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JOURNAL
Journal of Science and Medicine in Sport

DATE DEPOSITED
4 May 2020

This version available at
http://research.stmarys.ac.uk/id/eprint/3970/

Variations in Strength-Related Measures During the Menstrual Cycle in Eumenorrheic Women: A Systematic Review and Meta-Analysis

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Manuscript length: 3980 words

Abstract length: 224 words

Figures: 2

Tables: 1

Appendix: 1 (supplementary table)

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Abstract

Objectives: To systematically review the current body of research that has investigated changes in strength-related variables during different phases of the menstrual cycle in eumenorrheic women. *Design:* Systematic review and meta-analysis. *Method*: A literature search was conducted in Pubmed, SPORTDiscus and Web of Science using search terms related to the menstrual cycle and strength-related measures. Two reviewers reached consensus that 21 studies met the criteria for inclusion. Methodological rigor was assessed using the Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies. Random effects meta-analyses were used to compare the early-follicular, ovulatory and mid-luteal phases for maximal voluntary contraction, isokinetic peak torque, and explosive strength. *Results:* The assessment of study quality showed that a high level of bias exists in specific areas of study design. Non-significant and small or trivial effect sizes ($p \geq 0.26$, Hedges $g \leq 0.35$) were identified for all strength-related variables in each comparison between phases. 95% confidence intervals for each comparison suggested the uncertainty associated with each estimate extends to a small effect on strength performance with unclear direction ($-0.42 \leq g \leq 0.48$). The heterogeneity for each comparison was also small ($p \geq 0.83$, $I^2=0\%$). *Conclusions:* Strength status appears to be minimally altered ($g \leq 0.35$) by the fluctuations in ovarian sex hormones that occur during the menstrual cycle. This finding should be interpreted with caution due to the methodological shortcomings identified by the quality assessment.

Key words: period, menstruation, oestrogen, progesterone, power, athletes

1. Introduction

The menstrual cycle represents an important biological rhythm in females that serves to prepare the uterus for gestation. In eumenorrheic women, a menstrual cycle typically lasts 28 days, but can vary considerably[1]. It is well-established that over the course of a menstrual cycle, women are exposed to a constant and rapidly shifting profile of endogenous sex hormones. Aside from their principal roles in reproductive function and control of sexual characteristics, the main female ovarian hormones (oestrogen and progesterone) circulating in the blood, influence a multitude of different physiological systems. Fluctuations in these, and other sex hormones, can explain variations in physical performance and physiological responses to exercise over the course of a menstrual cycle[2], which has important implications for scientific research and the optimization of exercise prescription in females. In particular, the effect that changes in female reproductive hormones exert in strength-related tasks has received considerable attention and is widely debated[2–5].

The menstrual cycle is traditionally divided into two distinct phases (follicular and luteal), which are separated by ovulation. These two phases are defined by ovarian function and differentiated by varying concentrations of oestrogen and progesterone. The follicular phase begins on the first day of menses (days 1-5) and is characterized by low concentrations of both oestrogen and progesterone. Oestrogen gradually increases during the follicular phase and peaks ~1 day prior to ovulation (typically 12-14 days after menstruation onset), which is triggered by a surge in the luteinizing hormone (LH). The rise in oestrogen and LH is also accompanied by a sharp and brief increase in testosterone, which is a precursor for the biosynthesis of oestrogen, and is considered to be important for sexual function and desire in females[6]. Following the ovulatory period, the early-luteal phase is characterized by decreasing oestrogen levels and a gradual rise in progesterone. Through the mid-luteal phase, oestrogen displays a bi-phasic response, resulting in high levels of both hormones before a gradual decrease over the following 5-7 days. Although this pattern of hormonal physiology is broadly present in all eumenorrheic females, the concentration of hormones and timing of cycle events, displays large inter-individual variability[7], making scientific investigation in this area complex and challenging. Therefore, although many studies have investigated the effects of menstrual cycle phase on exercise performance, it is prudent to examine the internal validity of these studies to ensure that the conclusions generated are accurate.

Oestrogen is responsible for the regulation of a number of important anabolic processes[8] and can influence central nervous system function[9]. Dehydroepiandrosterone (DHEA), the precursor to oestrogen and testosterone that peaks prior to ovulation, produces a net excitatory effect via its action on several neurotransmitter receptors[10]. Specifically, oestrogen is known to bind to receptor sites that attenuate the release of γ-aminobutyric acid[11], a neurotransmitter responsible for reducing neuronal excitability and muscle tone. Additionally, oestrogen promotes the activation of glutamate releasing neuron receptors that cause an excitatory response in the nervous system[12]. In contrast, progesterone is known to exert a net inhibitory effect on the nervous system via enhancement of γ-aminobutyric acid action[13]. Variations in testosterone level across the menstrual cycle also produce physiological effects that may alter strength-related performance. Although absolute testosterone is low in females compared to males, a surge in testosterone during the late-follicular phase may benefit performance during short-intense activity, via increases in motivational drive[14], and enhanced calcium kinetics in the muscle cell[15]. It is also possible that the thermogenic action of progesterone, which causes an increase in core body and skin temperature during the luteal phase[16], positively influences nerve conduction velocity[17] and antagonistic co-contraction[18], and consequently may positively influence performance in explosive strength-related tasks. Based upon these theoretical mechanisms, it is conceivable that oestrogen has an inotropic effect on muscular strength-related capabilities.

Strength can be defined as the ability of an individual to apply force under a specified set of movement constraints[19]. Increases in strength are associated with improvements in important markers of metabolic health[20], everyday tasks[21], a lower risk of injury[22], and enhanced athletic performance[23]. Strength training is also important in counteracting conditions associated with muscle weakness, such as sarcopenia, musculoskeletal disorders, and prolonged immobilization[24]. Strength training also provides beneficial changes to the risk factors associated with anterior-cruciate ligament injury, which has a high incidence in female athletes injury[25].

