

TITLE

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

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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 eumenorrhoeic 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 eumenorrhic women, a menstrual cycle typically lasts 28 days, but can vary considerably¹. 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 cycle², 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 debated²⁻⁵.

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 females⁶. 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 eumenorrhic females, the concentration of hormones and timing of cycle events, displays large inter-individual variability⁷, 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 processes⁸ and can influence central nervous system function⁹. Dehydroepiandrosterone (DHEA), the precursor to oestrogen and testosterone that peaks prior to ovulation, produces a net excitatory effect via its action on several neurotransmitter receptors¹⁰. Specifically, oestrogen is known to bind to receptor sites that attenuate the release of γ -aminobutyric acid¹¹, 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 system¹². In contrast, progesterone is known to exert a net inhibitory effect on the nervous system via enhancement of γ -aminobutyric acid action¹³. 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 drive¹⁴, and enhanced calcium kinetics in the muscle cell¹⁵. It is also possible that the thermogenic action of progesterone, which causes an increase in core body and skin temperature during the luteal phase¹⁶, positively influences nerve conduction velocity¹⁷ and antagonistic co-contraction¹⁸, 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 constraints¹⁹. Increases in strength are associated with improvements in important markers of metabolic health²⁰, everyday tasks²¹, a lower risk of injury²², and enhanced athletic performance²³. Strength training is also important in counteracting conditions associated with muscle weakness, such as sarcopenia, musculoskeletal disorders, and prolonged immobilization²⁴. Strength training also provides beneficial changes to the risk factors associated with anterior-cruciate ligament injury, which has a high incidence in female athletes injury²⁵.

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 Group²⁷ 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.

