrong <i>et al.</i> (2005)	To measure the influence of different methods of exogenous	Healthy women (21 ± 3 y) who were not undertaking	Parallel group, intervention, repeated measures	Oral ethinyl oestradiol & progestin contraceptives	Women with a self-reported natural monthly MC, tested at the	$\dot{V}O_2$ peak ($ml \cdot kg^{-1} \cdot min^{-1}$) measured during an incremental	Low

	hormonal contraceptive (OCP, injectable steroid contraceptive, or no contraceptive) on thermal, metabolic, cardiorespiratory, performance, body composition and perceptual response of healthy young women (contraceptive) to a seven-eight week program of heat acclimation and physical training	frequent physical training	(Ortho-Novum, Ortho-Cyclen, Northi-TriCyclen, Marvelon or Femodene)	EF phase, verified by serum oestrogen and progesterone levels	run to volitional fatigue – E
Bell <i>et al.</i> (2011)	To measure the influence of OCP	Healthy women (20.2 ± 1.4 y)	Parallel group, observational, OCP	Women with a self-reported	Rate of force production (N·s ⁻¹)

on hamstring neuromechanics and leg stiffness across the MC who were physically active (defined as a minimum of 20 minutes of activity three times per week) repeated measures natural monthly MC for the previous six months, tested at the EF and ovulation phase, verified using urinary ovulation detection, and serum oestrogen and progesterone levels¹), and time to reach 50% peak (ms) measured during a maximal voluntary isometric hamstring contraction – S

Bemben <i>et al.</i> (1992)	To measure the influence of OCP on growth hormone and prolactin responses and on energy substrate utilisation during prolonged	Healthy, moderately active women (25.1 ± 1.4 y)	Parallel group, observational, single-measure	Multi or monophasic OCPs containing 35 µg of oestrogen (Ortho Novum 10/11, 7-7-7, 1/35 & Demulen)	Women with a self-reported natural monthly MC (cycles ranging from 28 to 35 days in length), for one year prior to the study, tested at	$\dot{V}O_2$ peak (ml·kg ⁻¹ ·min ⁻¹) and absolute workload (m·min ⁻¹) measured during an incremental run to volitional fatigue – E	Low
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	submaximal exercise				the EL, ML, and LL phases, verified by BBT and serum progesterone		
Bushman <i>et al.</i> (2006)	To measure the effect of menstruation and OCP on power performance	Healthy, moderately active women (21.6 ± 2.6 y)	Parallel group, observational, repeated measures	2 participants took a monophasic and 15 a multiphasic OCP	Women with a self-reported natural monthly MC tested at the EF and EL phases, verified by BBT and urinary ovulation detection test	Estimated $\dot{V}O_2$ peak (ml·kg·min ⁻¹) measured from the Forestry Step Test – E; peak power (W or W·kg ⁻¹), anaerobic capacity (W or W·kg ⁻¹) and power decline (W or W·kg ⁻¹) measured by the Wingate test - E and anaerobic	Low/ very low

							power ($\text{kg}\cdot\text{m}^{-1}\cdot\text{s}^{-1}$)
							measured in the
							Margaria
							Kalamen test - E
Casazza <i>et al.</i> (2009)	To measure the effects of MC phase and triphasic OCP use on peak exercise capacity	Healthy, habitually active women who were not competitive athletes (25.5 ± 1.5 y)	Within group, intervention	Standardized triphasic OCP (days 1-7: 0.035 mg ethinylestradiol & 0.18 mg norgestimate; days 8-14: 0.035 ethinylestradiol & 0.215 norgestimate; days 15-21: 0.035 mg ethinylestradiol & 0.25 mg norgestimate,	Women with a self-reported natural monthly MC (22 to 32 days in length) for at least six months, tested during the LF and ML phases, verified by a urinary ovulation detection test and serum oestrogen and progesterone	Peak $\dot{\text{V}}\text{O}_2$ (L·min ⁻¹), power (W) and time to exhaustion	Moderate (min) measured during an incremental cycle to volitional fatigue – E

				days 22-28: placebo pill)		
de Bruyn- Prevost <i>et al.</i> (1984)	To measure the effects of OCP and eumenorrheic MC on the physiological response to aerobic and anaerobic endurance tests	Women (22 ± 2.2 y)	Parallel group, observational, repeated measures	No information.	Women with a self-reported natural monthly MC, tested during the EF, ovulatory and LL phases, verified by BBT	VO ₂ peak (L·min ⁻¹) and working capacity at a heart rate of 170 bpm (W) measured using an incremental cycle to volitional fatigue - E, and maximal pedal time (s) during a fixed load (350 W) anaerobic endurance test – E
Drake <i>et al.</i> (2003)	To measure the effect of OCP and	Healthy women (24 ± 1 y) who	Parallel group, observational,	No information	Women with a self-reported	Maximal and submaximal

	eumenorrheic MC on electromyography and mechanomyograph y during isometric muscle contractions	were not involved in an exercise program	repeated measures	natural monthly MC (26 to 32 days in length) tested at the EF, LF, ovulation and EL, verified using urinary ovulation detection test	isometric extensor and flexor contraction at 100, 75, 50 and 25% of maximal torque (Nm) – S	
Ekenros <i>et al.</i> (2013)	To measure the effect of OCP and eumenorrheic MC on muscle strength and hop performance	Healthy women (26.7 ± 3.8 y)	Within-group, repeated measures	Low dose monophasic OCPs containing ethinyl oestradiol (20- 35 µg) combined with different progestogen (Levonorgestrel, Norgestimate, Drospirenone,	Women with a self-reported natural monthly MC who had not been taking any hormone- containing contraceptive for at least three months prior to the study, tested during the EF, ovulatory, and	Peak isokinetic knee extensor strength (Nm) - S, handgrip strength (kg) - S and jump height during the one leg hop test (cm) – S

					Desogestrel, Noretisterone & Lynestrenol)	ML phases, verified using urinary ovulation detection test and serum oestrogen and progesterone	
Elliott <i>et al.</i> (2005)	To measure the effect of OCP and MC on maximum force production	Healthy women (22 ± 4 y) who were sedentary (defined as not being involved in a strength or aerobic training program for the previous 6 months)	Parallel group, observational, repeated measures	Combined OCPs (Microgynon, Brevinor, Ovartette, Marvalon, Cilest)	Women with a self-reported natural monthly MC (mean cycle length of 29 days) who were not taken any hormonal based contraction for six months prior to the study, tested during the EF and ML phases, verified by BBT, urinary ovulation	Maximal voluntary isometric force of the first dorsal interosseus muscle (N) – S, isokinetic extension and flexion of the quadriceps and hamstring muscles at 1.04. 2.09 and 4.19 rad/S (Nm) – S,	Moderate

					detection test and serum oestrogen and progesterone	and isometric extension and flexion (Nm) – S	
Giacomoni & Falgairette (1999)	To measure the effect of time of day and OCP use on maximum anaerobic power	Physical education students (22.8 ± 2.8 y)	Parallel group, observational, repeated measures	Combined monophasic OCP (0.02-0.03 mg ethinylestradiol & 0.150 mg desogestrel or 0.075 mg gestodene)	Women with a self-reported natural monthly MC lasting 25 to 31 days in length, who had not used any OCP for at least four months before entering the study, tested during the LF and ML, verified by serum oestrogen and progesterone levels	Peak velocity (rpm) – E, peak force (kg) - S and peak power (W) – E, measured during a force velocity test	Moderate
Giacomoni et al. (2000)	To measure the effect of OCP and physical education		Parallel group, observational,	Combined monophasic	Women with a self-reported	Peak velocity (rpm) - E, peak	Moderate

	eumenorrheic MC on anaerobic performance	students (23 ± 3 y)	repeated measures	OCP with constant oestrogen and progesterone levels (0.02-0.03 mg ethinylestradiol & 0.150 mg desogestrel or 0.075 mg gestodene)	natural monthly MC lasting 25 to 31 days in length, who had not used any OCP for at least four months before entering the study, tested during the LF and ML, verified by serum oestrogen and progesterone levels	force (kg) - S and peak power (W) – E, measured during a force velocity test and jump height (cm) measured using multi and squat jump tests – S
Gordon <i>et al.</i> (2012)	To measure the effect of OCP and MC on peak isokinetic torque	Healthy, well- trained women (20.6 ± 1.2 y)	Parallel group, observational, repeated measures	Monophasic OCP	Women with a self-reported natural monthly MC (mean cycle length of 28 days) tested during the EF, LF, ML, and LL phases,	Peak concentric knee flexor and extensor torque at 60, 120, 18- and 240° (Nm) – S

					verified by salivary oestrogen and progesterone levels		
Gordon <i>et al.</i> (2018)	To measure the effect of OCP and eumenorrheic MC on incidence of $\dot{V}O_2$ max plateau and associated cardiorespiratory dynamics	Healthy, physically active women (21 ± 1.8 y)	Parallel group, observational, repeated measures	Monophasic OCP containing 30 µg ethinyl oestradiol and 150 µg levonorgestrel	Women with a self-reported natural monthly MC tested during the EF, LF, ML and LL, verified by MC history and salivary oestrogen and progesterone levels	Peak $\dot{V}O_2$ (L·min ⁻¹) and power (W) measured during an incremental run to volitional fatigue – E.	Moderate
Grucza <i>et al.</i> (1993)	To measure the effect of OCP and eumenorrheic MC on thermosensitivity	Healthy women (21.3 ± 1.8 y) who were undertaking approximately 2-3 hours of	Parallel group, observational, repeated measures	Monophasic OCP (Trikvilar or Neo-Gentrol 150/30)	Women with a self-reported natural monthly MC for one year preceding the experiment and	$\dot{V}O_2$ peak (ml·kg·min ⁻¹) measured during an incremental cycle to	Low

		various activity types per week			who had never taken OCPs, tested during the LF and ML phase, verified by BBT	volitional fatigue – E	
Grucza <i>et al.</i> (2002)	To measure the effect of OCP and eumenorrheic MC on cardiorespiratory responses to exercise	Healthy university students (21.3 ± 1.8 y)	Parallel group, observational, repeated measures	Monophasic OCP (Trikvilar or Neo-gentrol)	Women with a self-reported natural monthly MC for one year preceding the experiment and who had never taken OCPs, tested during the LF and ML phase, verified by BBT	VO ₂ peak (ml·kg ⁻¹ ·min ⁻¹) measured during an incremental cycle to volitional fatigue - E	Low
Hicks <i>et al.</i> (2017)	To measure the effect of OCP and eumenorrheic MC	Healthy, recreationally	Parallel group, intervention,	Combined monophasic OCP with	Women with a self-reported	Peak voluntary isometric torque (Nm) – S.	Moderate

	on exercise induced muscle damage, and tendon properties	active women (22.3 ± 2.3 y)	repeated measures	ethinyl oestradiol dosage between 20 and 30 µg	natural monthly MC (average cycle length of 28 days) and who had never taken the OCP, tested during the ovulatory phase, verified by serum oestrogen		
Isacco <i>et al.</i> (2015)	To measure the effect of OCP and eumenorrheic MC on lipid oxidation and cardiorespiratory parameters at the anaerobic threshold and maximum capacity	Weight stable, healthy women (22 ± 2.9 y) who were recreationally active (defined as those not involved in any regular exercise training)	Parallel group, observational, repeated measures	Low-dose monophasic OCP contained 20 (n = 8) or 30 (n = 3) µg of ethinylestradiol and gestodene or levonorgestrel	Women with a self-reported natural monthly MC (average cycle length of 28 days for at least one year) and had not taken any OCP for more than one year prior to the study	VO ₂ peak (ml·kg ⁻¹ ·min ⁻¹) measured during an incremental cycle to volitional fatigue - E	Moderate