Findings from studies examining the influence of female sex hormones on strength-related performance have previously been summarized in several non-systematic narrative reviews and book chapters[1–4,26]. However, these works typically address the effects of female reproductive hormones on athletic performance qualities more broadly and concluded that the effects on muscular strength are equivocal. Consequently, the aim of this study was to systematically review the current body of research that has investigated changes in strength-related variables during different phases of the menstrual cycle in eumenorrheic women, and to conduct a meta-analysis of the data.

2. Methods

The complete protocol for this study was registered with PROSPERO International prospective register of systematic reviews (registration number: CRD42019126598). The guidelines provided by the Cochrane Musculoskeletal Group[27] were used as the basis for this systematic review. Fig. 1 provides a visual overview of the review and study selection process.

An initial scoping search was carried out in PubMed PubReMiner using the terms 'strength' AND 'menstrual cycle'. The terms selected for the search strategy were defined *a priori* and were supplemented using medical subject headings provided by the scoping exercise. The search was conducted on October 8th 2018 in Pubmed, SPORTDiscus and Web of Science using the following search terms: ["menstrual cycle" OR "menstrual phase" OR "luteal phase" OR "follicular phase"] AND ["strength" OR "power" OR "torque" OR "force" OR "neuromuscular" OR "max* voluntary contraction" OR "isometric" OR "isokinetic" OR "muscular performance"] NOT ["postmenopausal"]. No restriction was placed upon date or language of publication.

Studies that met the following pre-defined criteria were included in the review:

- Participants were eumenorrheic females (operationally defined as regularly occurring menstrual cycles of between 21-35 days for >6 months)

- At least one maximal muscular strength- or power-related outcome measure was taken
- Outcome measurements occurred in two or more defined phases (e.g. follicular, ovulatory, luteal) of the menstrual cycle
- A physiological measure of hormone levels or body temperature was taken to identify and/or verify menstrual cycle phases
- Published in full, in a peer-reviewed journal

The following exclusion criteria were also applied:

- Participants used one of the following forms of contraception: oral, implanted, injected, intrauterine devices, patches
- Participants received hormone replacement therapy
- Comparative time points were separated by longer than a regular menstrual cycle
- Participants suffered from an injury, illness or disease that may have affected performance in a test
- Description of measurement protocols and/or results were incomplete
- Ergogenic aids were used as part of the study

No limits were placed upon the training or competitive status of participants.

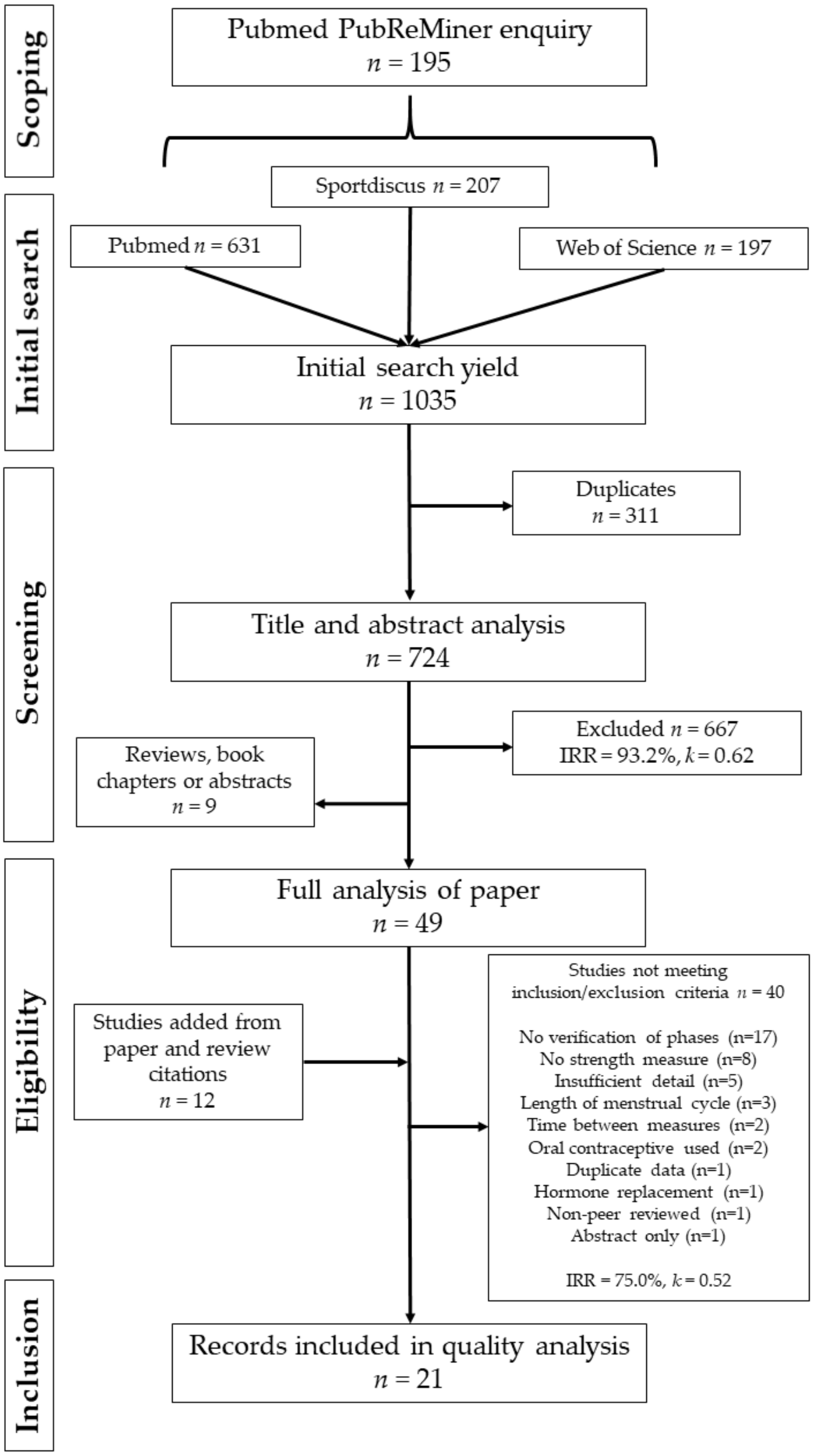

Fig. 1 Search, screening and selection process for suitable studies. IRR = inter-rater reliability, *k* = Cohen's kappa statistic

