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The influence of the menstrual cycle and hormonal contraceptives on cardiorespiratory fitness in physically active women: A systematic review and meta-analysis

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ABSTRACT

Objective: To systematically review and summarize the existing evidence related to the influence of the menstrual cycle (MC) and hormonal contraceptive (HC) use on $\dot{V}O_{2max}$ in physically active women.

Methods: This systematic review and meta-analysis conforms to the PRISMA statement guidelines. Four (sub-)meta-analyses were performed. Two focused on longitudinal studies examining the same women several times to compare the $\dot{V}O_{2max}$ during the different menstrual phases or oral contraceptive (OC) use and withdrawal. Two meta-analyses examined if there is a difference in $\dot{V}O_{2max}$ between OC users and normally menstruating women by analyzing cross-sectional studies assigning physically active women to one of these two groups as well as intervention-based studies (cross-over studies, randomized controlled trials considering only the data of the intervention group) comparing women intra-individually with and without OCs.

Results: Nine of the included studies (107 women) evaluated the influence of the MC, five studies (69 women) the impact of OCs on $\dot{V}O_{2max}$, and six studies investigated both topics (88 women). A mean difference of $\dot{V}O_{2max}$ −0.03 ml/kg/min (95%CI −1.06 to 1.01) between the early follicular and luteal menstrual phase was observed. Between the active and inactive phases of OCs, a mean difference of −0.11 ml/kg/min (95%CI −2.32 to 2.10) was found. The inter-individual comparison of naturally menstruating women and OC users showed a mean difference in $\dot{V}O_{2max}$ of 0.23 ml/kg/min (95% CI −2.33 to 2.79) in favor of OC use. The intra-individual comparison of the same women showed a mean decrease in $\dot{V}O_{2max}$ of −0.84 ml/kg/min (95% CI −2.38 to 0.70) after a new start with OCs.

Conclusions: Our meta-analyses showed no effects of the MC or the OCs on $\dot{V}O_{2max}$. More high-quality studies are needed determining the MC phases more precisely, including OCs with the current standard formulations and comparing the influence of different progestins.

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1. Introduction

Several studies have been conducted to investigate the effect of the menstrual cycle (MC) or hormonal contraceptives (HC) on exercise performance. A group of researchers summarized these studies in two systematic reviews and meta-analyses [1,2]. These analyses indicated that exercise performance might be slightly reduced during the early follicular phase of the MC and that the use of oral contraceptives (OC) might result in an inferior exercise performance compared to naturally menstruating women. Due to the trivial effect size, the large between-study variation, and the number of poor-quality studies included in these meta-analyses, general guidelines on exercise performance could not be deducted [1,2]. Another systematic review included studies on the effect of the MC and OCs on responses to resistance training [3]. The review article reported conflicting results, with studies often limited by small sample sizes and methodological issues, but do appear to suggest that female hormones may affect the resistance training response [3].

It should be noted that there are some limitations within studies in sport and exercise science with women as participants [4]. Due to a lack of agreement on the terminology and methodological approaches, MC phases were not uniformly defined and examined, OCs with variable dosages of ethinyl estradiol (EE) and different kinds of progestin were included and compared. Furthermore, exercise performance was measured using different parameters and participants ranged from sedentary to physically active to elite athletes [1,2,4].

The current systematic review and meta-analysis investigates the influence of endogenous and exogenous female steroid hormones on cardiorespiratory fitness. In addition to the reproductive system, these hormones have numerous physiological effects that could affect the cardiovascular system, respiratory function, thermoregulation, and substrate metabolism [5–8]. For example, progesterone augments body temperature and appears to stimulate minute ventilation [5,6], whereas estrogen seems to enhance muscular glycogen storage and increase lipid availability and utilization [7,8]. An understanding of this influence is important in terms of maximizing health benefits [9] and could also be relevant to optimizing training and competition practices [10].

Hence, previous reviews on the topic [1,2] have considered females in general with conflicting or trivial results, the present one focuses on physically active women in order to minimize the risk of potential changes in the outcome measures of the performance test due to the training effect, to reduce a large variability in the measures and to increase the sensitivity to detect smaller changes [11]. Furthermore, the current systematic review and meta-analysis is focused on a specific outcome, which is cardiorespiratory fitness (operationalized by the maximum oxygen uptake [$\dot{V}O_{2max}$]). $\dot{V}O_{2max}$ is an objective and standardized parameter that directly measures cardiorespiratory fitness. It represents the "gold standard" for assessing exercise capacity [9] and is one of the most important physiological determinants of endurance performance [12]. Specifically, $\dot{V}O_{2max}$ is a parameter to evaluate the integrated functioning of the pulmonary, cardiovascular, and muscle systems to uptake, transport, and utilize O_2 predominantly in the contracting muscle mitochondria [13].

Thus, the aim of this review and meta-analysis was to determine the influence of different MC phases as well as the use of HCs on $\dot{V}O_{2max}$ in physically active women.

2. Material and methods

This systematic review and meta-analysis is based on the PRISMA statement guidelines [14] and was conducted using a registered protocol (PROSPERO CRD42021291213).

2.1. Study inclusion and exclusion criteria

We defined the eligibility criteria using the PICOS model as follows:

Population: healthy, physically active women. A population was defined as "physically active" if the mean relative $\dot{V}O_{2max}$ was equal to or greater than 40 ml/min/kg [15].