Joyce <i>et al.</i> (2013)	To measure the effect of long-term OCP use on endurance performance	Healthy women (21 ± 2.7 y) who were recreationally active (defined as exercising > 3 days per week for at least 30 minutes per session)	Parallel group, observational, single measure	Combined monophasic OCP	Women with a self-reported natural monthly MC lasting between 28 and 30 days for at least 12 months before the study, tested during the EF phase, verified by serum oestrogen and progesterone levels	Peak $\dot{V}\text{O}_2$ (L·min ⁻¹) and power (W) measured during an incremental cycle to volitional fatigue – E, and time to exhaustion (s) on a submaximal cycling test – E	Moderate

					progesterone levels		
Joyce <i>et al.</i> (2014)	To measure the effect of sex and OCP on submaximal cycling performance following an eccentric exercise protocol	Healthy women (20.8 ± 2.4 y) who were regularly physically active, but not participating in any regular resistance-exercise training	Parallel group, intervention, repeated measures	Combined monophasic OCP	Women with a self-reported natural monthly MC lasting between 28 and 30 days for at least 12 months before the study, tested during the EF phase and verified serum oestrogen and progesterone levels	Peak $\dot{V}O_2$ (ml·kg $^{-1}$) and power (W) measured during an incremental cycle to volitional fatigue – E, and mean torque (Nm·kg $^{-1}$) and torque decline (Nm) measured across 240 maximal eccentric quadriceps contractions – S	Low
Lebrun <i>et al.</i> (2000)	To measure the effect of OCP and	Healthy, athletic women (18 – 40	Randomised controlled trial	Triphasic OCP (Synphasic,	Women with a self-reported	$\dot{V}O_2$ peak (L·min $^{-1}$)	Moderate

	eumenorrheic MC on exercise performance in highly active women	y), but none that competed in aerobic activities (cycling, triathlon, rowing, cross- country skiing)	0.035 mg ethinylestradiol and 0.5 – 1.0 mg norethindrone)	natural monthly MC (24 to 35 days in length) and no OCP use	measured during an incremental cycle to volitional fatigue - E, time to exhaustion (s) in a submaximal endurance test - E, time to exhaustion (s) in an anaerobic speed test – E and peak quadriceps and hamstring torque (Nm) – S		
Lee <i>et al.</i> (2014)	To measure the effect of OCP and eumenorrheic MC on anterior cruciate ligament elasticity,	Healthy, non- athletic women $(24.7 \pm 2 \text{ y})$	Parallel group, observational, repeated measures	Low dose OCP containing < 50 μg ethinyl- estradiol	Women with a self-reported natural monthly MC for at least six months, with	Knee flexion force (N) – S	Moderate

force to flex the knee and knee flexion-extension hysteresis

an average cycle length of 29 days, tested during the EF, LF, ovulatory and ML phases, verified by serum oestrogen and progesterone levels

Lynch & Nimmo (1998)	To measure the effect of OCP and eumenorrheic MC on intermittent exercise performance	Healthy women (25.3 ± 6 y) who were recreationally active but not training for any one sport exclusively	Parallel group, observational, repeated measures	Low-dose monophasic OCP (Femodene, Cilest, Ovranette, Microgynon).	Women with a self-reported natural monthly ovulatory MCs with an average cycle length of 29 days, and who had either never taken OCPs or had not taken an OCP in the last four months,	$\dot{V}O_2$ peak ($ml \cdot kg^{-1} \cdot min^{-1}$) measured during run to volitional fatigue – E, and time to exhaustion (s) in an intermittent sprint test – E	Moderate / low
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						tested during the LF and LL phases, verified by serum progesterone levels	
Lynch <i>et al.</i> (2001)	To measure the effect of OCP on performance and metabolic responses to, intermittent exercise during the 1 st or 3 rd week of the OCP cycle	Healthy, untrained women (23.1 ± 4 y)	Single group, observational, repeated measures	Low dose monophasic OCP (Ovranette, Femodene, Mercilon, Microgynon, Brevinor)	N/A	Time to exhaustion (s) in the final sprint of an intermittent sprint protocol – E	Moderate
Mackay <i>et al.</i> (2019)	To measure the effect of OCP use on indirect markers of muscle damage following eccentric cycling in women	Healthy women (27.7 ± 4.5 y) who were not actively participating in any resistance or	Parallel group, acute intervention, single measure	Third and fourth generation monophasic OCP (ethynl estradiol 0.02 μ g;	Women with a self-reported natural monthly MC (between 24 and 35 days) and who were not volitional	$\dot{V}O_2$ peak ($ml \cdot kg^{-1} \cdot min^{-1}$)	High/ moderate

	flexibility training in the 6 months prior to the study	drospirenone 3 µg)	using any form of hormone-based contraceptive methods for six months prior to the study, tested during the ovulatory phase, verified by urinary ovulation detection kit and salivary oestrogen and progesterone levels	fatigue – E, maximal voluntary knee extensor contraction at 90% knee flexion (N) – S, and mean power (W) during an eccentric cycling test - E			
Mattu <i>et al.</i> (2020)	To measure maximal and submaximal exercise outcomes at different phases of the menstrual and OCP cycle	Healthy, trained, women (25.5 ± 5.2 y) who performed moderate to vigorous physical activity	Parallel group, observational, repeated measures	Second or third generation monophasic OCP containing between 20 – 35 µg of ethinyl oestradiol and	Women with a self-reported natural monthly MC (cycle between 21 and 35 days in length) who were non volitional	VO ₂ peak (L·min ⁻¹ or ml·kg ⁻¹ ·min ⁻¹) during an incremental ramp test to volitional	High

	at least 4 times per week, and for at least 30 minutes per bout	100-200 µg of progestin)	hormonal contraceptive users for at least 12 months prior to the study, tested during the LF and ML phases, tested using urinary ovulation detection test	fatigue – E, and time to exhaustion (s) during a constant load test at 85% peak power – E			
Minahan <i>et al.</i> (2015)	To measure the effect of sex and OCP in the response to muscle damage after intense eccentric exercise	Healthy women (21 ± 2.7 y) who were habitually active (primarily moderate intensity endurance-based activities), but who were not undertaking a	Parallel group, intervention, repeated measures	Combined monophasic OCP	Women with a self-reported natural monthly MC that occurred every 28 to 30 days, tested during the EF phase, verified by serum oestrogen levels	Peak and mean isometric torque (Nm and Nm·kg ⁻¹) across 240 eccentric contractions – S	Low

		resistance training program					
Minahan <i>et al.</i> (2017)	To measure the effect of OCP and the eumenorrheic MC on core body temperature and skin blood flow at rest and during exercise (temperate and hot environments)	Healthy women (22 ± 3.4 y) who were recreationally active (300-500 minutes per week of moderate and hot intensity exercise)	Parallel group, observational, repeated measures	Low dose combined monophasic OCP	Women with a self-reported natural monthly MC (every 25 to 32 days) for more than 12 months and who had never taken any form of synthetic hormones, tested during the EF phase, verified by serum oestrogen and progesterone levels	Peak $\dot{V}O_2$ (ml·kg·min ⁻¹) and power (W)	Moderate measured during an incremental cycle to volitional fatigue – E, and mean power output (W) during a 3-stage submaximal test - E
Ortega-Santos <i>et al.</i> (2018)	To measure the effect of OCP and eumenorrheic MC on substrate	Healthy trained women (35.6 ± 4.2 y) who were training in either	Parallel group, observational, repeated measured	Stable monophasic	Women with a self-reported natural monthly MC tested during	$\dot{V}O_2$ peak (ml·kg·min ⁻¹)	Low measured during an incremental

	oxidation during steady-state exercise.	endurance or strength activities for 5 - 12 hours per week			the EF, LF and ML phase, verified by MC history and serum oestrogen and progesterone	run to volitional fatigue - E	
Peters & Burrows (2006)	To measure the effect of the androgenicity of progestins in OCP on leg strength	University athletes (20.2 ± 0.5 y) from a variety of sports (cricket, football, endurance running and swimming)	Parallel group, observational, repeated measures	Monophasic OCP containing 30 µg ethinylestradiol with 120µg levonorgestrel or 250µg norgestimate	N/A	Peak leg extension and flexion torque (Nm) - S	Moderate
Quinn <i>et al.</i> (2018)	To measure the effect of long-term OCP use on cerebral oxygenation during active (defined as 150–300	Healthy women (21 ± 3 y) who were recreationally-active (defined as 150–300	Parallel group, observational, single measure	28-day combined monophasic OCP	Women with a self-reported natural monthly MC (28-30 days in length) and had not taken any	Peak $\dot{V}O_2$ (ml·kg $^{-1}$ ·min $^{-1}$) and power (W) during an incremental cycle to	Moderate

	incremental cycling to exhaustion	minutes per week of moderate intensity exercise)		form of hormonal contraception for 12 months prior to the study, tested during the EF phase, verified by serum oestrogen and progesterone levels	volitional fatigue - E
Rebelo <i>et al.</i> (2010)	To measure the effect of OCP on peak aerobic capacity and at the anaerobic threshold level in active and sedentary young women	Healthy women (23 ± 2.1 y), who were active (running or spinning 4 – 5 times per week) or sedentary (not engaging in regular physical activity for the	Parallel group, observational, single measure	Monophasic OCP (0.2 mg ethinylestradiol and 0.15 mg gestodene)	N/A Peak $\dot{V}O_2$ (ml·kg $^{-1}$ ·min $^{-1}$) and power (W) during an incremental cycle to volitional fatigue - E