The initial search returned 1035 papers, which were imported into a published software for systematic reviews[28]. Two reviewers (RB and GB) independently conducted each step of the study selection process (Fig. 1), with reasons for study exclusion noted by each reviewer. Any conflicts were resolved after each stage via discussion and consensus agreement between the reviewers. Following the removal of duplicate papers (*n*=311), the title and abstract of each study were screened (*n*=724, inter-rater reliability (IRR): 93.2%, Cohens *k*=0.62). Nine works were identified that were review articles, conference abstracts or book chapters, leaving 49 studies that were taken forward for full analysis. A further 12 papers were added following a process of citation checking of relevant systematic reviews and individual studies that appeared to meet the criteria for inclusion. These 61 papers were read in full by the two reviewers to assess suitability for inclusion (IRR: 75.0%, Cohens *k*=0.52). This process resulted in the exclusion of a further 40 studies for the following reasons: no physiological verification of menstrual cycle phases (*n*=17), no maximal strength-related measure (*n*=6), results were not reported appropriately (*n*=4), method provided insufficient detail (*n*=3), menstrual cycle was longer than the pre-defined range or length unreported (*n*=3), measurements were separated by >1 menstrual cycle (*n*=2), participants used oral contraceptive (*n*=2), study was non-peer reviewed (*n*=1) or not published in full (*n*=1), duplicate data (*n*=1), and participants received hormone replacement injections (*n*=1).

Twenty-one studies were subsequently assessed for quality using the National Heart, Lung, and Blood Institute Quality Assessment Tool (NHLBI-QAT) for Observational Cohort and Cross-Sectional Studies. The tool compromises 14 items designed to assess the internal rigor of observational and cross-sectional research studies, with questions marked at 'yes' (low risk of bias), 'no' (high risk of bias) or 'other' (unclear risk of bias). A 15th item was added to identify whether the sequence of testing between menstrual cycle phases was randomized. This is important because, in the absence of sufficient familiarization to a strength-related task, a practice-effect may be present across trials, which may bias results. No studies were excluded based upon the results generated by the NHLBI-QAT and agreement between reviewers was high (IRR: 94.0%, Cohens *k*=0.87).

The following data were extracted by the lead author (RB) and recorded in a spreadsheet: (1) author names, publication year and country of origin; (2) sample size and participant characteristics; (3) the timing of strength measurements during the menstrual cycle; (4) how menstrual cycle phase was identified and verified (5) how strength was assessed; and (6) the main findings regarding strength values at the time points used. Accuracy of data extraction was verified by a co-author (GB).

Review Manager (v5.3) was used to conduct random effect meta-analyses using the inverse variance method to compare the effect of menstrual cycle phases on strength-measures. The inverse-variance random effects model was selected because it weights trials proportionally based upon standard error values and heterogeneity across studies is also accounted for. The first day of menstruation was used as a common reference point to define menstrual cycle phases. Three comparisons were made: early-follicular phase (≤5 days from menstruation onset) versus ovulatory phase (±2 days from ovulation), early-follicular phase versus mid-luteal phase (21±2 days from menstruation onset or 7±2 days following ovulation), and ovulatory phase versus mid-luteal phase[7]. Values and comparisons between other time points in individual studies were also calculated for review purposes but were not entered into the meta-analysis due to the lack of data across studies at specific time points.

Outcome measures used in studies could be grouped into three categories based upon the strength quality assessed: maximal voluntary contraction (MVC), isokinetic peak torque (IPT, knee extension and knee flexion), and explosive strength (maximal jumping tasks, cycle ergometer peak power output, and rate of force development). A total of nine meta-analyses were therefore performed (three menstrual cycle phase comparisons for each of the three strength-related categories). Where studies reported an outcome measure more than once for different tasks, the data were pooled and entered as a single observation in order to avoid bias in the effect calculation caused by sampling dependence[29].

Sample sizes and outcome measures with their respective standard deviation (SD) were inputted into the meta-analysis to calculate an effect size (ES) using Hedges *g* statistic with 95% confidence interval (CI). Values were interpreted as <0.2 (trivial); 0.2-0.59 (small); 0.6-1.19 (moderate); and ≥1.2

(large). The level of statistical heterogeneity between studies was quantified using the I^2 statistic and corresponding p-value. Results are displayed as mean ± SD, unless stated.

3. Results

The supplementary table provides a summary of the 21 studies that met the inclusion criteria. A total of 232 participants were included (mean age range: 19-30 years). Four studies used sedentary participants[30–33], six studies used recreational or active participants[34–39], five studies used moderately-trained participants[40–44], three investigations used well-trained or Collegiate athletes[45–47], and two studies used highly-trained or elite performers[41,48]. Two studies did not mention the training status of their participants[49,50].