Intervention: the influence of the cyclic hormone changes of endogenous hormones throughout the MC in eumenorrheic women and the influence of exogenous hormones in women taking HCs on cardiorespiratory fitness. Eumenorrhea was defined as an MC ranging between 21 and 35 days in length. All forms of HCs were considered: OC, vaginal ring, patch, progestin-only contraceptive (pill, implant, intrauterine device [IUD])

Comparator and **study design**: Four comparison/(sub-)meta-analyses were performed. Two focused on longitudinal studies examining the same women several times in order to compare the $\dot{V}O_{2max}$ during the different menstrual phases or during OC use and withdrawal. The other two meta-analyses assessed a potential difference in $\dot{V}O_{2max}$ between OC users and eumenorrheic women by analyzing cross-sectional studies assigning physically active women to one of these two groups (inter-individual comparison) as well as intervention-based studies (randomized-controlled trials [RCT], cross-over studies) comparing the same women with and without HCs (intra-individual comparison).

Outcome: cardiorespiratory fitness measured by relative $\dot{V}O_{2max}$ assessed in ml/kg/min.

2.2. Search strategy

The electronic search was conducted on PubMed, Web of Science, Embase, Cochrane Library, and Google Scholar [16]. The Google Scholar search was limited to the first 300 articles [17]. The search strategy was based on combinations of "menstrual cycle" or "hormonal contraceptives" and "exercise performance" terms and was designed and supported by a clinical librarian. The following

search terms and their combinations were used: ('oral contraceptive' OR 'levonorgestrel' OR 'ethinyl estradiol' OR 'contraceptive') OR ('menstrual cycle' OR 'menstrual phase', OR 'follicular phase', OR 'luteal phase') AND ('aerobic', OR 'aerobic power', OR 'aerobic capacity', OR 'endurance', OR 'endurance capacity', OR 'anaerobic', OR 'anaerobic capacity' OR 'aerobic threshold' OR 'oxygen consumption' OR 'oxygen uptake' OR 'VO_{2peak}' OR 'VO_{2max}'). The electronic database search was conducted by two reviewers (C.B., MJ.S.) on November 2nd, 2021. No language or date restrictions were applied.

2.3. Data selection and extraction

All duplicates were removed by the Endnote "find duplicates" function. Two independent reviewers (C.B., LF.S.) screened the titles and abstracts as well as, in a second stage, the full articles with the Rayyan QCRI app [18]. Only published full-text articles were taken into consideration. Any disagreement about the inclusion of studies was resolved by consensus or a third reviewer (MJ.S.) where necessary.

Two reviewers (C.B., LF.S.) independently extracted data using a predesigned data collection form that captured information on study design, sample size, performance test, methods of MC verification, definition of test phases, formulation and application period of the used OC and outcome (relative $\dot{V}O_{2max}$, assessed in ml/kg/min). If studies just published the absolute $\dot{V}O_{2max}$ value (assessed in l/min), authors were contacted in order to obtain the relative $\dot{V}O_{2max}$ value. Thus, one of six contacted authors [19] provided us with unpublished information, the other five studies were excluded.

2.4. Quality assessment

The methodological quality of the included articles was assessed with the Newcastle-Ottawa Scale (NOS) [20] for the non-randomized studies and with the Cochrane Collaboration's tool for assessing risk of bias (RoB 2) [21] for the RCTs.

NOS assesses the quality of the articles in three domains of selection, comparability and exposure. An adapted version of the NOS for case-control studies was used for the cross-sectional studies. An adapted version of NOS for cohort studies was applied for the longitudinal studies examining the same women at different phases of the MC, during the inactive/active OC phase or with/without OCs. In both adapted versions, specific quality characteristics relevant to the conclusion of the current meta-analysis were included. Studies that received a score of eight to nine stars were judged to be at low risk of bias, studies that scored seven stars were considered at medium risk, and studies that scored less than six stars were considered at high risk of bias.

With the RoB 2 tool, studies are judged to be at low, some concern or high risk of bias on the basis of criteria evaluating the randomization process, deviation from the intended interventions, missing outcome data, measurement of outcome and selection of the reported results [21].

Two reviewers (C.B., LF.S.) performed the assessment independently. Scores were compared, and any inter-reviewer disagreements were resolved by consensus or by a third reviewer (MJ.S.) where necessary.

2.5. Data analysis

Most of the included studies differentiated solely the follicular and the luteal phase of the MC. The follicular phase should be divided into an early follicular (low progesterone, low estrogen) and late follicular (low progesterone, high estrogen) phase [22]. Based on serum hormone analysis, the "follicular" phase was interpreted as the "early follicular" phase of the MC in the included studies. Only two [23,24] studies correctly examined three phases and made a serum measurement of estrogen and progesterone to verify them. Therefore, we could just examine the early follicular and the luteal phase of the MC.

Just two RCTs [25,26] met the inclusion criteria for the intra-individual comparison of women with and without OCs, whereas one of them did not publish the results of the placebo group [25]. Since OC use causes alterations in the pattern of the normal MC and bleeding, performing true double-blind studies is highly challenging. In the study of Lebrun et al. [26], approximately half of the participants were aware that they were taking OCs or the placebo. Therefore, we merged the data of the intervention group (OC use) of the RCTs with the data of studies analyzed women prior to and after OC treatment in a cross-over design.