		previous 12 months)					
Rechichi <i>et al.</i> (2008)	To measure the effect of OCP cycle on endurance performance	Trained cyclists and triathletes (34 ± 7 y)	Single group, repeated measures, observational	Monophasic OCP (20-35 µg ethinylestradiol and 100-3000 µg progestin)	N/A	Mean power output (W) during a 1 h time-trial - E	High
Rechichi <i>et al.</i> (1996)	To measure the effect of OCP cycle on common team sport performance variables	Team sport athletes (23.5 ± 4.5 y).	Single group, observational, repeated measures	Monophasic OCP (30 mcg ethinylestradiol with 150 mcg levonorgestrel, 2000 mcg cyproterone acetate, 3 mg drospirenone or 500 mcg norethisterone)	N/A	Jump height (cm) measured during a countermoveme nt and a reactive strength (30 and 45 cm) jumps - S; 10 second cycle peak power (W·kg ⁻¹) and total work done (J·kg ⁻¹) - E; 5X6 second	High

repeated sprint
total work ($J \cdot kg^{-1}$)
¹) and power
decrement (%) -
E

Rechichi <i>et al.</i> (2012)	To measure the effect of OCP cycle on 200m swimming performance and associated measures of heart rate, blood lactate, pH and blood glucose	Competitive swimmers and water polo players (26 ± 4 y)	Single group, repeated measures, observational	Monophasic OCP (30 µg ethinylestradiol and 150 µg levonorgestrel)	N/A	Time to complete (s) a 200 m swim - E	High
Redman & Weatherby (2004)	To measure the effect of OCP cycle on anaerobic performance	Elite and sub-elite rowers (20 ± 1.9 y)	Single group, repeated measures, observational	Combined triphasic OCPs (Triphasil-28)	N/A	Peak power output (W) during a 10s maximal row - E, and time to	High

						complete (s) a
						1000 m row - E
Sarwar <i>et al.</i> (1996)	To measure the effect of eumenorrheic MC on muscle strength, contractile properties, and fatigability in eumenorrheic and OCP users	Healthy, relatively sedentary women (20.6 ± 1.2 y)	Parallel group, observational, repeated measures	Combined (monophasic) OCPs with low dose ethinyl oestradiol ($20-35 \mu\text{g}$) together with progestins in different doses	Women with a self-reported natural monthly MC lasting between 26 and 32 days (mean cycle length of 28 days), tested during the EF, LF, ovulatory, ML, and LL phase, verified by counting of days	Peak handgrip and quadriceps strength (N) - S
Schaumberg <i>et al.</i> (2017)	To measure the effect of OCP use on peak physiological, cardiovascular and performance	Healthy women (25.5 ± 5.4 y) who were recreationally active, but not competitive at	Parallel group, intervention, repeated measures	Combined monophasic ($20-30 \mu\text{g}$ ethinylestradiol and n = 5 androgenic, n =	Women with a self-reported natural monthly MC, tested during the ML phase, measured during verified by MC	$\dot{\text{V}}\text{O}_2$ peak ($\text{L} \cdot \text{min}^{-1}$) and peak power output (W) measured during an incremental

	adaptations to sprint interval training	state or national level in any sport	5 anti-androgenic, and n = 15 non-androgenic progestins)	history, counting of days, urinary ovulation detection kit and serum oestrogen and progesterone levels	cycle to volitional fatigue - E		
Sunderland <i>et al.</i> (2011)	To measure the effect of OCP and eumenorrheic MC on the growth hormone response to sprint exercise	Physically active women who regularly participated in repeated sprint type activities (21.5 ± 3.8 y)	Parallel group, observational, repeated measures	Monophasic OCP with high androgenicity (Microgynon, Ovranette, Mercilon, Loestrin)	Women with a self-reported natural monthly MC that varied in length from 27 to 35 days, tested during the LF and ML phase, verified by urinary ovulation detection test and serum oestrogen and progesterone levels	Mean and peak power output (W) during a 30 s treadmill sprint	Moderate

Vaiksaar <i>et al.</i> (2011)	To measure the effect of OCP cycle on substrate use and lactate level over a 1h submaximal rowing exercise	Trained rowers (21 ± 2.8 y)	Single group, observational, repeated measures	Monophasic OCP (20 µg ethinylestradiol and 75 µg gestodene)	N/A	$\dot{V}O_2$ peak (L·min ⁻¹) measured from a maximal rowing test – E, and submaximal mean power output (W) measured during a submaximal rowing test – E	Moderate
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Vaiksaar <i>et al.</i> (2011)	To measure the effect of OCP and eumenorrheic MC on endurance performance	Recreational OCP users (21.0 ± 2.6 y), trained eumenorrheic (18.8 ± 2.1 y), recreational eumenorrheic (18.0 ± 0.9 y)	Parallel group, observational, repeated measures	Monophasic OCP (20 µg ethinylestradiol and 75 µg gestodene)	Women with a self-reported natural monthly MC (24–35 days), with at least six months of documented MC, tested during the	$\dot{V}O_2$ peak (ml·kg·min ⁻¹) and peak power (W) measured during a maximal rowing test - E	High
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					LF and ML phases, verified by MC history and serum oestrogen and progesterone levels		
Wirth & Lohman (1982)	To measure the effect of OCP and vitamin B6 supplementation on static muscle function	Women (18-33 y)	Parallel group, observational, repeated measures	No information provided	Women with a self-reported natural monthly MC (25 to 30 days in length) who had not used an OCP agent for a period of one year prior to the study. Tested during the LF and ML phases and verified by counting of days	Grip strength (kg) and endurance time (s) measured during a handgrip test - S	Very low

OCP: oral contraceptive pill; MC: menstrual cycle; EF: early follicular; LF: late follicular; EL: early luteal; ML: mid-luteal; LL: late luteal;
BBT: basal body temperature; $\dot{V}O_2$ peak: peak oxygen uptake; E: endurance; S: strength.

Appendix J: Screening Questionnaire for Inclusion and Exclusion Criteria.

Screening Questionnaire for Inclusion and Exclusion Criteria.

CHAPTER 9 Page 1: Study screening questionnaire for inclusion and exclusion criteria

Thank you for your interest in this study.

Prior to enrolling you on the study we must make sure you meet the study inclusion and exclusion criteria. This questionnaire is designed to make sure you meet these criteria, and covers physical activity readiness, medical history, menstrual cycle/ hormonal contraceptive history and training history.

If you are eligible for this study following the completion of this questionnaire the lead investigator will be in touch via email to arrange a pre-testing session date. If you are deemed not eligible on completion of the screening questionnaires the information obtained will be disregarded and disposed of following university guidelines.

Any data is provided anonymously and only a code will be used to identify any data given from these screening questionnaires. Only the lead researcher will have access to any identifying information (e.g., consent forms) which will be stored separately from other data under a password protected device. All questions are directly related to the study. If you feel uncomfortable at any point you are free to withdraw from the study.

If you have any further questions, please do not hesitate to get in touch by emailing Kelly McNulty at kelly.mcnulty@northumbria.ac.uk

Filling out the applicable questions will take approx. 20 minutes - please note you can stop and save answers and all answers are entirely confidential.

Please enter the unique participant code given to you by the lead researcher: *Required*

If eligible, are you willing to be contacted via post (*i.e.*, to send ovulation detection kits and thermometers if in the naturally menstruating group) or via text SMS and email for daily reminders to complete questionnaires? *Required*

- Yes
 No

If eligible, are you willing to complete the training sessions and follow up sessions virtually via Zoom or another form of virtual meeting (*i.e.*, Teams etc.)? *Required*

- Yes
 No

If eligible, do you have an iPhone or smartphone that has a camera capable of recording slow motion video in 240 FPS? *Please note all iPhones from the 6 range and upwards have this capability (and you will be taken through a step-by-step guide for this), for other phone devices this can be found via a Google search if not already known.* *Required*

- Yes
 No

The below set of questions will be used to determine your eligibility to participate in the current research study.

Date of birth: *Required*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.

Country of residence: *Required*

Height (cm): *Required*

Weight (kg): *Required*

Have you ever suffered from any of the following medical conditions? *Required*

Heart disease or attack

- High or low blood pressure
- Stroke
- Cancer
- Diabetes
- Asthma
- High cholesterol
- Epilepsy
- None of the above

If you selected Yes to any of these, please give further details:

Do you suffer from any other medical conditions? *Required*

If you selected Yes, please specify:

Are you currently or have you taken any medication regularly within the last year? If yes, please give details. *Required*

If you selected Yes, please specify:

 Have you had any musculoskeletal injuries in the past 6 months which have affected your capacity to exercise, or caused you to take time off work or seek medical advice? *Required*

 If you selected Yes, please specify:

 Do you currently smoke? *Required*

 Do you currently drink alcohol? *Required*

 Are you currently taking part in any other research trials? *Required*

 If you selected Yes, please specify:

The below set of questions will be used to determine your eligibility to participate in the current research study.

At what age did you have your first period? Required

Please enter a whole number (integer).

On average, would you consider yourself to have a regular menstrual cycle length (days between a period)? The UK average length of cycle is between 21 and 35 days. *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* Required

- Yes
- No
- Not applicable

On average, how long does your period (days bleeding) last? *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* Required

- 0-2 days
- 2-5 days
- 5-7 days
- 7+ days
- Not applicable

Have you had a regular period for the last 12 months (a minimum of nine cycles per calendar year and a cycle that ranges between 21 and 35 days in length, with no spotting between periods)? *Please note if you are currently on any form of hormonal contraceptive please select not applicable.* Required

- Yes
- No
- Not applicable

Do you have any children? □ Required

Please list the date/s you had your child/ children (DD/MM/YYYY):

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



Please list the date/s you had your child/ children (DD/MM/YYYY):

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



Please list the date/s you had your child/ children (DD/MM/YYYY):

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



Please list the date/s you had your child/ children (DD/MM/YYYY):

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



In the last year, have you experienced any of the following (please select all that apply)? □

Required

- Given birth
- Pregnancy
- Breast fed
- None of the above

Within the last year, have your periods stopped at all? *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* Required

What was the date of your last period (DD/MM/YYYY)? *Please note if you cannot remember exact day, please make sure month or year is correct.*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



Is there a chance you might be pregnant?

Have you been diagnosed as post-menopausal?

Have you ever had a hysterectomy?

Have you ever had your ovary / ovaries removed?

Are you currently or have you ever taken an oral contraceptive pill? *Required*

What type of pill did / do you take (name and dose of oestrogen and progesterone)? *Dose values can be found on the medication box. If you are unsure, please ask.*

When did you start taking the pill (DD/MM/YYYY)? *Please note if you cannot remember exact day, please make sure month and year is correct.*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.
 

If you have, when did you stop taking the pill (DD/MM/YYYY)? *Please note if you cannot remember exact day, please make sure month and year is correct.*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.
 