Fig. 2 provides an overview of the results from the NHLBI-QAT scores to highlight which features of study design present the highest risk of bias. Scores for studies ranged from 6 to 13 points out of total of 15 points (see supplementary table), with a mean score of 8.8 ± 1.9 points. The physiological method used to identify and verify menstrual cycle phases varied considerably. Fifteen studies attempted to identify menstrual cycle phases/events prior to data collection using an estimate of basal body temperature[30,32,36,38,39,43,49,50] and/or LH concentration in the urine[30–32,34,35,37,42,46], with the other six studies using only self-report strategies[33,41,44,45,47,48]. Twelve investigations measured oestrogen and progesterone concentrations prior to each trial in the blood[32–35,37,38,42,43,47,50], saliva[45] or urine[46], and a further three studies measured only progesterone in the blood[36,44,48]. One study assessed only salivary testosterone concentrations[41], and five investigations did not verify differences between measurement time points with hormone measurements[30,31,39,40,49]. The validity and reliability of both the independent variables (hormones, item #9) and the dependent variables (strength measures, item #11) were reported in less than half of the studies. One study used a single-blind design[34], and all but two studies[41,42] collected data over the course of a single menstrual cycle. Many studies had a low number of participants (mean: n=11) and only four provided a sample size power analysis[32,34,35,43]. Eleven of the 21 included studies conducted trials in a random order[32,33,49,36,38–41,43–45], and ten studies were deemed to have adequately controlled for confounding variables[30,32,36,39–41,43,44,47,48].

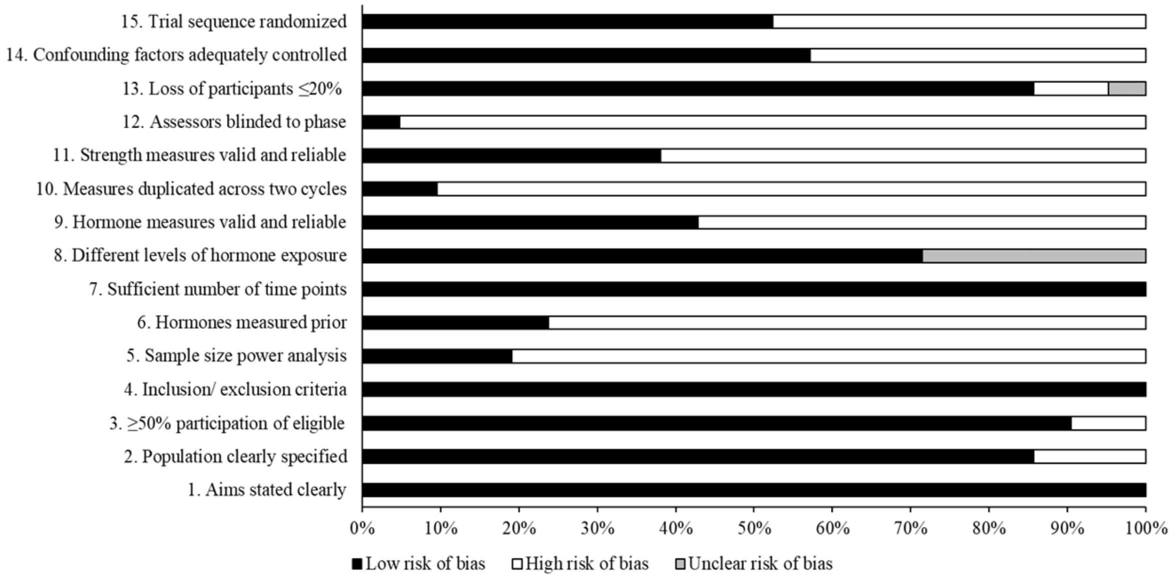

Fig. 2 Summary of assessment of quality results using the National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, to highlight areas where a high risk of bias exists.

The results of the random-effects meta-analyses are summarized in Table 1. Heterogeneity for each variable and sub-group was very small ($p \geq 0.83$, $I^2=0\%$). A MVC task was used in eleven studies[30,31,50,32,35,37–40,42,49] and all were entered in the meta-analysis ($n=98$). Results showed non-significant and trivial differences ($p \geq 0.93$, ES≤0.01) in each of the three comparisons, with the uncertainty around effect size estimates extending to a small effect without clear direction (supplementary table). Three investigations observed significantly higher ($p<0.05$) MVC measures around ovulation compared to other menstrual cycle phases[30,37,39].

Isokinetic peak torque was assessed in seven studies[30,35,42,43,45,46,50] (*n*=139), with all but one[43] eligible for various meta-analytical comparisons between phases. Every study used knee extension dynamometry at angular velocities of 30 $^{\circ}.\mathrm{sec}^{-1}$ [43], 60 $^{\circ}.\mathrm{sec}^{-1}$ [30,45,50], 120 $^{\circ}.\mathrm{sec}^{-1}$ [35,42,45,46], 180 $^{\circ}.\mathrm{sec}^{-1}$ [30,45] and 240 $^{\circ}.\mathrm{sec}^{-1}$ [45,50]. Five of the seven studies also evaluated IPT in the knee flexors at the same angular velocities used to assess the knee extensors[30,43,45,46,50]. Taken together, results show that differences between menstrual cycle phases were non-significant and trivial for measures of IPT ($p \geq 0.26$, ES≤0.08). Sub-category analysis for IPT in the knee flexors revealed small differences between the early-follicular and ovulatory phases in favour of the early-follicular phase ($p=0.34$, ES=-0.35, 95% CI: -1.07 to 0.37, *n*=15). Three of the seven studies[30,35,45] observed significantly lower ($p<0.05$) values around menses compared to other times of the cycle, and Bambaeichi et al.[30] noted significantly higher scores around ovulation compared to menses, mid-follicular and luteal phases. One paper[42] reported a difference that was close to the threshold of significance ($p=0.06$) in favour of the luteal phase compared to menses. The magnitude of the differences observed in these studies was trivial or small (ES≤0.49).

A test of explosive strength capability was utilized in ten studies (*n*=96), with measures categorized as: a maximal vertical or horizontal jumping task[35,36,42,47,48], peak power output on a cycle ergometer[33,36,41,44], and single joint isometric rate of force development or time to peak force[34,38]. Only one study was not entered into the meta-analysis[44] as the time points used did not fall within the pre-determined phases identified for comparison. Trivial differences between phases were noted for each comparison (Table 1, $p \geq 0.74$, ES≤0.06). The uncertainty of this estimate, reflected in the 95% CI, shows no clear direction to the differences for any phase comparisons. All ten individual studies reported non-significant differences ($p>0.05$) between time points with magnitudes considered trivial or small (ES≤0.44).