Some studies examined $\dot{V}O_{2peak}$ instead of $\dot{V}O_{2max}$ [19,27,28]. These studies were included in the current meta-analysis using $\dot{V}O_{2peak}$ as an indicator for $\dot{V}O_{2max}$ based on the suggestion that the $\dot{V}$ O_{2peak} attained on a maximum-effort incremental test in subjects exercising to the limit of tolerance is likely to be a valid index of $\dot{V}O_{2max}$ [29].

Depending on the range of mean $\dot{V}O_{2max}$ and the number of subjects included, the highly trained women with a $\dot{V}O_{2max} > 53$ ml/kg/min [15] would be considered separately because, especially for this population, even a small difference could be relevant.

For each of the four meta-analyses (see chapter 2.1.), a random-effect model with the REML (restricted maximum likelihood) estimation method was applied. Between-study heterogeneity was determined using I^2. Effect estimates for $\dot{V}O_{2max}$ were provided per study and as mean differences with corresponding 95% confidence intervals and visualized using forest plots. Given the small sample size of several included studies, the robustness of the estimates was assessed by sensitivity analyses utilizing fixed-effects inverse-variance models. Analyses were undertaken using Stata (Version 16.1, StataCorp, College Station, Texas, USA).

3. Results

3.1. Literature search

The literature search and selection of studies are presented in Fig. 1.

3.2. Study characteristics

Details of the included studies are shown in Tables 1–4. A total of 20 studies were included in this systematic review and meta-analysis. Nine of the 20 studies examined the influence of the MC on $\dot{V}O_{2max}$ (including 107 women) [19,23,24,30–35], five studies examined the influence of OCs on $\dot{V}O_{2max}$ (including 69 women) [26,27,36–38] and six assessed both topics (including 88 women) [11,25,28,39–41].

All 15 studies examining the influence of the MC phases on $\dot{V}O_{2max}$ used a calendar-based counting method to identify the different phases of the MC. To estimate the day of ovulation, two studies included daily recordings of basal body temperature [23,31], four studies used an ovulation prediction kit identifying the urinary LH surge [11,19,28,30] and one study performed a transabdominal ultrasound to confirm that ovulation did occur [25]. Ten studies measured serum concentrations of estrogen and progesterone [19,23,24,28,30,32,34,35,39,41], two studies serum progesterone only [31,33], one study conducted a salivary hormone analysis [40], and in two studies no hormones were measured [11,25].

Most studies analyzed the effect of monophasic pills on $\dot{V}O_{2max}$ [11,25,27,36–41], two studies the effect of triphasic pills [26,28]. The utilized pills contained a total of five different progestins (levonorgestrel, desogestrel, norethisterone, gestodene, and norgestimate). The dosing of EE varied between 20 and 35 mcg per pill. None of the included studies analyzed progestin-only pills.

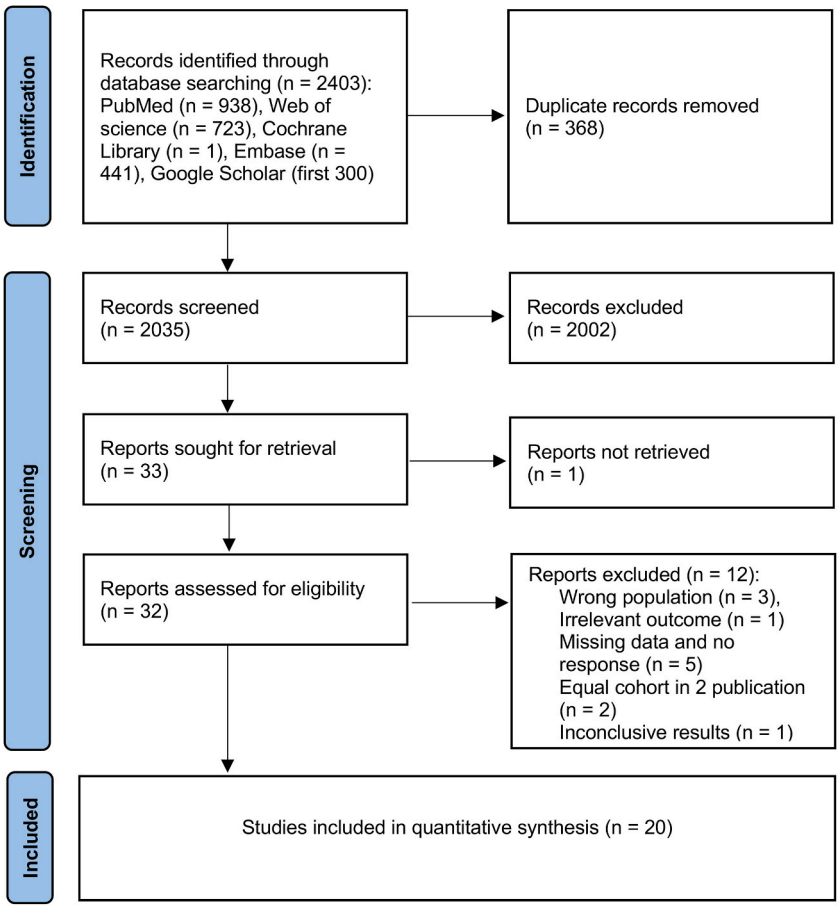

Fig. 1. PRISMA flow diagram presenting screening process and search results.

Table 1
Longitudinal studies, examining the effect of menstrual cycle phases on $\dot{V}O_{2max}$.