Are you currently or have you ever used any other form of hormone-based birth control (i.e., injection, implant, patch, vaginal ring, hormonal intrauterine system (IUS) or copper coil (non-hormonal intrauterine device [IUS]) etc.)? *Required*

What type of hormone-based birth control did / do you take (name and dose of oestrogen and progesterone)? *If you are unsure, please ask. Link to hormonal contraception types and delivery*

forms if unsure: https://drive.google.com/file/d/1SeMaqVzLd7a9qwvEqs2tmc_k1UyxnjNs/view?usp=sharing

When did you start using the contraception (DD/MM/YYYY)? *Please note if you cannot remember exact day, please make sure month and year is correct.*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



If you have, when did you stop using the contraception (DD/MM/YYYY)? *Please note if you cannot remember exact day, please make sure month and year is correct.*

Dates need to be in the format 'DD/MM/YYYY', for example 27/03/1980.



If you are currently using any form of hormonal contraception, what is your reason (please select all that apply)? *Please note if you are not currently on any form of hormonal contraceptive, please select not applicable.* *Required*

- Birth control to avoid pregnancy
- Eliminate/ control bleeding
- Manage menstrual cycle symptoms
- Not applicable
- Other

If you selected Other, please specify:

 Have you ever used hormone replacement therapy? *Required*

 Have you ever sought help from a medical professional for any menstrual cycle related reason? *Required*

 If you selected Yes, please specify:

 Have you ever been diagnosed with any of the following (please select all applicable)?

Required

Menorrhagia or heavy menstrual bleeding (i.e., blood loss of more than 80 ml, requires frequent period product changing and any excessive blood loss that interferes with your day- to-day life)

Polycystic ovary syndrome

Endometriosis

Amenorrhea (lack of or no periods)

Thyroid dysfunction

Ovarian cyst

Iron-deficiency

Iron-deficiency anaemia

Polyps and fibroids

None of the above

Other

 If you selected Other, please specify:

On average, do you feel your periods are... *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* *Required*

- Very light/ spotting (*i.e.*, needing to change a low-absorbency tampon or pad one or two times per day)
- Light (*i.e.*, needing to change a low- or regular-absorbency tampon or pad two or three times per day)
- Moderate (*i.e.*, needing to change a regular-absorbency tampon or pad every three to four hours)
- Heavy (*i.e.*, needing to change a high-absorbency tampon or pad every three to four hours)
- Very heavy (*i.e.*, protection hardly works at all; you would need to change the highest absorbency tampon or pad every hour or two)
- Variable month to month
- I don't know/ never think about this
- Not applicable

During your periods do you regularly (please select all relevant to you) ... *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* *Required*

- Flood through clothes or bedding
 - Need to frequently change period products (*i.e.*, changing pads or tampons every 2 hours or less)
 - Need double period product protection (*i.e.*, use of tampon and pad)
 - Pass large blood clots
-
- None of the above
 - Other
 - Not applicable

If you selected Other, please specify:

Throughout the menstrual cycle do you experience any of the following symptoms? *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.*

Frequency *Required*

	Not applicable	Never	Rarely	Sometimes	Often
Changes to/ difficulties in breathing	<input type="radio"/>				
Nausea, sickness & vomiting	<input type="radio"/>				
Constipation	<input type="radio"/>				
Dizziness/ light headedness/ reduced coordination	<input type="radio"/>				
Poor concentration/ memory	<input type="radio"/>				
Joint pain/ muscle aches & cramps	<input type="radio"/>				
Temperature fluctuations	<input type="radio"/>				
Disturbed sleep	<input type="radio"/>				
Diarrhoea	<input type="radio"/>				
Headaches/ migraines	<input type="radio"/>				
Lower back pain	<input type="radio"/>				
Water retention	<input type="radio"/>				
Bloating/ increased gas	<input type="radio"/>				
Period cramps/ pain & pelvic/uterine/ovarian pain	<input type="radio"/>				
Tiredness/ fatigue	<input type="radio"/>				
Breast pain/ tenderness	<input type="radio"/>				
Cravings/ changes in appetite	<input type="radio"/>				
Mood changes/ irritability/ anxiety	<input type="radio"/>				

 Do you experience any other menstrual cycle related symptoms (i.e., those not listed above)?
Please note if you are currently on any form of hormonal contraceptive, please select not applicable. Required

- Yes
- No
- Not applicable

 If you selected Yes, please specify:

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Please indicate on the following scale, how severe your menstrual cycle symptoms have been on average in the last 12 months. *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* *Required*

Please don't select more than 1 answer(s) per

row. Please select at least 1 answer(s).

	Please select
N/A - Not applicable	<input type="checkbox"/>
0 - Absent	<input type="checkbox"/>
1 - Mild	<input type="checkbox"/>
2 - Moderate	<input type="checkbox"/>
3 - Severe	<input type="checkbox"/>

Do you regularly take pain relief for any menstrual cycle related symptom (*i.e.*, period pain, tender breasts etc.)? *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.* *Required*

- Yes, every cycle
- Yes, sometimes (roughly every 3 cycles)
- Yes, rarely (once/twice a year)
- No
- Not applicable

If you are on the combined, monophasic, oral contraceptive pill, do you suffer from any of these side effects? *Please note if you are currently naturally menstruating or on any other form of hormonal contraceptive, please select not applicable.*

	Frequency <input type="checkbox"/> <i>Required</i>				
	Not applicable	Never	Rarely	Sometimes	Often
Changes to/ difficulties in breathing	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Nausea, sickness & vomiting	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Constipation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Dizziness/ light headedness/ reduced coordination	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Poor concentration/ memory	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Joint pain/ muscle aches & cramps	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Temperature fluctuations	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Disturbed sleep	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Diarrhoea	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Headaches/ migraines	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Lower back pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Water retention	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Bloating/ increased gas	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Period cramps/ pain & pelvic/uterine/ovarian pain	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Tiredness/ fatigue	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Breast pain/ tenderness	<input type="radio"/>				
Cravings/ changes in appetite	<input type="radio"/>				
Mood changes/ irritability/ anxiety	<input type="radio"/>				

If you are on the combined, monophasic, oral contraceptive pill, do you suffer from any other side effects not listed above? *Please note if you are currently naturally menstruating or on any other form of hormonal contraceptive, please select not applicable.* *Required*

- Yes
- No
- Not applicable

If you selected Yes, please specify:

Please indicate on the following scale, how severe your oral contraceptive pill cycle side effects/ symptoms have been on average in the last 12 months. *Please note if you are currently naturally menstruating or on any other form of hormonal contraceptive, please select not applicable.*

Please don't select more than 1 answer(s) per

row. Please select at least 1 answer(s).

	Please select
N/A - Not applicable	<input type="checkbox"/>
0 - Absent	<input type="checkbox"/>
1 - Mild	<input checked="" type="checkbox"/>
2 - Moderate	<input type="checkbox"/>

Do you regularly take pain relief for any oral contraceptive pill cycle related side effects/symptom? Please note if you are currently naturally menstruating or on any other form of hormonal contraceptive, please select not applicable.

- Yes, every cycle
- Yes, sometimes (roughly every 3 cycles)
- Yes, rarely (once/twice a year)
- No
- Not applicable

Do you currently track your menstrual cycle (including any menstrual cycle symptoms etc.) or hormonal contraceptive use (including any side effects and symptoms)? *Required*

- Yes, manually through a diary or calendar
- Yes, using a smartphone app
- I don't feel the need to track my cycle
- No, I have never considered this/ I don't know how to track my cycle

CHAPTER 13 Page 5: Study eligibility: Training history

On average, how many minutes of moderate (i.e., hard breathing but can hold a conversation) physical activity do you take part in per-week? *Required*

- >Less than 150 minutes (>2 hours 30 mins)
- Around 150 minutes (2 hours 30 mins)
- <More than 150 minutes (<2 hours 30 mins)

On average, how often do you take part in any type of body strength/ weight-based activity?

Required

- Never
- Occasionally (1 day per week)
- Often (2 days per week)
- Regularly (more than 2 days per week)

What forms of exercise do you regularly take part in? Required

- Running
- Swimming
- Cycling
- Team sport (*i.e.*, hockey, netball, rugby)
- Athletics
- Gymnastics
- Rowing
- Boxing
- Martial arts (*i.e.*, judo/karate)
- Golf
- Gym-based classes (*i.e.*, spinning, body pump)
- Home based activity (*i.e.*, strength training and HIIT)
- Weight training

- Cross trainer or similar cardio-based exercise machines
- Cross fit
- Yoga/ Pilates
- Dance class/ dance-based fitness
- Other

If you selected Other, please specify:

Have you ever, or do you, regularly exercise from home? *Required*

Are you familiar with squat/lunge movement patterns? *Required*

- Highly familiar (confident and proficient with these movement patterns)
- Moderately familiar (fairly confident in ability to produce these movement patterns)
- Not familiar (I have never completed these movement patterns before)

Has the amount of exercise you complete on a weekly basis increased or decreased in the last year? *Required*

- Increased
- Decreased
- Stayed the same

Do you... *Required*

- Following a structured training program, set out by a coach etc.
- Follow your own structured training program
- Decide exercise/ sport on the day
- Other

If you selected Other, please specify:

Do you play any sport at a competitive (regularly partake in events in your sport or activity) or elite (compete at a world-class level in your sport) level? *Required*

If you selected Yes, please specify:

Do you consider your menstrual cycle to affect any of the following? *Please note if you are currently on any form of hormonal contraceptive, please select not applicable.*

	<input type="checkbox"/> <i>Required</i>				
	Yes, often (every cycle)	Yes, sometimes (every few cycles)	Yes, rarely (once or twice)	No, never	Not applicable
Training participation/adherence	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Training performance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Competitive participation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Competitive performance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Does any phase of your menstrual cycle effect any of the following? Please note if you are currently on any form of hormonal contraceptive, please select not applicable. Link to explain menstrual cycle phases if unsure:

<https://drive.google.com/file/d/1BoO8irkLyI4zkpH5w6vjmeIoWc7jr4G-/view?usp=sharing>

□ Required						
	Phase 1: Menstrual (the days during period/ bleeding, roughly days 1 to 5)	Phase 2: Follicular (the days after bleeding before ovulation, roughly days 5 to 14)	Phase 3: Luteal (the days immediately after ovulation up to 7 to 9 days after ovulation, roughly days 15 to 24)	Phase 4: Premenstrual (the days before your period/ bleeding = roughly 1 to 4 days before period/ bleeding, roughly days 24 to 28)	Don't experience this symptom	Not applicable
Decrease number of training sessions/ participation in sport & exercise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Increase number of training sessions/ participation in sport & exercise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Miss a training session	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Miss a competition						

Perceive a training session to be harder	<input type="checkbox"/>					
Perceive a training session to be easier	<input type="checkbox"/>					
Perform to the best of my ability	<input type="checkbox"/>					
Performance is negatively affected	<input type="checkbox"/>					
Feel more fatigued during training session	<input type="checkbox"/>					
Feel more energised during training session	<input type="checkbox"/>					
Decreased motivation to train						
Increased motivation to train	<input type="checkbox"/>					
Feel more fatigued/ take longer to recover following training	<input type="checkbox"/>					

Feel less fatigued / quicker recovery following training	<input type="checkbox"/>						
--	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------	--------------------------

If you are currently using the combined, monophasic, oral contraceptive pill, do you consider your use to affect any of the following? Please note if you are currently naturally menstruating or on any form of hormonal contraceptive, please select not applicable.