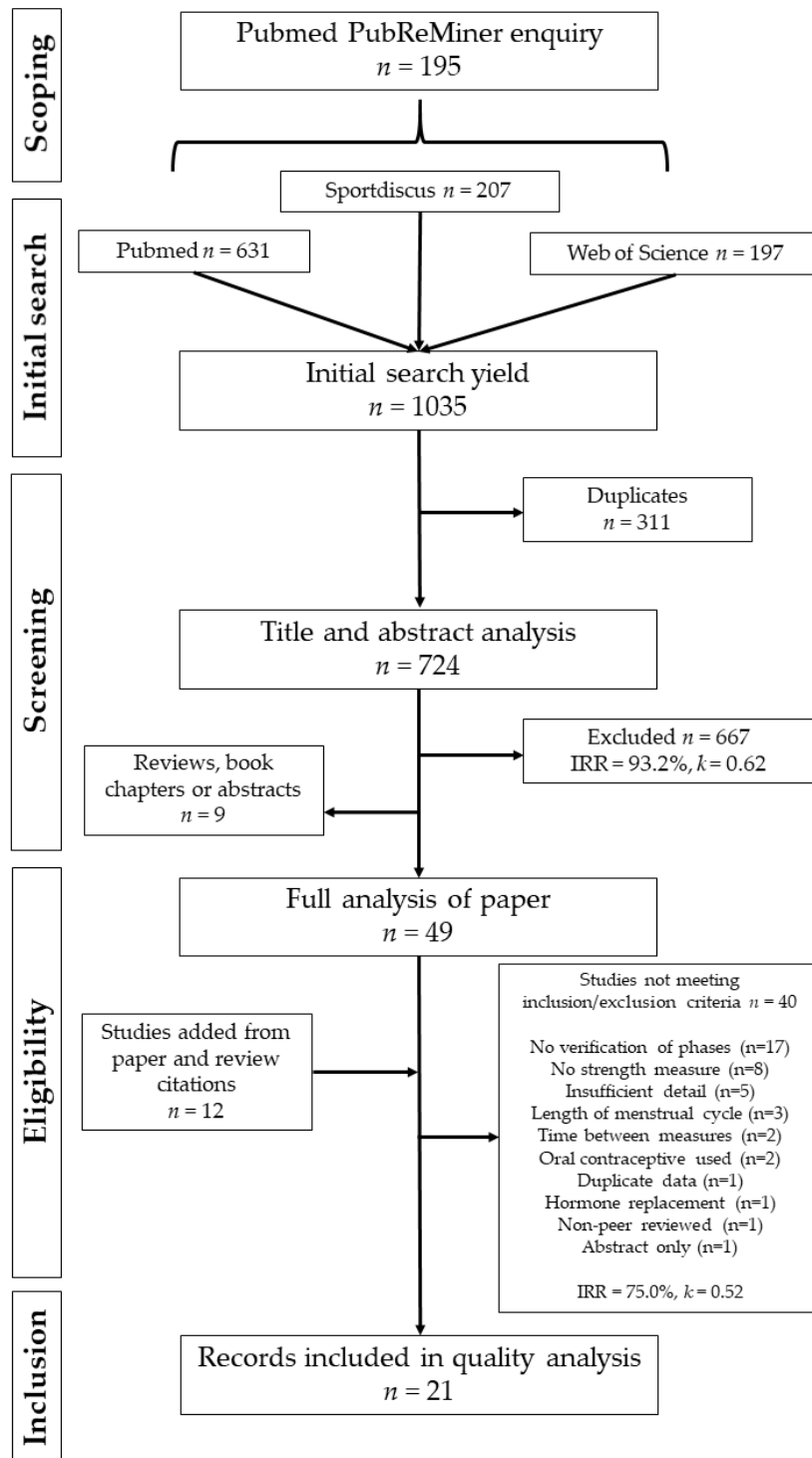


Fig. 1 Search, screening and selection process for suitable studies. IRR = inter-rater reliability, $k =$ Cohen's kappa statistic

The initial search returned 1035 papers, which were imported into a published software for systematic reviews²⁸. 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 comprises 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 phase⁷. 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 dependence²⁹.

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 \pm 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 participants³⁰⁻³³, six studies used recreational or active participants³⁴⁻³⁹, five studies used moderately-trained participants⁴⁰⁻⁴⁴, three investigations used well-trained or Collegiate athletes⁴⁵⁻⁴⁷, 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}, saliva⁴⁵ or urine⁴⁶, and a further three studies measured only progesterone in the blood^{36,44,48}. One study assessed only salivary testosterone concentrations⁴¹, 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 design³⁴, 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}.

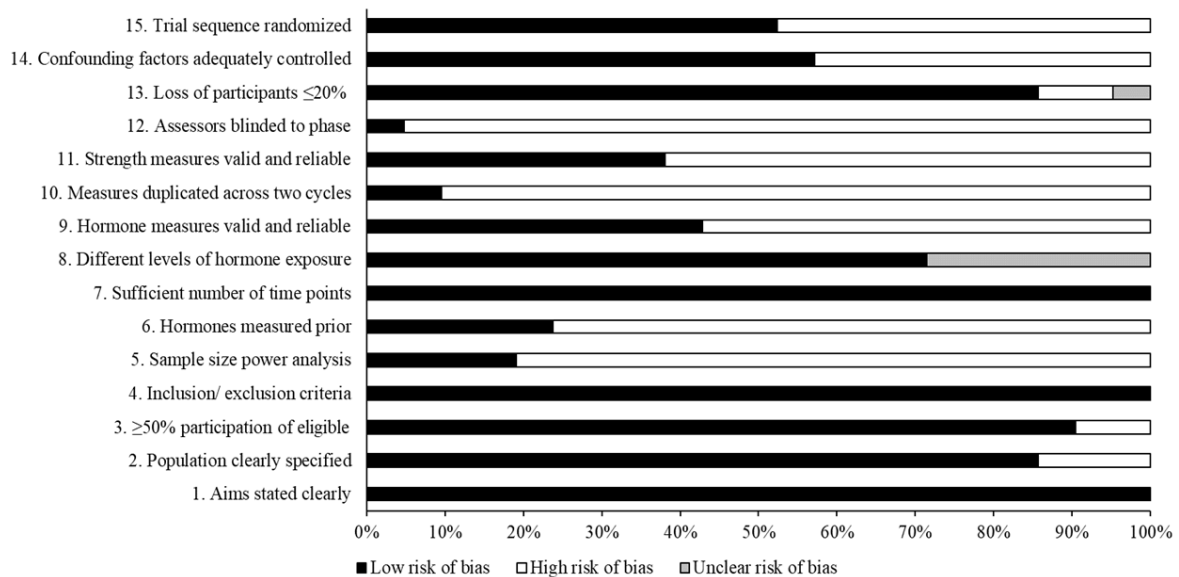


Fig. 2 Summary of assessment of quality results using the National Heart, Lung, and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies, to highlight areas where a high risk of bias exists.