Author(s), year	n	Performance test	Method of MC phase verification	Phase of MC			Results	Risk of bias (NOS)
				Definition of the different MC phases	Serum estradiol (pmol/L)	Serum progesterone (nmol/L)	$\dot{V}O_{2max}$ (ml/kg/min)	
Beidleman et al., 1999 [] [30]	8	treadmill	calendar-based counting method, urinary LH, serum hormone analysis	EF (day 3–6)	143.2 +/− 80.8	1.5 +/− 0.6	46.8 +/− 4.0	moderate
				L (6–9 days after LH surge)	411.2 +/− 139.5	42.7 +/− 28.1	46.3 +/− 5.6	
Bemben et al., 1995 [] [31]	5	treadmill	calendar-based counting method, basal body temperature, serum hormone analysis	EF (day 2–5)	not examined	1.4 +/− 0.2	42.0 +/− 7.6	high
				LF (day 12–15)	not examined	1.3 +/− 0.2	42.1 +/− 7.8	
				L (day 20–23)	not examined	21.2 +/− 13.9	43.6 +/− 6.5	
Bryner et al., 1996 [25]	10	treadmill	calendar-based counting method (ovulation = cycle length minus 12–14 days), transabdominal ultrasound to confirm ovulation	F (day of ovulation divided by two)	not examined	not examined	41.6 +/− 12.1	high
				L (6–8 days after ovulation)	not examined	not examined	39.7 +/− 11.4	
Casazza et al., 2002 [28]	6	cycle ergometer	calendar-based counting method, urinary LH, serum hormone analysis	F (day 4–8)	125.2 +/− 38.9	1.2 +/− 0.1	42.3 +/− 8.1[a]	moderate
				L (day 17–25)	271.3 +/− 56.2	33.7 +/− 7.6	42.6 +/− 7.8[a]	
Dean et al., 2003 [23]	8	cycle ergometer	calendar-based counting method, basal body temperature, serum hormone analysis	EF (day 3 +/− 1.6)	121.2 +/− 38.5	2.5 +/− 0.8	43.0 +/− 6.5	low
				LF (day 10 +/− 2.6)	433.2 +/− 244.1	4.1 +/− 2.8	42.7 +/− 6.5	
				L (day 21 +/− 1.8)	422.2 +/− 88.2	37.2 +/− 25.2	42.5 +/− 5.1	
De Souza et al., 1990 [32]	8	treadmill	calendar-based counting method, urinary LH, serum hormone analysis	EF (day 2–4)	135.4 +/− 71.3	not examined	53.1 +/− 4.5	moderate
				L (6–8 days after ovulation)	554.9 +/− 258.2	not examined	53.7 +/− 3.8	
Frandsen et al., 2020 [24]	19	cycle ergometer	calendar-based counting method, serum hormone analysis	EF (tested at 25% of the MC length)	155 +/− 68.5	0.8 +/− 0.3	43.9 +/− 5.71	moderate
				LF (tested at 40–45% of the MC length)	574 +/− 437.8	0.9 +/− 0.5	43.9 +/− 5.4	
				L (tested at 75% of the MC length)	581 +/− 438.8	37.6 +/− 24.1	43.3 +/− 5.6	
Goldsmith & Glaister, 2020 [33]	10	treadmill	calendar-based counting method, serum hormone analysis	EF (day 2 +/− 2)	not examined	3.7 +/− 4.3	58.2 +/− 4.2	moderate
				LF (4 +/− 2 days prior to ovulation)	not examined	1.5 +/− 1.4	58.4 +/− 4.7	
				L (2 +/− 1 days from the progesterone peak)	not examined	32.7 +/− 30.8	59.7 +/− 4.7	
Gorden et al., 2018 [40]	10	cycle ergometer	calendar-based counting method, salivary hormone analysis	menstruation (day 1–5, interpreted as EF)	not examined	not examined	41.6 +/− 3.7	high
				LF (day 9–11)	not examined	not examined	44.1 +/− 3.9	
				L (day 19–20)	not examined	not examined	42.6 +/− 2.9	
Lebrun et al., 1995 [34]	16	treadmill	calendar-based counting method, serum hormone analysis	EF (day 3–8)	141.4 +/− 63.2	1.2 +/− 0.4	53.7 +/− 3.6	moderate
				L (4–9 days after ovulation)	461.4 +/− 147.6	40.6 +/− 14.8	52.8 +/− 3.2	
Mattu et al., 2019 [11]	15	cycle ergometer	calendar-based counting method, urinary LH	F (day 5–10)	not examined	not examined	47.1 +/− 4.1	high
				L (day 19–24)	not examined	not examined	46.0 +/− 3.9	
Nakamura & Nose-Ogura 2021 [39]	10	cycle ergometer	calendar-based counting method, serum hormone analysis	EF (day 4–8)	249.7 +/− 185.8	1.0 +/− 1.3	41.8 +/− 6.1	moderate
				L (5–15 days after ovulation)	397.2 +/− 208.5	22.9 +/− 16.9	41.9 +/− 5.3	

(*continued on next page*)

Table 1 (*continued*)