	Required				
	Yes, often (every pill cycle)	Yes, sometimes (every few pill cycles)	Yes, rarely (once or twice)	No, never	Not applicable
Training participation/adherence	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Training performance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Competitive participation	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Competitive performance	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

If you are on the combined, monophasic, oral contraceptive pill, does any phase of your pill cycle effect any of the following? *Please note if you are currently naturally menstruating or on any other form of hormonal contraceptive, please select not applicable. Link to explain oral contraceptive phases if unsure:*

<https://drive.google.com/file/d/17v37nSVTYPQnfGhIBOHhD0VZJbggXBZ4/view?usp=sharing>

Required

	Oral contraceptive pill withdrawal phase days 1-7 (pill-free days/ placebo pill days)	Oral contraceptive pill consumption phase days 1-7 (21 pill-taking days/ active pill days)	Oral contraceptive pill consumption phase days 8-14 (21 pill-taking days/ active pill days)	Oral contraceptive pill consumption phase days 15-21 (21 pill-taking days/ active pill days)	Don't experience this	Not applicable
Decrease number of training sessions/ participation in sport & exercise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Increase number of training sessions/ participation in sport & exercise	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Miss a training session	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Miss a competition	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Perceive a training session to be harder	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Perceive a training session to be easier	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Perform to the best of my ability	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Performance is negatively affected	<input type="checkbox"/>					
Feel more fatigued during training session	<input type="checkbox"/>					
Feel more energised during training session	<input type="checkbox"/>					
Decreased motivation to train	<input type="checkbox"/>					
Increased motivation to train	<input type="checkbox"/>					
Feel more fatigued/ take longer to recover following training	<input type="checkbox"/>					
Feel less fatigued / quicker recovery following training	<input type="checkbox"/>					

Do you currently have a coach, exercise mentor, personal trainer etc.? *Required*

Is your coach, exercise mentor, physical trainer, male or female?

Do you discuss your menstrual cycle or hormonal contraceptive use with your coach, exercise mentor or personal trainer?

If not, why not (please select all applicable to you)?

- Never felt the need to
- Too embarrassed
- My own lack of education and knowledge
- Fear of judgement
- Male coach
- Other
- Not applicable

Have you ever been given any information/ education on how your menstrual cycle or hormonal contraceptive use might impact your training or performance? *Required*

If you selected Yes, please specify (*i.e.*, how did you receive this information, who gave you this information):

 Do you think understanding more about your menstrual cycle and hormonal contraceptive use will benefit your training and performance? *Required*

Appendix K: Daily Cycle Related Data and Symptom Tracking Forms.

- 1) Form for naturally menstruating group



THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

MENSTRUAL CYCLE SYMPTOM DAILY QUESTIONNAIRE.



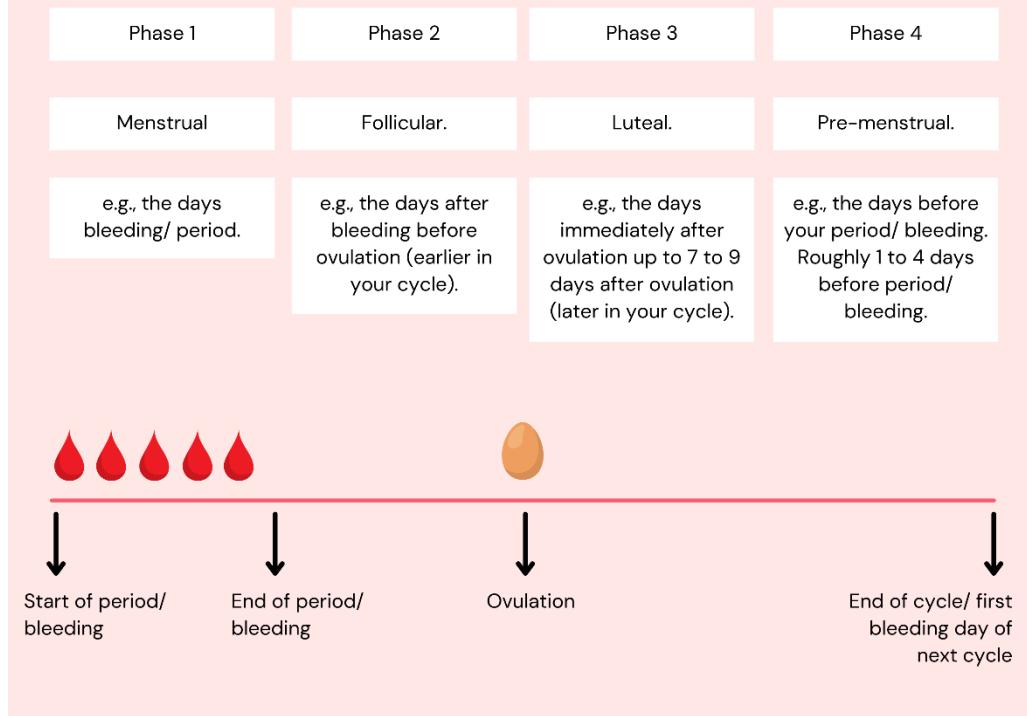
MENSTRUAL CYCLE RELATED DATA AND SYMPTOM TRACKING FORM

Please complete this form daily for the duration of the study.

Question 1: Are you currently on your period (menstrual bleeding)? Please use diagram below to help if unsure.

- Yes
- No

Menstrual cycle phases.



Question 2: What is your blood flow amount?

- None
- Very light/ spotting (*i.e.*, needing to change a low-absorbency tampon or pad one or two times per day)
- Light (*i.e.*, needing to change a low- or regular-absorbency tampon or pad two or three times per day)
- Moderate (*i.e.*, needing to change a regular-absorbency tampon or pad every three to four hours)
- Heavy (*i.e.*, needing to change a high-absorbency tampon or pad every three to four hours)
- Very heavy (*i.e.*, protection hardly works at all; you would need to change the highest absorbency tampon or pad every hour or two)

Question 3: Have you had a positive ovulation test today? Please note ovulation testing is not for medical use and should not replace your normal method of contraception and is solely for use in this study.

- Yes, non-flashing smiley face

- Yes, flashing smiley face
- No

Question 4: What was your daily basal body temperature reading today?

- Enter temp here

Question 5: What does your cervical fluid look like today?

- None/ dry phase (*i.e.*, dry or a hint of moisture)
- Sticky phase (*i.e.*, white/ cloudy in colour, thick and/or sticky/ forms small sticky globs)
- Creamy phase (*i.e.*, milky, creamy or lotion like)
- Clear phase (*i.e.*, like raw egg whites, stretchy & slippery, increased volume)
- Other (please specify)

Symptoms section

Question 6: Are you experiencing any of the following symptoms, and if so, how severe are your symptoms?

Symptom	Absent	Mild	Moderate	Severe
Changes to/ difficulties in breathing				
Nausea, sickness & vomiting				
Constipation				
Dizziness/ light headedness/ reduced coordination				
Poor concentration/ memory				
Joint pain/ muscle aches & cramps				
Temperature fluctuations				
Disturbed sleep				
Diarrhoea				
Headaches/ migraines				
Lower back pain				
Water retention				
Bloating/ increased gas				
Period cramps/ pain & pelvic/uterine/ovarian pain				
Tiredness/ fatigue				
Breast pain/ tenderness				
Cravings/ changes in appetite				
Mood changes/ irritability/ anxiety				

Question 7: Are you experiencing any other symptoms. If yes, please specify.

- No
- Yes (please specify)

Question 8: Have you trained today?

- Yes
- No

Training section

If you selected 'Yes', this section is to input more data regarding your training.

Additional question 1: What type of training did you complete?

- Strength training (*i.e.*, body weight or weight-based strength training)
- Interval training
- Continuous endurance training
- Speed training
- Plyometric training
- Circuit training
- Exercise class (*i.e.*, yoga, dance etc.)
- Other (please specify)

Additional question 2: How long did you train for (in minutes)?

- Enter training minutes here

Additionally question 3: What was your session rating of perceived exertion (RPE)? Please see image below for details.

- Enter session RPE here

0–10 Borg Rating of Perceived Exertion Scale	
0	Rest
1	Really easy
2	Easy
3	Moderate
4	Sort of hard
5	Hard
6	
7	Really hard
8	
9	Really, really, hard
10	Maximal: just like my hardest race

- 2) Form for oral contraceptive group



THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.



OCP CYCLE SYMPTOM DAILY QUESTIONNAIRE.



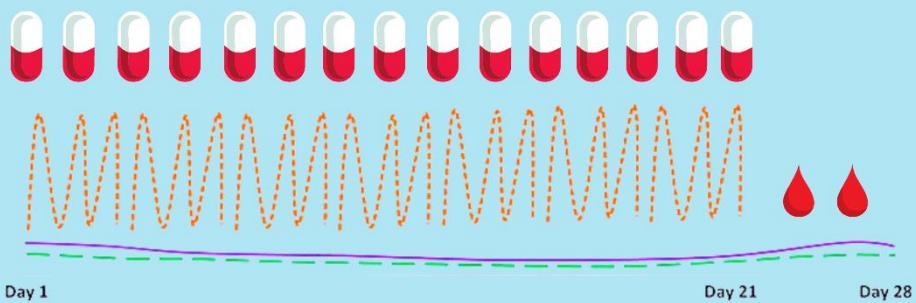
ORAL CONTRACEPTIVE PILL CYCLE RELATED DATA AND SYMPTOM TRACKING FORM

Please complete this form daily for the duration of the study.

Question 1: Are you currently on an oral contraceptive pill taking day (please note this does not include inactive or placebo pills)? Please use diagram below to help if unsure.

- Yes
- No

Oral contraceptive cycle phases



Pill consumption section

If you answered 'Yes' to the above, this section is for more details.

Additional question 1: What day of your oral contraceptive pill are you on?

- Enter day here

Pill withdrawal section

- *If you answered 'No' to the above, this section is for more details.*

Additional question 1: What day of your oral contraceptive pill withdrawal are you on?

- Enter day here

Additional question 2: Are you currently experiencing your withdrawal bleed (i.e., bleeding because of your pill withdrawal or bleeding because of placebo pill)?

- Yes
- No

Additional question 3: What is your blood flow amount?