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 ($p \geq 0.93$, $ES \leq 0.01$) 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 one⁴³ eligible for various meta-analytical comparisons between phases. Every study used knee extension dynamometry at angular velocities of $30\text{ }^{\circ}\cdot\text{sec}^{-1}$ ⁴³, $60\text{ }^{\circ}\cdot\text{sec}^{-1}$ ^{30,45,50}, $120\text{ }^{\circ}\cdot\text{sec}^{-1}$ ^{35,42,45,46}, $180\text{ }^{\circ}\cdot\text{sec}^{-1}$ ^{30,45} and $240\text{ }^{\circ}\cdot\text{sec}^{-1}$ ^{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 ($p\geq 0.26$, $ES\leq 0.08$). 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 Bambaiechi et al.³⁰ noted significantly higher scores around ovulation compared to menses, mid-follicular and luteal phases. One paper⁴² 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 ($ES\leq 0.49$).

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-analysis⁴⁴ 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, $p\geq 0.74$, $ES\leq 0.06$). 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 ($ES\leq 0.44$).

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

3

| Variables and sub-categories | Early-follicular vs ovulatory | | | Early-follicular vs mid-luteal | | | Ovulatory vs mid-luteal | | |
|------------------------------|-------------------------------|------------------------------|-----------------|--------------------------------|------------------------------|-----------------|-------------------------|------------------------------|-----------------|
| | <i>n</i> | Hedges <i>g</i> (95% CI) | <i>p</i> -value | <i>n</i> | Hedges <i>g</i> (95% CI) | <i>p</i> -value | <i>n</i> | Hedges <i>g</i> (95% CI) | <i>p</i> -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 | - | - | - | - | - | - |

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

5 development

6 4. Discussion

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

16 Theoretically, maximal physical performance during the menstrual cycle is at its lowest during
17 menstruation and/or the luteal phase³. The results of the meta-analyses conducted in this review
18 largely refute this suggestion. For the majority of studies that were entered into the meta-analyses,
19 results displayed a high level of similarity between menstrual cycle phases, as demonstrated by
20 narrow 95% CIs, and low heterogeneity values ($p \geq 0.83$, $I^2 = 0\%$). For the phases of the menstrual cycle
21 that were compared, fluctuations in hormones have, at most, a small effect ($ES \leq 0.35$) upon strength
22 performance. Although a similar pattern of results was observed across the investigations in this
23 review, a number of studies did note significant ($p < 0.05$) and/or moderate differences ($ES \geq 0.6$)
24 between phases^{30,35,37,39,45}. The reasons for these discrepancies are likely to be multi-factorial, thus it is
25 important to discuss these anomalies in the context of other findings and the results of the assessment
26 of study quality.

27 The inclusion of reliability statistics for dependent variables when reporting study outcomes is
28 recommended⁵¹, however these were only provided in eight studies^{32,34-36,39,42,43,50}. Reliability was
29 generally reported as being high in most studies (intra-class correlation coefficient > 0.9)^{34-36,42} and the
30 coefficient of variation has been reported at $< 6\%$ for the tasks used in the studies^{43,52,53}. It is therefore
31 likely that the trivial-small differences ($ES < 0.4$) observed in strength values between phases in many

32 studies can be explained by random error. Furthermore, a number of the statistically significant
33 differences identified in several studies^{30,35,45} were trivial or small in magnitude (<5%, ES<0.3), and
34 fell within the 95% CI for the phases compared. Additionally, six studies did not report with sufficient
35 accuracy the reliability of the assays used to evaluate different hormone concentrations^{37,38,44,46,48,50},
36 therefore it is unknown the extent to which the differences observed in hormones in these studies can
37 be attributed to measurement error.