Author(s), year	n	Performance test	Method of MC phase verification	Phase of MC			Results	Risk of bias (NOS)
				Definition of the different MC phases	Serum estradiol (pmol/L)	Serum progesterone (nmol/L)	$\dot{V}O_{2max}$ (ml/kg/min)	
Redman et al., 2003[19]	14	cycle ergometer	calendar-based counting method, urinary LH, serum hormone analysis	F (day 5–7)	131.7 +/− 130.6	1.7 +/− 0.8	42.1 +/− 8.4[a]	low
				L (day 21–23)	348.0 +/− 230.5	26.8 +/− 20.1	44.3 +/− 6.2[a]	
Smekal et al., 2007 [35]	19	cycle ergometer	calendar-based counting method, basal body temperature, serum hormone analysis	F (day 9 +/− 1)	203.3 +/− 108.3	2.3 +/− 0.6	43.2 +/− 5.1	high
				L (day 25 +/− 2)	456.3 +/− 187.9	27.4 +/− 13.8	43.5 +/− 5.1	
Vaiksaar et al., 2011 [41]	8[a]	rowing ergometer	calendar-based counting method, serum hormone analysis	F (day 8 +/− 3)	176.8 +/− 51.9	1.9 +/− 0.5	49.0 +/− 6.6	moderate
				L (day 20 +/− 2)	481.4 +/− 131.0	38.9 +/− 11.0	50.6 +/− 7.1	
	7[b]			F (day 8 +/− 3)	163.4 +/− 98.2	1.3 +/− 0.7	45.2 +/− 9.4	
				L (day 20 +/− 2)	517.7 +/− 21.7	30.1 +/− 0.7	45.4 +/− 4.1	

Note. Values are reported as means +/− SD. Vaiksaar et al. [41] distinguished between competitive cyclic athletes (a) and recreationally trained cyclic athletes (b).
EF: early follicular phase, F: follicular phase, L: luteal phase, LF: late follicular phase, LH: luteinizing hormone, MC: menstrual cycle, n: number of participants, NOS: Newcastle-Ottawa Quality Assessment Scale.
[a] $\dot{V}O_{2peak}$ was measured.

Table 2
Cross-sectional studies, examining the inter-individual difference between oral contraceptive users and naturally menstruating women.

Author(s), year	n	Performance test	Oral contraceptive	EE	Progestin	Duration of use	Test phase	Results	Risk of bias (NOS)
								$\dot{V}O_{2max}$ (ml/kg/min)	
Gordon et al., 2018 [40]	16	cycle ergometer	mono-phasic	30 mcg 150 mcg	levonorgestrel	>3 months	OC users (n = 6): day 19–20, interpreted as active-pill phase	44.3 +/− 3.6	high
							NCOC users (n = 10): menstruation, interpreted as F	41.6 +/− 3.7	
Mattu et al., 2019 [11]	30	cycle ergometer	mono-phasic	20–35 mcg	levonorgestrel (n = 10) desogestrel (n = 5)	>6 months	OC users (n = 15): active-pill phase	45.2 +/− 4.3	moderate
							NOC users (n = 15): F (day 5–10)	47.1 +/− 4.1	
Quinn et al., 2018 [27]	16	cycle ergometer	mono-phasic		not specified	>12 months	OC users (n = 8): active-pill phase	44.5 +/− 4.2[a]	high
							NOC users (n = 15): F (day 4–10)	43.5 +/− 5.2[a]	
Vaiksaar et al., 2011 [41]	16	rowing ergometer	mono-phasic	20 mcg	gestodene 75 mcg	>3 months	OC users (n = 9): day 20 +/− 2, interpreted as active-pill phase	44.5 +/− 5.2	moderate
							NOC users (n = 7): F (day 8 +/−3)	45.2 +/− 9.4	

Note. Values are reported as means +/− SD.
OC: combined oral contraceptive, EE: Ethinyl estradiol, F: follicular phase, n: number of participants, NOC: non-combined oral contraceptive, NOS: Newcastle-Ottawa Quality Assessment Scale.
[a] $\dot{V}O_{2peak}$ was measured.

3.3. Quality

The quality classifications are presented in Tables 1–4

The studies were considered at high (34.5%), moderate (51.7%) to low (13.8%) risk of bias as described in the methodology section.

Table 3
Longitudinal studies, examining the effect of the active/inactive phase of the oral contraceptive cycle on $\dot{V}O_{2max}$.

Author(s), year	n	Performance test	Oral contraceptive	EE	Progestin	Duration of OC use	Test phase	Results	Risk of bias (NOS)
								$\dot{V}O_{2max}$ (ml/kg/min)	
Gordon et al., 2018[40]	6	cycle ergometer	mono-phasic	30 mcg	levonorgestrel 150 mcg	>3 months	day 1–3, interpreted as inactive-pill phase	44.9 +/− 5.0	high
							day 19–20, interpreted as active-pill phase	44.3 +/− 3.6	
Mattu et al., 2019 [11]	15	cycle ergometer	mono-phasic	20–35 mcg	levonorgestrel (n = 10) desogestrel (n = 5)	>6 months	inactive-pill phase	45.5 +/− 5.3	moderate
							active-pill phase	45.2 +/− 4.3	
Nakamura & Nose-Ogura, 2021 [39]	10	cycle ergometer	mono-phasic	20 mcg	norethisterone 1 mg	3 months	inactive-pill phase	40.7 +/− 5.3	low
							active-pill phase	41.1 +/− 5.3	
Vaiksaar et al., 2011 [36]	8	rowing ergometer	mono-phasic	20 mcg	75 mcg gestodene	>3 months	active-pill phase	45.9 +/− 5.7	low
							inactive-pill phase	44.3 +/−5.5	

Note. Values are reported as means +/− SD.
OC: oral contraceptive, EE: Ethinyl estradiol, n: number of participants, NOS: Newcastle-Ottawa Quality Assessment Scale.