Table 1. Results of random effects meta-analysis on differences between strength-related measures in menstrual cycle phases. Early-follicular phase (≤7 days from menstruation onset), ovulatory phase (±2 days from ovulation), mid-luteal phase (21±2 days from menstruation onset or 7±2 days following ovulation).

Variables and sub-categories	Early-follicular *vs* ovulatory			Early-follicular *vs* mid-luteal			Ovulatory *vs* mid-luteal		
	n	Hedges *g* (95% CI)	*p*-value	*n*	Hedges *g* (95% CI)	*p*-value	*n*	Hedges *g* (95% CI)	*p*-value
MVC	**98**	**0.04 (-0.24 to 0.32)**	**0.80**	**98**	**-0.01 (-0.29 to 0.27)**	**0.93**	**82**	**0.01 (-0.30 to 0.31)**	**0.97**
Isok peak torque	**85**	**-0.17 (-0.47 to 0.14)**	**0.28**	**139**	**0.03 (-0.21 to 0.26)**	**0.82**	**85**	**0.04 (-0.26 to 0.34)**	**0.78**
Knee extension	56	-0.06 (-0.43 to 0.31)	0.76	83	0.03 (-0.27 to 0.34)	0.84	48	0.09 (-0.31 to 0.49)	0.66
Knee flexion	29	-0.38 (-0.90 to 0.14)	0.16	56	0.02 (-0.37 to 0.41)	0.92	37	-0.02 (-0.48 to 0.44)	0.94
Explosive strength	**79**	**0.09 (-0.22 to 0.40)**	**0.58**	**90**	**0.02 (-0.28 to 0.31)**	**0.91**	**56**	**-0.06 (-0.43 to 0.31)**	**0.76**
Jumping	19	-0.04 (-0.67 to 0.60)	0.91	46	-0.04 (-0.45 to 0.37)	0.86	19	-0.03 (-0.67 to 0.60)	0.92
Cycle erg PPO	37	0.13 (-0.33 to 0.58)	0.58	44	0.07 (-0.35 to 0.49)	0.74	37	-0.07 (-0.53 to 0.38)	0.76
RFD	23	0.12 (-0.45 to 0.70)	0.67	-	-	-	-	-	-

CI = confidence interval, MVC = maximum voluntary contraction, Isok = isokinetic, erg = ergometer, PPO = peak power output, RFD = rate of force development

4. Discussion

The purpose of this systematic review was to collate and evaluate the literature that has investigated the effect of the menstrual cycle on strength-related measures in eumenorrheic women. Based upon the results of 21 studies that met the criteria for inclusion, differences between phases within the menstrual cycle for measures of MVC, IPT and explosive strength are regarded as trivial to small. The assessment of study quality revealed that a number of important features of study design were consistently overlooked. Small sample sizes, absence of hormonal measures to identify and verify menstrual cycle phase, lack of assessor blinding, poor control of confounding factors, and non-randomization of trials is likely to explain the inconsistent findings in this area. Future investigations should endeavour to address the important methodological issues highlighted here (Fig. 2).

Theoretically, maximal physical performance during the menstrual cycle is at its lowest during menstruation and/or the luteal phase[3]. The results of the meta-analyses conducted in this review largely refute this suggestion. For the majority of studies that were entered into the meta-analyses, results displayed a high level of similarity between menstrual cycle phases, as demonstrated by narrow 95% CIs, and low heterogeneity values ($p \geq 0.83$, $I^2=0\%$). For the phases of the menstrual cycle that were compared, fluctuations in hormones have, at most, a small effect (ES≤0.35) upon strength performance. Although a similar pattern of results was observed across the investigations in this review, a number of studies did note significant ($p<0.05$) and/or moderate differences (ES≥0.6) between phases[30,35,37,39,45]. The reasons for these discrepancies are likely to be multi-factorial, thus it is important to discuss these anomalies in the context of other findings and the results of the assessment of study quality.

The inclusion of reliability statistics for dependent variables when reporting study outcomes is recommended[51], however these were only provided in eight studies[32,34–36,39,42,43,50]. Reliability was generally reported as being high in most studies (intra-class correlation coefficient >0.9)[34–36,42] and the coefficient of variation has been reported at <6% for the tasks used in the studies[43,52,53]. It is therefore likely that the trivial-small differences (ES<0.4) observed in strength values between phases in many studies can be explained by random error. Furthermore, a number of the statistically significant differences identified in several studies[30,35,45] were trivial or small in magnitude (<5%, ES<0.3), and fell within the 95% CI for the phases compared. Additionally, six studies did not report with sufficient accuracy the reliability of the assays used to evaluate different hormone concentrations[37,38,44,46,48,50], therefore it is unknown the extent to which the differences observed in hormones in these studies can be attributed to measurement error.

The number of participants used in many studies included in this review was small (mean: n=11). Several studies provided statistical verification that the sample size was sufficiently powered to detect meaningful changes[32,34,35,43], however this calculation was not always based upon the strength variable measured[34]. Other studies did not include a power calculation; therefore, it is likely that for a number of the studies included in this review, sample sizes may not have been adequate to detect differences in strength values.