- None
- Very light/ spotting (*i.e.*, needing to change a low-absorbency tampon or pad one or two times per day)
- Light (*i.e.*, needing to change a low- or regular-absorbency tampon or pad two or three times per day)
- Moderate (*i.e.*, needing to change a regular-absorbency tampon or pad every three to four hours)
- Heavy (*i.e.*, needing to change a high-absorbency tampon or pad every three to four hours)
- Very heavy (*i.e.*, protection hardly works at all; you would need to change the highest absorbency tampon or pad every hour or two)

Symptoms section

Question 2: Are you experiencing any of the following symptoms, and if so, how severe are your symptoms?

Symptom	Absent	Mild	Moderate	Severe
Changes to/ difficulties in breathing				
Nausea, sickness & vomiting				
Constipation				
Dizziness/ light headedness/ reduced coordination				
Poor concentration/ memory				
Joint pain/ muscle aches & cramps				
Temperature fluctuations				
Disturbed sleep				
Diarrhoea				
Headaches/ migraines				
Lower back pain				
Water retention				
Bloating/ increased gas				
Period cramps/ pain & pelvic/uterine/ovarian pain				
Tiredness/ fatigue				
Breast pain/ tenderness				

Cravings/ changes in appetite				
Mood changes/ irritability/ anxiety				

Question 7: Are you experiencing any other symptoms. If yes, please specify.

- No
- Yes (please specify)

Question 8: Have you trained today?

- Yes
- No

Training section

If you selected 'Yes', this section is to input more data regarding your training.

Additional question 1: What type of training did you complete?

- Strength training (*i.e.*, body weight or weight-based strength training)
- Interval training
- Continuous endurance training
- Speed training
- Plyometric training
- Circuit training
- Exercise class (*i.e.*, yoga, dance etc.)
- Other (please specify)

Additional question 2: How long did you train for (in minutes)?

- Enter training minutes here

Additionally question 3: What was your session rating of perceived exertion (RPE)?

Please see image below for details.

- Enter session RPE here

0–10 Borg Rating of Perceived Exertion Scale	
0	Rest
1	Really easy
2	Easy
3	Moderate
4	Sort of hard
5	Hard
6	
7	Really hard
8	
9	Really, really, hard
10	Maximal: just like my hardest race

Appendix L: Exercise Sheets Detailing How to Perform Each Exercise for Participants.



The exercise session.



STEP BY STEP GUIDE

For more info, please contact Kelly McNulty
E: kelly.mcnnulty@northumbria.ac.uk

Basic introduction.

All training sessions will be monitored over Zoom (or a similar platform) with one of the research team.

Details of the warm-up and exercise session are provided on the next pages.

The entire protocol will take approx. 30 minutes to complete and all you will be verbally encouraged during the session to complete the whole protocol.

Each exercise will be coached during the familiarisation session to ensure you are performing the exercise session correctly. Additionally, during the exercise session itself you will be coached on technique if deemed required.

Your heart rate will be monitored during the session and your rating of perceived exertion will also be monitored using a questionnaire scale after each circuit.

Warm up.

Everyone will complete a standard warm up prior to the exercise session. This includes...

EXERCISE	TIME/ REPS
Jogging on the spot	60 s
Low level high knees	30 s
Heel flicks	30 s
Inch worms	10 reps
Standing hurdle stretch	5 reps each leg
Side lunge	5 reps each leg
Squat	5 reps
Lunge	5 reps each leg

The training stimulus.

Everyone will complete the exercise session consisting of six lower body focused exercises, separated by 20 s rest: The exercises include:

EXERCISE	TIME/ REPS
Bodyweight squat	20 reps
Bodyweight lunge	10 reps each leg
Bodyweight step up	10 reps each leg
Bodyweight jump squat	10 reps
Bodyweight split squat	10 reps each leg
Squat hold	30 s

This circuit will be repeated 5 times with one minutes rest between each circuit.

You will try to complete each exercise at a standardised tempo whereby the goal is to complete one repetition per second for the bodyweight squat, step ups and split squats, and as close to one repetition per second as possible on the jump squat and lunge exercises.

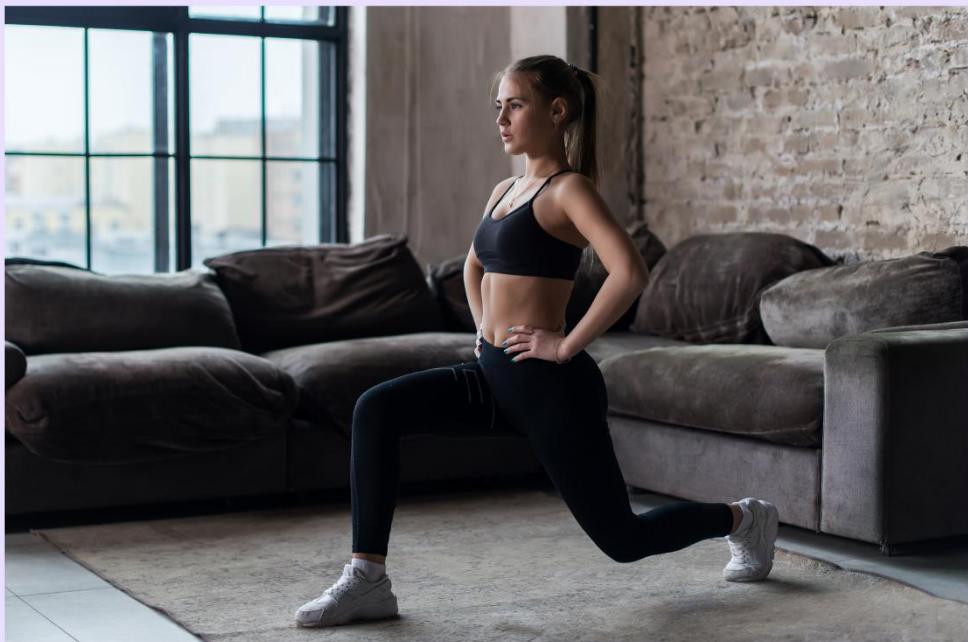
Each exercise in detail.



1. SQUAT

Stand with feet roughly shoulder-width apart and toes pointing slightly out. Squat down until thighs are at least parallel to the floor whilst keeping chest lifted. Return to start position and repeat.

Each exercise in detail.



2. LUNGE

Step forward with one foot until the distance is roughly as long as the length of your leg and bend to a 90-degree angle before returning to the start position. Repeat.

Each exercise in detail.



3. STEP UP

Step up onto a box (or whatever equipment you have which is a hard surface to step up onto, ensure you step up to the same height of roughly 90-degree knee angle and use the same equipment during each session) with one foot, bring the opposite foot up to meet the foot on the box and then return to the starting position by stepping down. Repeat alternatively.

Each exercise in detail.



4. JUMP SQUAT

Perform a squat movement and then explode off the floor and jump as high as you can, before landing and sticking this landing for 1 second before starting the next jump from a standing position. During this exercise always keep your hands on your hips.

Each exercise in detail.



5. SPILT SQUAT

To perform the split squat get into a lunge position with the heel of your back foot raised, whilst keeping your torso upright lower until your back knee almost touches the floor and then push back up. Repeat and then switch legs.

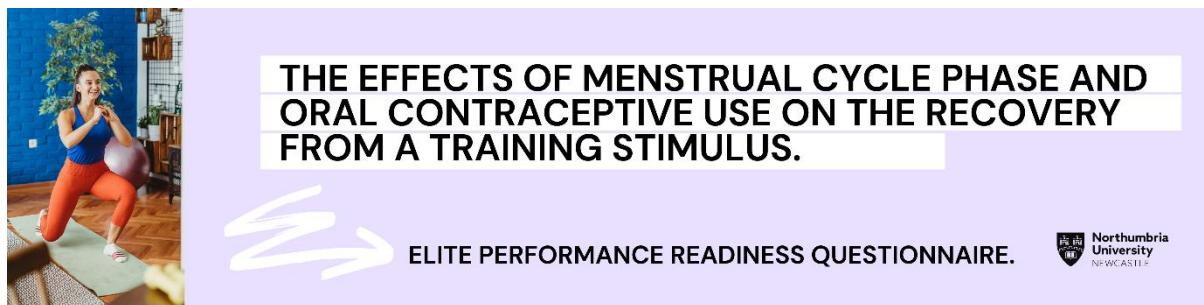
Each exercise in detail.



6. SQUAT HOLD

To perform the squat hold, get into a squat position, with your knees at 90-degrees and hold this position for the required duration.

Appendix M: The ‘Elite Performance Readiness Questionnaire’.

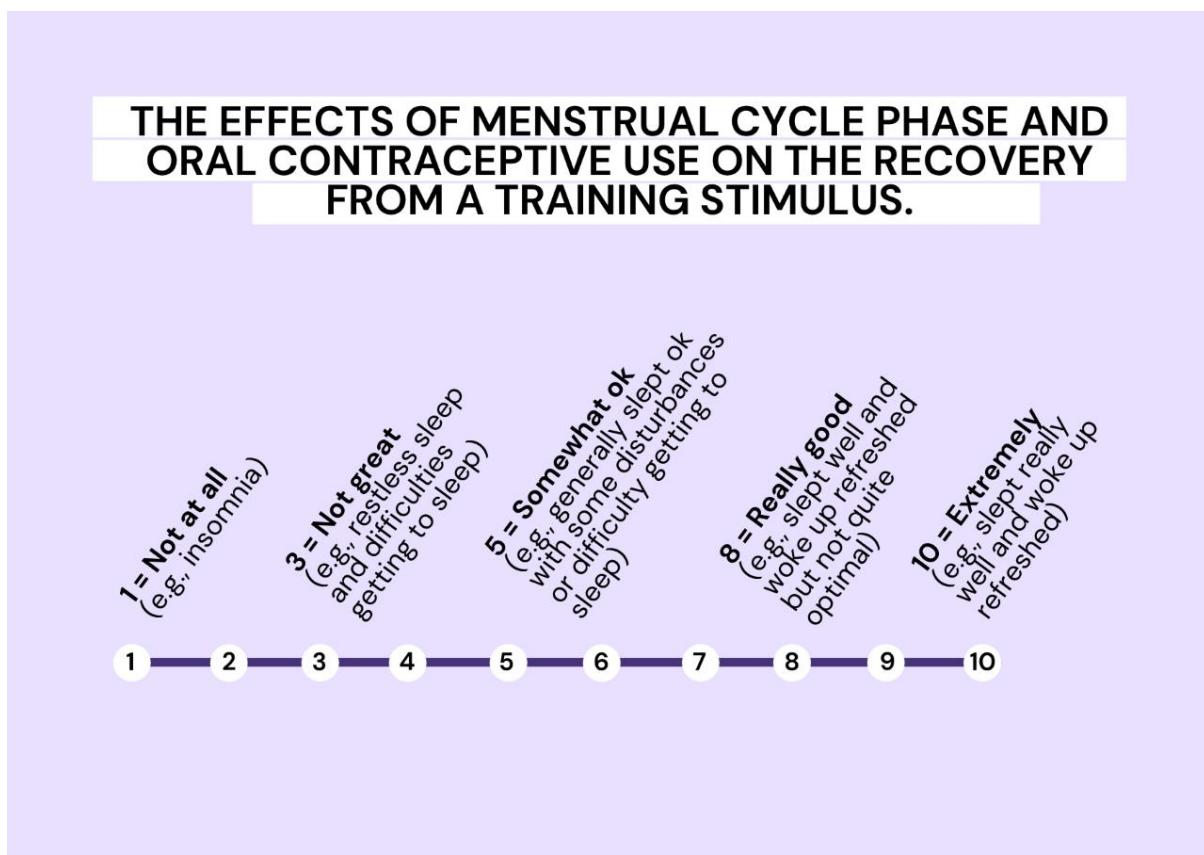


THE ELITE PERFORMANCE READINESS QUESTIONNAIRE

Below are 12 questions we would like you to answer concerning how you feel. These questions are answered by indicating your feelings on a scale that ranges from ‘not at all’ to ‘extremely.’ Please read each one carefully then mark your place on the scale that best describes **HOW YOU FEEL RIGHT NOW.**