In 80% of the included studies [11,19,23,24,26–28], [32–39,41], two identical performance tests were conducted, also considering testing at the same time of day as well as controlling diet and activities on the days before the test. In 90% [11,19,23,24,26–28], [32–39,41], care was taken to include women with similar fitness levels. Of the studies examining the same women several times, just 22% [19,32,33,40] made one familiarization trial prior to the test phase. Hence, to minimize test order effects the test conditions were randomized or the order of testing was counterbalanced in 80% of the longitudinal studies examining the influence of the different menstrual/OC phases on $\dot{V}O_{2max}$ [19,24,25,30,31,34–36,39].

The primary sources of bias for studies considered at high or moderate risk were insufficient precision in the determination of the different menstrual phases and inaccurate consideration of the different properties of OCs. In the adapted version of NOS, trials were considered if the three phases of MC (early follicular, late follicular and luteal phase) were correctly examined and a verification of the MC phase was performed by measuring serum estrogen and progesterone concentrations at the time of testing [22] which was the case in two studies only [23,24]. In two of the four cross-sectional studies [11,27], not all participants received an OC with the same progestin. In 50% of the cross-sectional [11,27] as well as the intervention-based studies [25,37,38] examining a possible inter-/, respectively intra-individual influence of OCs on $\dot{V}O_{2max,}$ it remains unclear whether the women were in the active or the pill-free interval at the moment of the investigation. Furthermore, two [25,26] of the six intervention-based studies chose an interval shorter than three months between new start with OCs and test phase [25,26]. Common side effects of OCs are generally self-limiting and improve with the duration of use [42]. Therefore, testing after at least three or even six pill cycles seems more reasonable to ensure that any short-term effects are also long-term effects and vice-versa [10].

3.4. *Effect of the menstrual cycle phases on $\dot{V}O_{2max}$*

A total of 15 studies (including 173 women) investigated the effect of the MC phase on $\dot{V}O_{2max}$[11,19,23–25,28,30–35,37,39–41] . Our meta-analysis found a mean decrease in $\dot{V}O_{2max}$ of −0.03 ml/kg/min (95% CI –1.06 to 1.01; Fig. 2) during the early follicular compared with the luteal phase of the MC. If the highly trained women with a $\dot{V}O_{2max}$ > 53 ml/kg/min [15] were considered separately, the results did not change substantially (0.09 ml/kg/min (95% CI –1.72 to 1.90; Fig. 3).

3.5. *Effect of oral contraceptives on $\dot{V}O_{2max}$*

Four longitudinal studies (including 39 women) [11,36,39,40] analyzed the influence of different OC phases on $\dot{V}O_{2max}$. The current meta-analysis showed a mean decrease in $\dot{V}O_{2max}$ of −0.11 ml/kg/min (95% CI –2.32 to 2.10; Fig. 4) during the inactive compared with the active OC phases.

Four cross sectional studies [11,27,40,41] analyzed the potential inter-individual difference in $\dot{V}O_{2max}$ between OC users and eumenorrheic women (including 78 women). A mean difference in $\dot{V}O_{2max}$ of 0.23 ml/kg/min (95% CI –2.33 to 2.79; Fig. 5) use was found in favor of OC use.

Table 4
Intervention studies, examining the intra-individual effect of $\dot{V}O_{2max}$ after initiating oral contraceptive.

Author(s), year,	n	Performance test	Oral contraceptive	EE	Progestin	Duration of OC use	Test phase	Results $\dot{V}O_{2max}$ (ml/kg/min)	Risk of bias
Bryner et al., 1996[25]	10	treadmill	mono-phasic	35 mcg	norethisterone 1 mg	first intake cycle	without OC: F (day of ovulation divided by two)	41.6 +/− 12.1	high (RoB2)
							with OC: third week (interpreted as active-pill phase)	41.0 +/− 12.4	
Casazza et al., 2002 [28]	6	cycle ergometer	triphasic	35 mcg	norgestimatep2p0.18 mg−0.25 mg	4 months	without OC: F (day 4–8)	42.3 +/− 8.1[a]	moderate (NOS)
							with OC: active-pill phase	36.9 +/− 5.4[a]	
Lebrun et al., 2003[26]	7	treadmill	triphasic	35 mcg	norethisterone 0.5 mg–1.0 mg	2 months	without OC: F (day 3–8)	54.7 +/− 4.3	some concerns (RoB2)
							with OC: active-pill phase	52.0 +/− 4.2	
Nakamura & Nose-Ogura, 2021 [39]	10	cycle ergometer	mono-phasic	20 mcg	norethisterone 1 mg	3 months	without OC: F (day 4–8)	41.8 +/− 6.1	moderate (NOS)
							with OC: active-pill phase	41.1 +/− 5.3	
Notelovitz et al., 1987 [38]	6	treadmill	mono-phasic	35 mcg	norethisteronep2p0.4 mg	6 months	without OC (phase not specified)	41.2 +/− 11.8	moderate (NOS)
							with OC (phase not specified)	38.4 +/− 9.4	
Rickenlund et al., 2004 [37]	13[a]	treadmill	mono-phasic	30 mcg	levonorgestrel 150 mcg	10 months	without OC: F (day 1–5)	55.3 +/− 4.4	high (NOS)
							with OC: active-pill phase	55.6 +/− 3.1	
	12[b]						without OC: F (day 1–5)	41.9 +/− 3.3	
							with OC: active-pill phase	41.7 +/− 3.1	

Note. Values are reported as means +/− SD. Rickenlund et al. [37] distinguished between athletes (a) and sedentary controls (b).
OC: oral contraceptive, EE: Ethinyl estradiol, F: follicular phase, n: number of participants, NOS: Newcastle-Ottawa Quality Assessment Scale, RoB2: Cochrane Collaboration's tool for assessing risk of bias.
[a] $\dot{V}O_{2peak}$ was measured.