Accurate determination of the days within the menstrual cycle to test each participant is a critical aspect of research in this area[3]. Inconsistencies between studies may therefore, in part, be attributed to the methods used to determine the most appropriate day to test strength-status within these phases, and the actual day selected. All included studies estimated hormonal status by counting days from self-reported menstruation onset. Many studies employed urinary ovulation tests to detect a surge in LH[30–32,34,35,37,42,46], and/or monitoring of basal body temperature[30,32,36,38–40,43,49,50], in the cycle prior to data collection to identify the idiosyncrasies in hormone fluctuations that were subsequently used to assist with the scheduling of tests for each participant. This may, in part, ameliorate the limitations associated with testing only within a single cycle. However, it is well-established that substantial variability exists in menstrual cycle lengths and timing of phases in eumenorrheic women[7], thus targeting specific days beyond menses onset and/or ovulation, may not capture the phases with sufficient accuracy[54]. Although false-positive results are rare with urinary LH tests, these rely on participants conducting the test correctly and interpreting results accurately, which may not always be the case[54]. In studies that did not rely upon urinary testing or tracking of basal body temperature to estimate ovulation[33,41,44,45,47,48], the likelihood of including participants in the data collection with an anovulatory cycle is increased.

Most investigations also assessed hormone concentrations on the day of testing using a blood[32,33,47,48,50,34–38,42–44], saliva[41,45] or urine sample[46] to verify that differences existed between time-points. Nevertheless, it is problematic to determine from a single measurement whether the hormone was rising, peaking or falling, particularly during the ovulatory phase, where the rise in oestrogen concentration is short-lived. Five studies did not ascertain hormonal concentrations alongside strength testing trials[30,31,39,40,49]. Consequently, some uncertainty exists over whether the hormonal milieu differed between measurements, despite proxy physiological measures being used to identify appropriate time-points. Additionally three investigations, that did not aim to measure strength during the ovulatory phase, measured only progesterone[36,44,48], thus the role of oestrogen in explaining the patterns of results observed in these studies cannot be discerned. It is also noteworthy that three of the five studies[30,39,45] that observed significant differences between phases included a greater number of time points (four or five), compared to the smaller number of time points (two or three) measured in 14 of the studies observing no significant differences. A greater number of trials across the menstrual cycle may therefore have captured subtle differences between important phases, which studies with fewer measurement points may have missed.

Research in this area is potentially confounded by high levels of inter-individual variability in hormonal concentrations across the menstrual cycle[7]. This is illustrated in the study by Cook and co-workers[41], which reported significantly higher changes in testosterone values across the menstrual cycle in elite female athletes compared to a group of non-elite but active females. Indeed, training alters the level of circulating androgens[55] and ovarian hormones[56] during the menstrual cycle, thus strength status through the menstrual cycle in well-trained females may differ from that of untrained females. Training status was not used as a moderating variable in the meta-analyses due to the lack of detail provided on strength-training history for participants in most studies. Highly- or well-trained athletes were used in a number of investigations[41,45–48], but it was often unclear how much strength-training experience participants possessed.

Despite several studies recognizing the issue of individuality[32,47,50], there are currently no investigations that have attempted to objectively quantify the degree to which observed differences in strength between menstrual cycle phases, are individual in nature. Within the context of personalized medicine and exercise programming, a study of this nature would be valuable. A robust methodological and statistical approach to addressing this important issue would involve repeated measurements in a randomized order over two menstrual cycles[57]. Although two existing studies duplicated measures over two menstrual cycles[41,42], individual differences were not quantified.

The nature of the strength task and muscle groups tested might also be factors that explain the ambiguity in results, however the findings from this meta-analysis refute this (Table 1). The IPT knee flexor sub-category produced the greatest ES for the comparison between early-follicular phase and ovulatory phase, with the 95% CI extending to a moderate difference in the direction of the early-follicular phase (p=0.34, ES=-0.35, 95% CI: -1.07 to 0.37). However, it is important to note that this sub-analysis comprised only one study (n=15), therefore more data are required to provide a firmer conclusion.

Potential confounding factors were adequately controlled in ten of the 21 studies (Fig. 2). In particular, standardizing the time of day that trials are conducted is important, because ovarian hormones are known to have a diurnal variation, with progesterone[58], estradiol and testosterone concentrations[59] highest in the morning, and gradually decreasing throughout the day. Around half of the studies conducted tests in a fully randomized or quasi-randomized sequence[32,33,49,36,38–41,43–45]. A non-randomized order was applied in the other studies, which typically involved sequencing tests chronologically, starting from the onset of menses (day 0). This approach to study organization brings ‘design bias’, which is inconsistent with the principle of equipoise, and raises the possibility that a degree of systematic bias exists in the results of studies. In particular, for non-strength trained females who were unfamiliar with a strength task, a learning effect is likely to occur, which benefits the trials taking place later in the study[51]. Appropriate randomization of trials also facilitates no *a priori* knowledge amongst the researchers of a participants menstrual cycle phase. Knowledge of the participants hormonal status at the time of a test generates a cognitive bias that may influence behaviour and creates self-deception[60]. Although fully blinding the participant to their menstrual cycle phase would be impossible, the absence of a single-blind design may also have contributed to the conflicting findings reported in this review.

There are several limitations associated with this review that should be recognized. We addressed variations in strength status in eumenorrheic females only, however it should be recognized that a high number (~30-50%) of active females use hormonal contraceptives[61], which contain exogenous hormones that may influence physical performance and adaptation to training[62]. A review that captures this group of females would potentially be useful but is beyond the scope of a single article. In addition to the numerous confounding factors that influence the results in this area of research, there was also a high level of inconsistency in the number and choice of time points used to compare strength, making inter-study comparison problematic. Even within the phases used for comparison in the meta-analysis, timings of measurements varied across studies, which within the context of rapidly shifting concentrations of hormones, is likely to have influenced the results. Six studies only took measurements at two time points[32,34,40,43,44,47] and three of these studies scored the highest in the quality assessment (≥10 out of 15 points)[32,34,43]. It is therefore intriguing what additional insight these higher quality studies could have provided had more phases been selected for testing. Finally, at the eligibility stage of the systematic review, 40 studies were excluded. Although there were validity-related issues within these studies that precluded their inclusion in the review, there may have been important results contained in some studies that were worthy of consideration in this analysis.