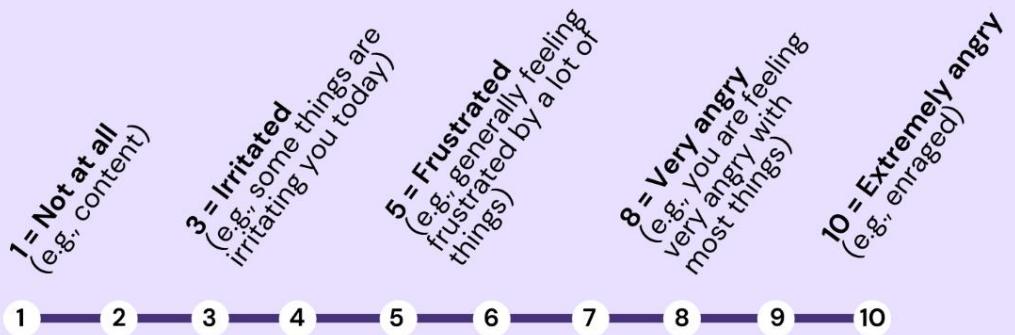
Please make sure you answer every question.

Question 1: How well do you think you have slept?



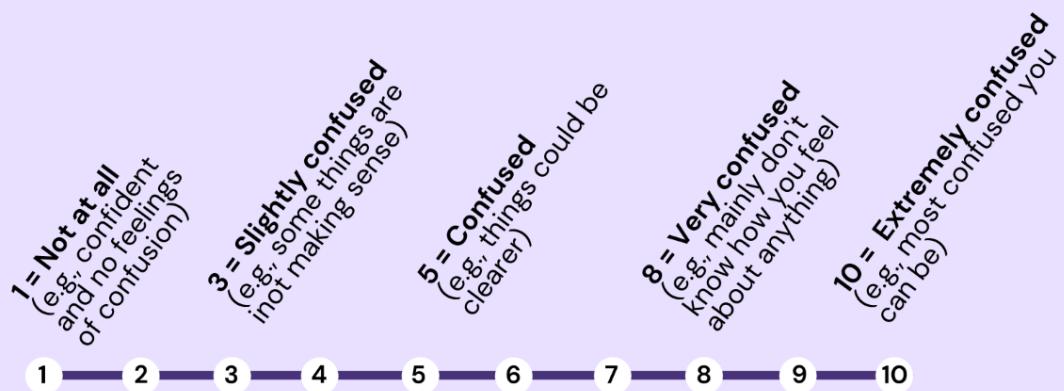
Question 2: How angry do you feel?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

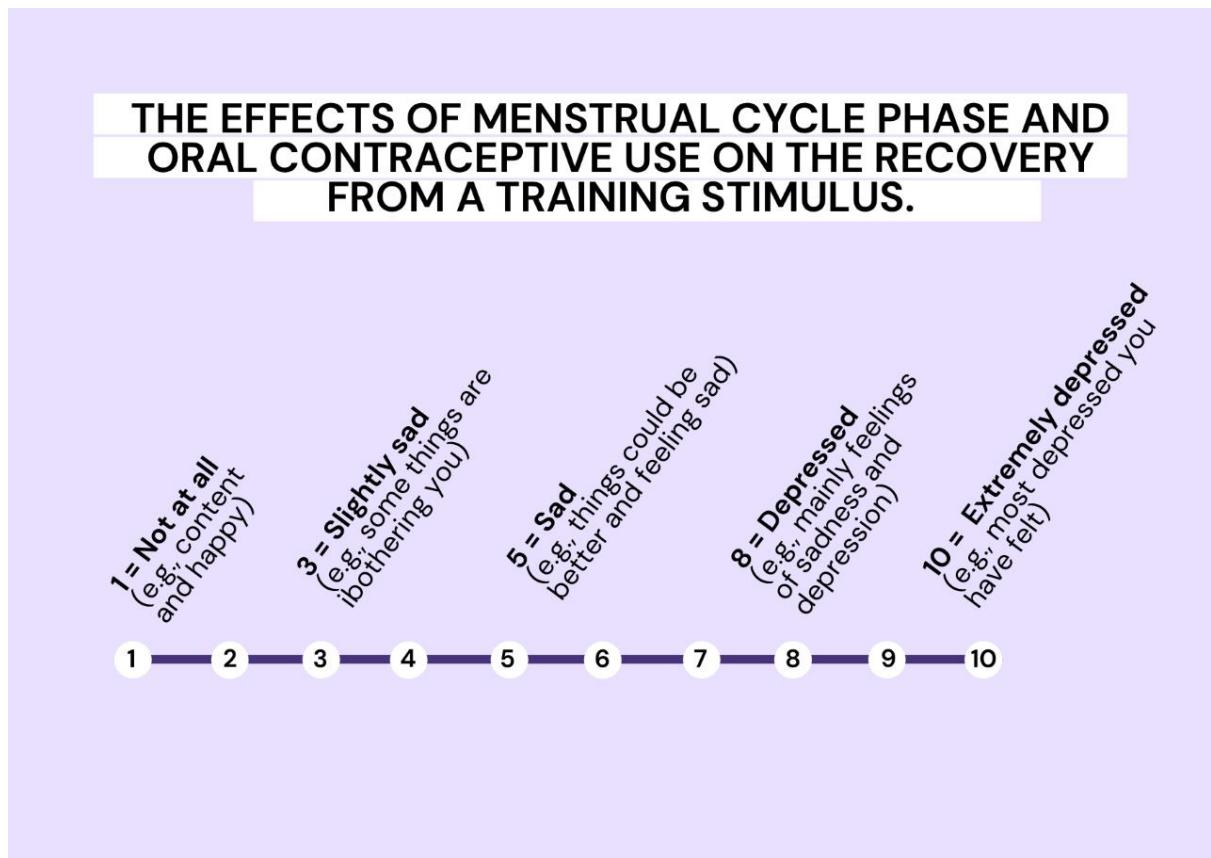


Question 3: How confused do you feel?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

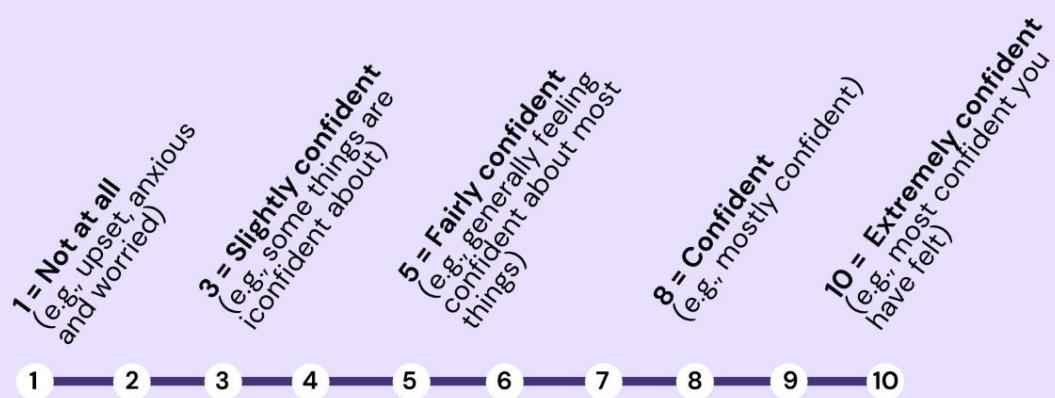


Question 4: How depressed do you feel?



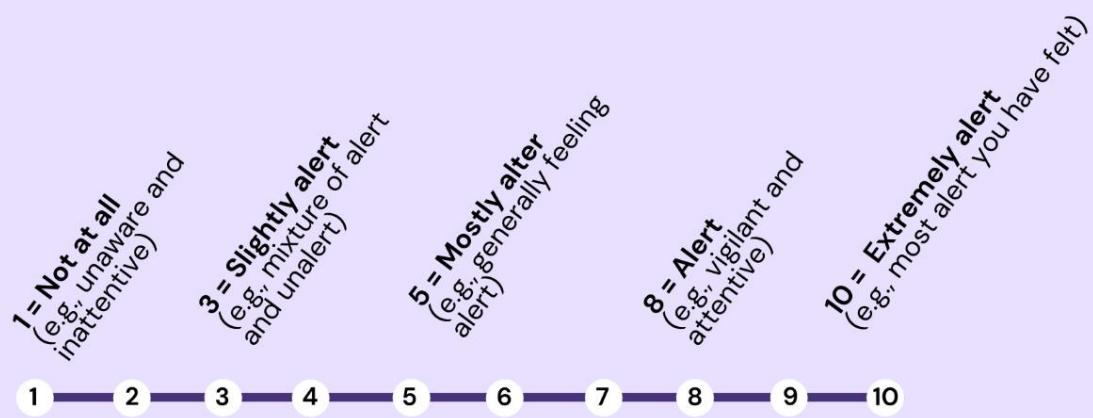
Question 5: How confident do you feel?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