Six studies were intervention-based studies (including 71 women) examining a possible intra-individual difference in $\dot{V}O_{2max}$ comparing the same women without and with OCs. Four studies analyzed women prior to and after 3–10 months of OC treatment in a cross-over design (including 47 women) [28,37–39]. Two studies were randomized double-blind placebo-controlled (including 24 women) [25,26]. While Bryner et al. [25] observed no difference in $\dot{V}O_{2max}$, Lebrun et al. [26] showed a decrease of $\dot{V}O_{2max}$ in the OC group (−2.7 ml/kg/h), whereas $\dot{V}O_{2max}$ in the placebo group slightly increased (+0.8 ml/kg/min) over the same time period. Overall, the meta-analysis combining the data of the cross-over studies and of the intervention groups of the RCT showed a mean intra-individual decrease in $\dot{V}O_{2max}$ of −0.84 ml/kg/min (95% CI –2.38 to 0.70; Fig. 6) after new start with OCs.

3.6. Sensitivity analysis

The robustness of the estimations of the meta-analyses was confirmed by sensitivity analyses utilizing fixed-effects inverse-variance models. Since heterogeneity between studies was relatively low with regard to the outcomes of interest (mostly even $I^2 = 0$, except $I^2 = 32\%$ for the assessment of the OC effect in the cross-sectional studies), the fixed-effects models provided very similar, often even identical estimates. The results were persistent and robust when the available absolute values of $\dot{V}O_{2max}$ (l/min) were analyzed.

4. Discussion

4.1. Main implications

Our meta-analyses did not find changes in $\dot{V}O_{2max}$ between the early follicular and the luteal phases of the MC or during the active

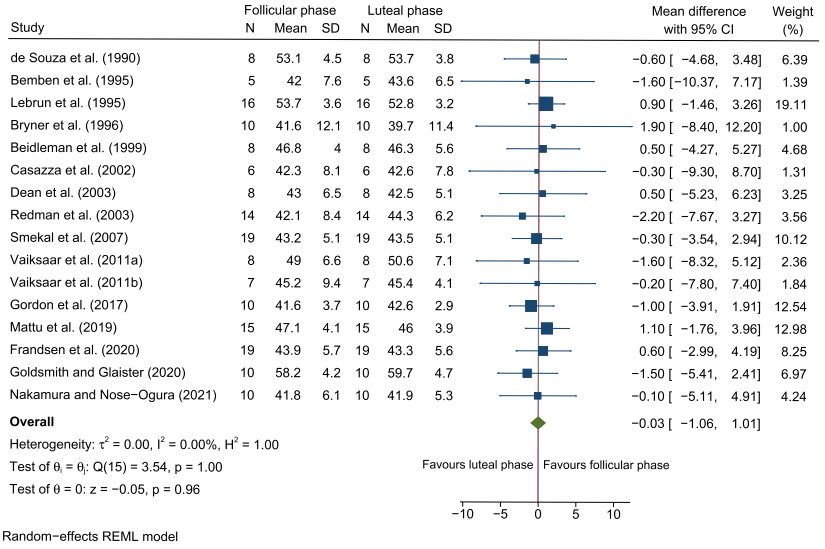

Fig. 2. Forest plot of studies examining the effect of the early follicular and the luteal phases of the menstrual cycle on $\dot{V}O_{2max}$ in physically active women. Mean difference represents $\dot{V}O_{2max}$ assessed in ml/kg/min. Note: Vaiksaar et al. [41]distinguished between competitive cyclic athletes (a) and recreationally trained cyclic athletes (b).

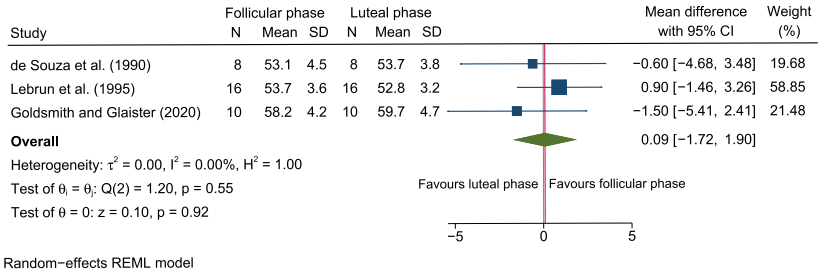

Fig. 3. Forest plot of studies examining the effect of the early follicular and the luteal phases of the menstrual cycle on $\dot{V}O_{2max}$ in highly trained women with a $\dot{V}O_{2max} > 53$ ml/kg/min. Mean difference represents $\dot{V}O_{2max}$ assessed in ml/kg/min.