38 The number of participants used in many studies included in this review was small (mean: $n=11$).
39 Several studies provided statistical verification that the sample size was sufficiently powered to detect
40 meaningful changes^{32,34,35,43}, however this calculation was not always based upon the strength variable
41 measured³⁴. Other studies did not include a power calculation; therefore, it is likely that for a number
42 of the studies included in this review, sample sizes may not have been adequate to detect differences
43 in strength values.

44 Accurate determination of the days within the menstrual cycle to test each participant is a critical
45 aspect of research in this area³. Inconsistencies between studies may therefore, in part, be attributed to
46 the methods used to determine the most appropriate day to test strength-status within these phases,
47 and the actual day selected. All included studies estimated hormonal status by counting days from
48 self-reported menstruation onset. Many studies employed urinary ovulation tests to detect a surge in
49 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
50 data collection to identify the idiosyncrasies in hormone fluctuations that were subsequently used to
51 assist with the scheduling of tests for each participant. This may, in part, ameliorate the limitations
52 associated with testing only within a single cycle. However, it is well-established that substantial
53 variability exists in menstrual cycle lengths and timing of phases in eumenorrheic women⁷, thus
54 targeting specific days beyond menses onset and/or ovulation, may not capture the phases with
55 sufficient accuracy⁵⁴. Although false-positive results are rare with urinary LH tests, these rely on
56 participants conducting the test correctly and interpreting results accurately, which may not always be
57 the case⁵⁴. In studies that did not rely upon urinary testing or tracking of basal body temperature to

58 estimate ovulation^{33,41,44,45,47,48}, the likelihood of including participants in the data collection with an
59 anovulatory cycle is increased.

60 Most investigations also assessed hormone concentrations on the day of testing using a
61 blood^{32,33,47,48,50,34–38,42–44}, saliva^{41,45} or urine sample⁴⁶ to verify that differences existed between time-
62 points. Nevertheless, it is problematic to determine from a single measurement whether the hormone
63 was rising, peaking or falling, particularly during the ovulatory phase, where the rise in oestrogen
64 concentration is short-lived. Five studies did not ascertain hormonal concentrations alongside strength
65 testing trials^{30,31,39,40,49}. Consequently, some uncertainty exists over whether the hormonal milieu
66 differed between measurements, despite proxy physiological measures being used to identify
67 appropriate time-points. Additionally three investigations, that did not aim to measure strength during
68 the ovulatory phase, measured only progesterone^{36,44,48}, thus the role of oestrogen in explaining the
69 patterns of results observed in these studies cannot be discerned. It is also noteworthy that three of the
70 five studies^{30,39,45} that observed significant differences between phases included a greater number of
71 time points (four or five), compared to the smaller number of time points (two or three) measured in
72 14 of the studies observing no significant differences. A greater number of trials across the menstrual
73 cycle may therefore have captured subtle differences between important phases, which studies with
74 fewer measurement points may have missed.

75 Research in this area is potentially confounded by high levels of inter-individual variability in
76 hormonal concentrations across the menstrual cycle⁷. This is illustrated in the study by Cook and co-
77 workers⁴¹, which reported significantly higher changes in testosterone values across the menstrual
78 cycle in elite female athletes compared to a group of non-elite but active females. Indeed, training
79 alters the level of circulating androgens⁵⁵ and ovarian hormones⁵⁶ during the menstrual cycle, thus
80 strength status through the menstrual cycle in well-trained females may differ from that of untrained
81 females. Training status was not used as a moderating variable in the meta-analyses due to the lack of
82 detail provided on strength-training history for participants in most studies. Highly- or well-trained
83 athletes were used in a number of investigations^{41,45–48}, but it was often unclear how much strength-
84 training experience participants possessed.

85 Despite several studies recognizing the issue of individuality^{32,47,50}, there are currently no
86 investigations that have attempted to objectively quantify the degree to which observed differences in
87 strength between menstrual cycle phases, are individual in nature. Within the context of personalized
88 medicine and exercise programming, a study of this nature would be valuable. A robust
89 methodological and statistical approach to addressing this important issue would involve repeated
90 measurements in a randomized order over two menstrual cycles⁵⁷. Although two existing studies
91 duplicated measures over two menstrual cycles^{41,42}, individual differences were not quantified.