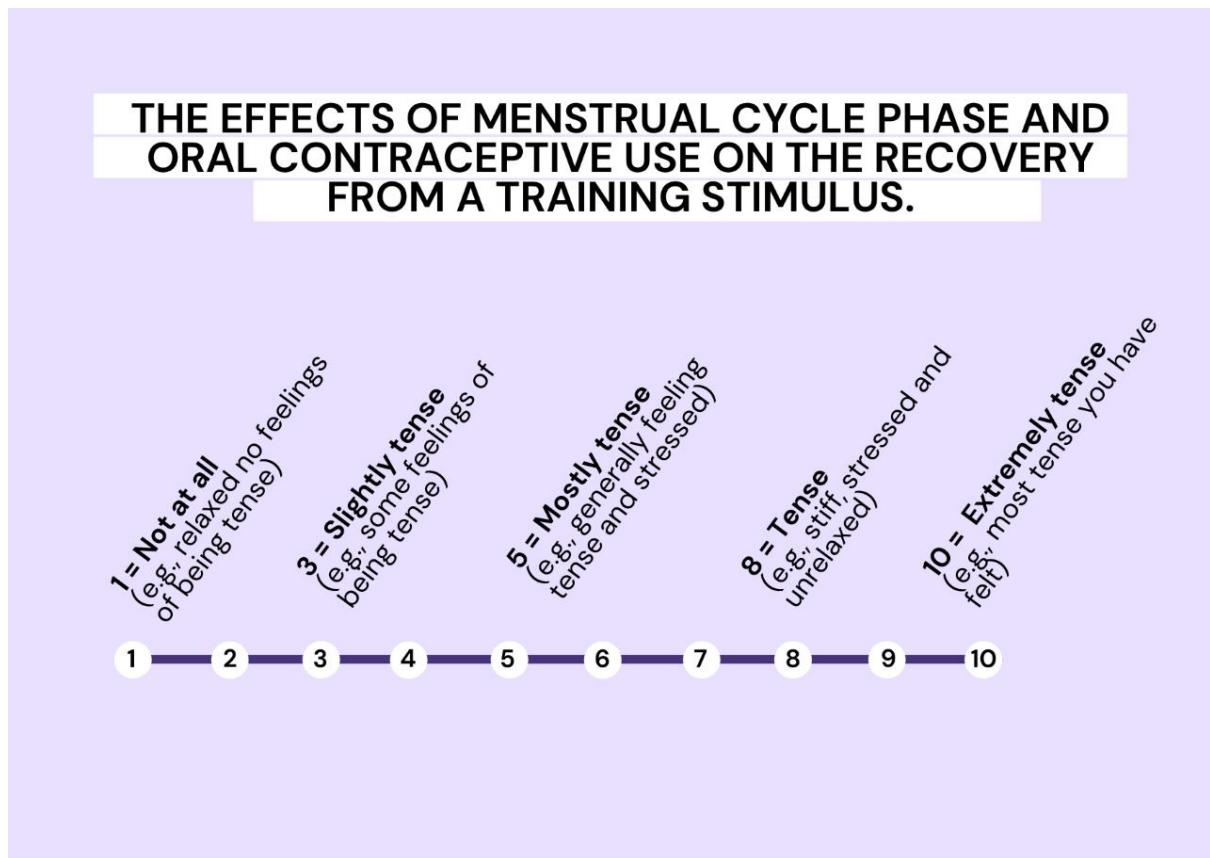


Question 6: How alter do you feel?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

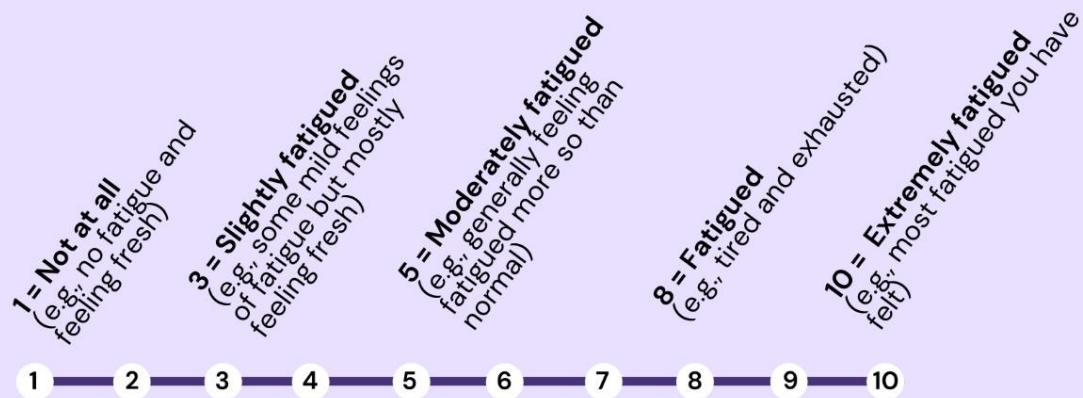


Question 7: How tense do you feel?



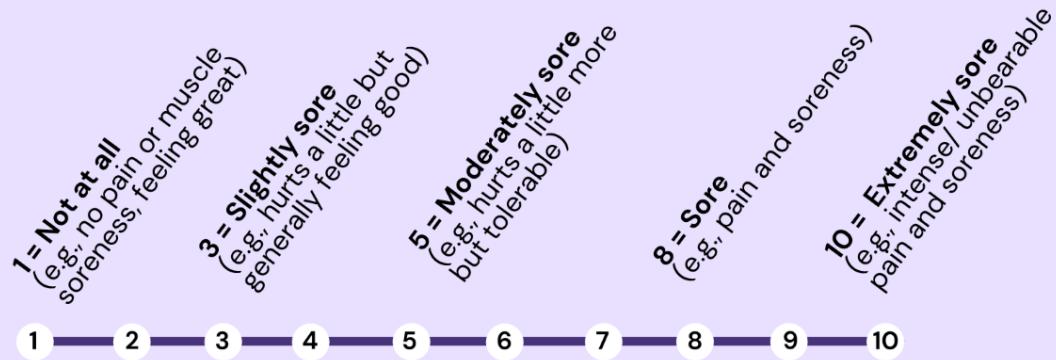
Question 8: How fatigued do you feel?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

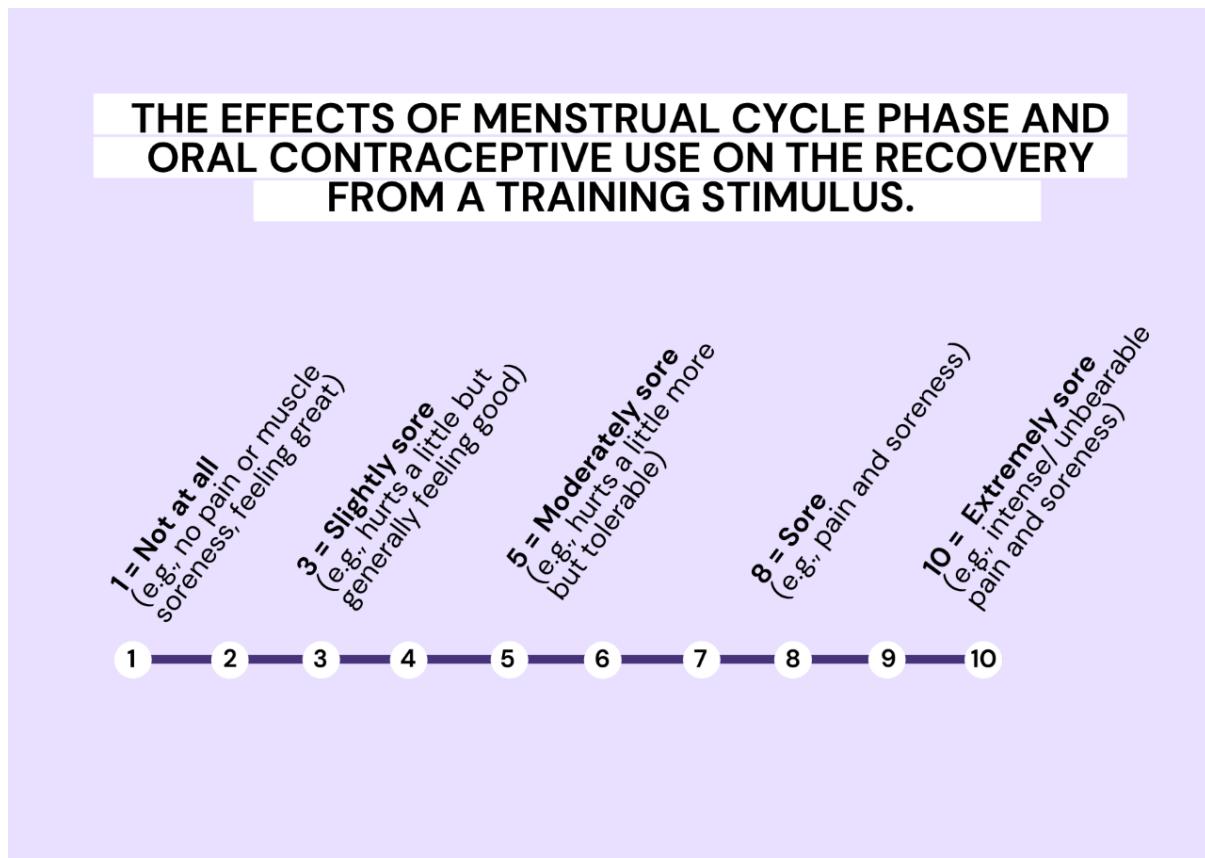


Question 9: How sore do your muscles feel (passive muscle soreness)?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

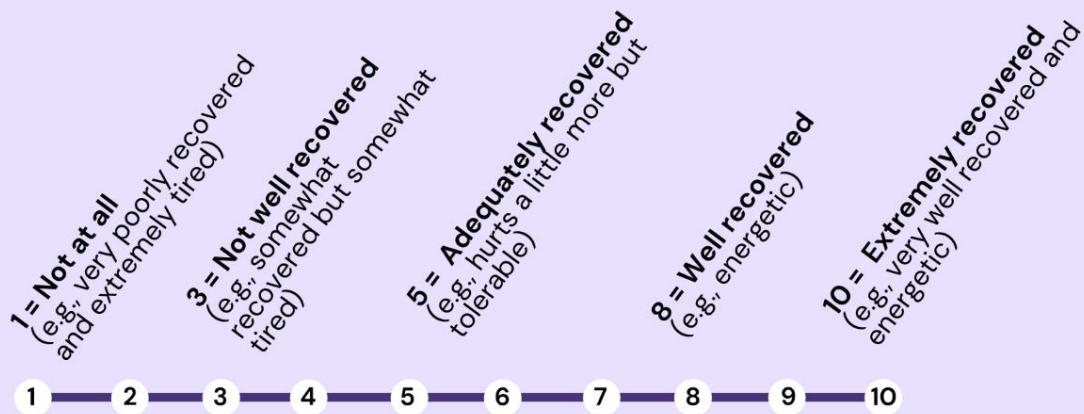


Question 10: How sore do your muscles feel (active soreness during a squat to 90-degrees)?



Question 11: How well do you think you have recovered?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.



Question 12: How motivated to train are you?

THE EFFECTS OF MENSTRUAL CYCLE PHASE AND ORAL CONTRACEPTIVE USE ON THE RECOVERY FROM A TRAINING STIMULUS.