5. Conclusion

Strength-related characteristics appear to remain invariable between menstrual cycle phases, despite fluctuations in concentrations of circulating levels of oestrogen and progesterone. Practically, these findings suggest that eumenorrheic females participating in sports or activities that rely heavily on maximal or explosive strength, are not disadvantaged by their menstrual cycle phase on any given day. Research in this area is immensely challenging due to problems associated with accurate identification of cycle phases in each participant and control of other confounding factors that may also cause variations in strength performance. Consequently, many of the studies in this area are limited by small sample sizes and methodological issues, therefore future experiments should endeavour to address these shortcomings.

6. Practical Implications

- Fluctuations in female sex hormones over the course of the menstrual cycle may explain variations in physical performance
- Strength-related qualities are minimally affected by changes in sex hormones over the course of the menstrual cycle
- Regularly menstruating females who participate in strength-related exercise activities or strength-dominant sports do not need to adjust for menstrual cycle phase to maximize their performance

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Supplementary Table. Participant characteristics, main study design features and results of studies that have investigated variability in strength-related measures through the menstrual cycle.

Authors; country of origin	*n*	Age (y)	Training status	Phase identification / hormone verification	Measures	Timing of measurements	Main findings	Quality score (0-15)
Studies showing significant differences								
Bambaeichi et al. (2004); U.K.	8	30 ± 5	Sedentary	Self-report menses; oral temp; urine / -	Knee ext and flex isok (60, 180°.s^{-1}): peak torque Knee ext and flex: MVC (at 60°)	Menses+1-4d, mid-FP (+7-9d), OP, mid-LP (+19-21d), late-LP (+25-27d); Measures taken 06:00h and 18:00h.	Time of day effect: NSD, ES=0.20 Knee ext torque 180°.s^{-1}: OP sig higher ($p<0.05$) than menses (ES=0.22, 4.7%), mid-LP sig higher ($p<0.05$) than menses (ES=0.25, 4.8%) & mid-FP (ES=0.34, 6.2%) Knee flex torque 60°.s^{-1}: OP sig higher ($p<0.05$) than mid-FP (ES=0.53, 9.1%) & mid-LP (ES=0.49, 9.4%) Knee flex MVC: OP sig higher ($p<0.05$) than mid-FP (ES=0.27, 6.5%) & mid-LP (ES=0.39, 10.2%) Knee ext torque 60°.s^{-1}, knee flex torque 180°.s^{-1}, knee ext MVC: NSD, ES<0.2	7
Ekenros et al. (2013); Sweden	9	27 ± 5	Recreational (2 sessions per week)	Self-report menses; urine / blood	Knee ext isok (120°.s^{-1}): peak torque Handgrip: MVC 1-leg hop distance	Menses+2-4d, OP (within 48h of peak LH), LP (ovulation+7-8d)	Knee ext torque: LP sig higher ($p=0.02$) than menses (ES=0.22, 4.3%), NSD (ES<0.2) between other phases and MVC and hop	10
Gordon et al. (2013); U.K.	11	21 ± 1	Well-trained	Self-report menses / saliva	Knee ext and flex isok: 60, 120, 180, 240°.s^{-1}	Menses+1-3d, mid-FP (+9-11d), mid-LP (+19-20d), pre-menses (+27-28d)	Knee ext 60, 180, 240°.s^{-1}: NSD, ES=0.15-0.28 between phases 120°.s^{-1}: mid-LP sig higher ($p=0.02$) than menses (ES=0.15, 2.9%) Knee flex 180, 240°.s^{-1}: NSD, ES=0.13-0.33 between phases	9

							60º.s^{-1}: pre-menses sig higher (p=0.02) than menses (ES=0.47, 14.2%) 120º.s^{-1}: pre-menses sig higher (p=0.02) than menses (ES=0.37, 8.9%)	
Iwamoto et al. (2002); Japan	6	22 ± 4	Active	Self-report menses; urine / blood	Elbow flexion (90º): MVC	Menses (+1-3d), OP (+11-13d), LP (+21-23d)	MVC: OP sig higher than menses (p<0.05, ES=0.46, 12.7%) and LP (p<0.01, ES=0.72, 21.1%)	7
Tenan et al. (2016); U.S.A.	9	25 ± 5	Recreational	Self-report menses; oral temp / -	Knee ext (90º): MVC	Early-FP, late-FP, OP, mid-LP, late-LP (individualized)	MVC: sig diff across cycles (p<0.01). Mid-LP sig lower than late-FP (p=0.01, ES=0.58, 16.9%), OP (p=0.02, ES=0.55, 16.9%), late-LP (p<0.01, ES=0.65, 18.5%) Early-FP v mid-LP: NSD (ES=0.44, 13.9%), favour early-FP	10
Studies showing non-significant differences								
Bell et al. (2011); U.S.A.	15	20 ± 2	Physically active	Self-report menses; urine / blood	Prone knee flex 30º: RFD, time to peak force$_{50\%}$	Menses+3-5d Ovulation+2-4d	RFD and peak force$_{50\%}$: NSD, ES<0.2	11
Birch and Reilly (1999); U.K.	17	18-32	Not reported	Self-report menses; oral temp / -	Rack pull: MVC @knee and waist height	Menses, mid-FP, within 48h of ovulation, mid-LP, pre-menses	MVC @knee: NSD, OP vs mid-LP: ES=0.22 (favour LP), other comparisons ES<0.2	6
Birch and Reilly (2002); U.K.	10	24 ± 3	Moderately active	Self-report menses; oral temp / -	Rack pull: MVC @knee height	Mid-FP, mid-LP Measures taken 06:00h and 18:00h	MVC: phase x time of day interaction (p<0.05) 06:00: NSD, ES=0.20 (favour mid-FP) 18:00: NSD, ES=0.16 (favour mid-LP)	8
Cook et al. (2018); U.K.	22	21 ± 1	6 elite athletes, 16 non-elite; multi-sport; >2y RT	Self-report menses / saliva	Static cycle: peak power	Menses+7d, +14d, +21d	Peak power: NSD 7d v 14d: ES=0.07 14d v 21d: ES=0.09 7d v 21d: ES=0.01	9