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

99 Potential confounding factors were adequately controlled in ten of the 21 studies (Fig. 2). In
100 particular, standardizing the time of day that trials are conducted is important, because ovarian
101 hormones are known to have a diurnal variation, with progesterone⁵⁸, estradiol and testosterone
102 concentrations⁵⁹ highest in the morning, and gradually decreasing throughout the day. Around half of
103 the studies conducted tests in a fully randomized or quasi-randomized sequence^{32,33,49,36,38-41,43-45}. A
104 non-randomized order was applied in the other studies, which typically involved sequencing tests
105 chronologically, starting from the onset of menses (day 0). This approach to study organization brings
106 ‘design bias’, which is inconsistent with the principle of equipoise, and raises the possibility that a
107 degree of systematic bias exists in the results of studies. In particular, for non-strength trained females
108 who were unfamiliar with a strength task, a learning effect is likely to occur, which benefits the trials
109 taking place later in the study⁵¹. Appropriate randomization of trials also facilitates *no a priori*
110 knowledge amongst the researchers of a participants menstrual cycle phase. Knowledge of the
111 participants hormonal status at the time of a test generates a cognitive bias that may influence

112 behaviour and creates self-deception⁶⁰. Although fully blinding the participant to their menstrual cycle
113 phase would be impossible, the absence of a single-blind design may also have contributed to the
114 conflicting findings reported in this review.

115 There are several limitations associated with this review that should be recognized. We addressed
116 variations in strength status in eumenorrheic females only, however it should be recognized that a
117 high number (~30-50%) of active females use hormonal contraceptives⁶¹, which contain exogenous
118 hormones that may influence physical performance and adaptation to training⁶². A review that
119 captures this group of females would potentially be useful but is beyond the scope of a single article.
120 In addition to the numerous confounding factors that influence the results in this area of research,
121 there was also a high level of inconsistency in the number and choice of time points used to compare
122 strength, making inter-study comparison problematic. Even within the phases used for comparison in
123 the meta-analysis, timings of measurements varied across studies, which within the context of rapidly
124 shifting concentrations of hormones, is likely to have influenced the results. Six studies only took
125 measurements at two time points^{32,34,40,43,44,47} and three of these studies scored the highest in the
126 quality assessment (≥ 10 out of 15 points)^{32,34,43}. It is therefore intriguing what additional insight these
127 higher quality studies could have provided had more phases been selected for testing. Finally, at the
128 eligibility stage of the systematic review, 40 studies were excluded. Although there were validity-
129 related issues within these studies that precluded their inclusion in the review, there may have been
130 important results contained in some studies that were worthy of consideration in this analysis.

131 **5. Conclusion**

132 Strength-related characteristics appear to remain invariable between menstrual cycle phases, despite
133 fluctuations in concentrations of circulating levels of oestrogen and progesterone. Practically, these
134 findings suggest that eumenorrheic females participating in sports or activities that rely heavily on
135 maximal or explosive strength, are not disadvantaged by their menstrual cycle phase on any given
136 day. Research in this area is immensely challenging due to problems associated with accurate
137 identification of cycle phases in each participant and control of other confounding factors that may

138 also cause variations in strength performance. Consequently, many of the studies in this area are
139 limited by small sample sizes and methodological issues, therefore future experiments should
140 endeavour to address these shortcomings.

141

142 **6. Practical Implications**

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

150

151

Accepted

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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) |
|--|----|---------|------------------------------------|---|--|---|--|----------------------|
| <i>Studies showing significant differences</i> | | | | | | | | |
| 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 |

| | | | | | | | | |
|---|----|--------|---|-----------------------------------|---|---|---|----|
| | | | | | | | 60°.s ⁻¹ : pre-menses sig higher (p=0.02) than menses (ES=0.47, 14.2%) 120°.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 (90°): 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 (90°): 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 |
| <i>Studies showing non-significant differences</i> | | | | | | | | |
| Bell et al. (2011); U.S.A. | 15 | 20 ± 2 | Physically active | Self-report menses; urine / blood | Prone knee flex 30°: 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)

Accepted