de Jonge et al. (2001); Australia	15	30 ± 8	Not reported	Self-report menses; oral temp / blood	Knee ext: MVC and Knee ext and flex isok (60, 240°.s^{-1}): peak torque Handgrip: MVC	Menses (+1-3d), late-FP (pre-ovulation), LP	Handgrip and knee ext MVC, peak torque 60°.s^{-1}, 240°.s^{-1}: NSD, ES<0.2 Knee flex 60°.s^{-1}: NSD, menses v late-FP: ES=0.41 (favour menses) Knee flex 240°.s^{-1}: NSD, menses v late-FP: ES=0.29 (favour menses)	6
Drake et al. (2003); U.S.A.	7	24 ± 1	Sedentary	Self-report menses; urine / -	Knee ext 45°: MVC	Menses(+1-3d), early-FP (+4-7d), late-FP (+9-11d), OP, early-LP (ovulation+5d)	MVC: NSD between any phase Early-FP v early-LP: ES=0.25 (favour early-FP) Early-FP v menses: ES=0.22 (favour early-FP) Other comparisons ES<0.2	6
Elliott et al. (2003); U.K.	7	25 ± 5	Sedentary*	Self-report menses; urine and oral temp / blood	First dorsal interosseous: MVC	Early FP (menses+2d), mid-LP (+21d)	MVC: NSD (p=0.1), ES=0.43, 9.2% (favour mid-LP)	13
Fridén et al. (2003); Sweden	10	25 ± 4	Moderately active	Self-report menses; urine / blood	Handgrip: MVC Knee ext isok (120°.s^{-1}): peak torque 1-leg hop distance	Early-FP (menses+3-5d), OP (LH surge), mid-LP (ovulation+7d); 2 cycles	MVC: NSD between phases, OP v LP: ES=0.27 (favour LP) Peak torque: p=0.06 between phases, FP v LP: ES=0.36 (favour LP) 1-leg hop: NSD, all ES=0.07	10
Giacomoni et al. (2000); France	7	23 ± 3	Physically active	Self-report menses; rectal temp / blood	Cycle ergometer: peak power, optimal force Multi-jumps: peak power Squat jump height	Menses (+1-4d), mid-FP (+7-9d), mid-LP (+19-21d)	Cycle power: NSD between phases, menses v mid-FP: ES=0.24 (favour mid-FP) Multi-jump: NSD between phases, ES<0.2 Squat jump: NSD (p=0.48) between phases, menses v mid-FP: ES=0.31 (favour mid-FP)	11

Hertel et al. (2006); U.S.A.	14	19 ± 1	Collegiate athletes (soccer or cheer-leading)	Self-report menses; urine / urine	Knee ext and flex isok (120°.s^{-1}): peak torque	Mid-FP (menses+4-7d), OP (ovulation±2d), mid-LP (ovulation+7-10d)	Knee ext: NSD, mid-FP v OP: ES=0.40 mid-FP v mid-LP: ES=0.31 Knee flex: NSD, mid-FP v OP: ES=0.36 mid-FP v mid-LP: ES=0.41	8
Julian et al. (2017); Germany	9	19 ± 4	Sub-elite soccer players	Self-report menses / blood	CMJ	Mid-FP (menses+5-7d), mid-LP (+21-22d)	NSD; ES=0.17	8
Kubo et al. (2009); Japan	8	23 ± 1	Sedentary or mild-moderately active	Self-report menses; oral temp / blood	Knee ext and plantar flex: MVC, time to peak torque	Menses (+1-3d), OP (ovulation±2d), LP (ovulation+7-10d)	Knee ext and plantar flex MVC: NSD, ES<0.2 Knee ext time to peak: NSD, OP v LP: ES=0.35 (favour LP) Plantar flex time to peak: NSD, menses v LP: ES=0.38 (favour menses)	9
Lebrun et al. (1995); Canada	16	28 ± 4	Aerobically trained athletes (multi-sport)	Self-report menses; oral temp / blood	Knee ext and flex (30°.s^{-1}): peak torque (R and L)	Early FP (menses+3-8d), mid-LP (ovulation+4-9d)	Knee ext and flex (R and L): NSD Flex R: ES=0.71, Flex L: ES=0.22 (both favour mid-LP)	11
Middleton & Wenger (2006); Canada	6	25 ± 3	Moderately active	Self-report menses / blood	Cycle ergometer 10x6s sprint (30s rec): peak power	FP (menses+6-10d), LP (+20-24d)	Peak power: NSD, ES=0.17	9
Okudan et al. (2005); Turkey	15	19-23	Sedentary	Self-report menses / blood	Cycle ergometer Wingate test: peak power	Menses+7d, +14d, +21d	NSD 7d v 14d: ES=0.22 (favour 14d)	8
Tounsi et al. (2018); Tunisia	11	21 ± 3	High-level soccer	Self-report menses / blood	5-step bounds	Menses (+2-4d), mid-FP (+7-9d), LP (+20-22d). Each (am) and (pm)	Cycle phase (am): NSD, Menses v LP: ES=0.44 (favour menses); mid-FP v LP: ES=0.33 (favour mid-FP) (pm): NSD, ES<0.15	8

temp = temperature, d = days after the beginning of menstrual bleeding, h = hours, ext = extension, flex = flexion, isok = isokinetic, NSD = no significant difference, MVC = maximal voluntary contraction, FP = follicular phase, OP = ovulatory phase, LP = luteal phase, ES = effect size (Hedges *g*), sig = significant, RFD = rate of force development, RT = resistance training, LH = luteinizing hormone, reps = repetitions, CMJ = counter-movement jump, R = right side, L = left side, rec = recovery, * obtained from Elliott et al. (2005)