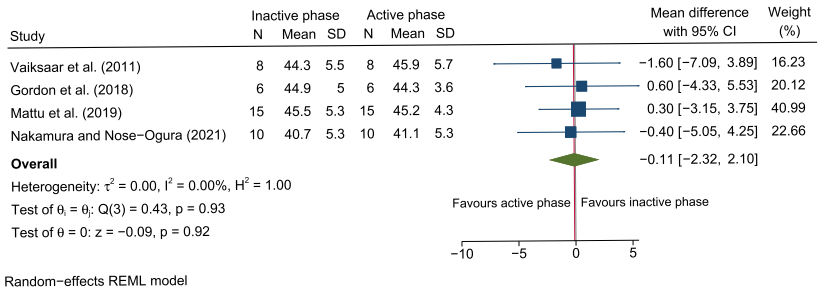

Fig. 4. Forest plot of studies examining the effect of the inactive and the active phase of the oral contraceptive cycle on $\dot{V}O_{2max}$ in physically active women. Mean difference represents $\dot{V}O_{2max}$ assessed in ml/kg/min.

and inactive pill phases in physically active women using an OC. Furthermore, no difference in $\dot{V}O_{2max}$ was found in the inter-individual comparison between OC users and eumenorrheic women as well as in the intra-individual comparison of the same women without and with OCs.

The results of the current meta-analysis are not in line with two meta-analyses published in 2020 investigating women regardless of their training level and an unspecific dependent variable (i.e. exercise performance) [1,2]. They concluded that exercise performance

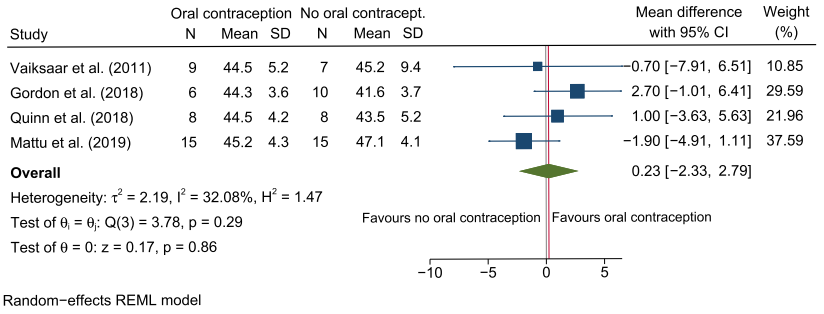

Fig. 5. Forest plot of cross-sectional studies examining the inter-individual difference in $\dot{V}O_{2max}$ between OC users and non-OC users in physically active women. Mean difference represents $\dot{V}O_{2max}$ assessed in ml/kg/min.

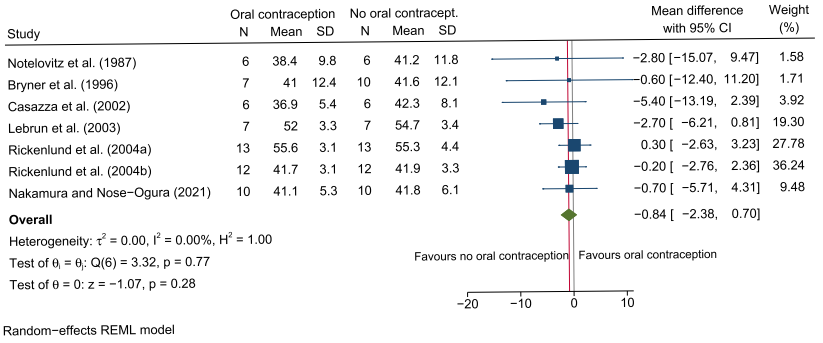

Fig. 6. Forest plot of interventional-based studies examining the intra-individual difference in $\dot{V}O_{2max}$ prior und after OC treatment. Mean difference represent $\dot{V}O_{2max}$ assessed in ml/kg/min. Note: Rickenlund et al.[37]distinguished between athletes (a) and sedentary controls (b).

is slightly reduced during the early follicular phase of the MC compared to all other phases and that the use of OCs might result in a slightly reduced exercise performance compared to naturally menstruating women. The results of the current meta-analysis do not confirm this observation in regard of a change in $\dot{V}O_{2max}$. Endogenous hormonal fluctuations between the early follicular and luteal phase of MC or exogenous hormone application may have a different effect in a homogenous population of physically active women.

In line with the results of the previously mentioned meta-analysis [1] no change in $\dot{V}O_{2max}$ during the inactive compared to the active pill phase was observed. This could be due to a slow elimination of EE from the bloodstream and affected organs, only resulting in little changes in endogenous concentration of estradiol and progesterone within the seven days of OC free interval [43].

The only accurate randomized double-blind placebo-controlled study examining a potential intra-individual difference in $\dot{V}O_{2max}$ with and without OCs [26] showed that the use of a triphasic OCs resulted in a mean decrease of −2.7 ml/kg/h compared with a +0.8 ml/kg/min improvement with placebo. However, the small number of participants (n = 14) limits the validity of this result and could also not be strengthened by our meta-analysis. Moreover, the studies investigating the effect of the OCs and MC phases on $\dot{V}O_{2max}$ or exercise performance have several deficits. Thus, there is insufficient data to discourage a woman from OCs due to potentially adverse effects on physical potential. The magnitude of the effect of endogenous and exogenous hormones on physical performance may vary substantially between subjects and be important on an individual basis. If a possible effect on physical performance in women is of interest, individualised recommendations should be made. In particular, the large variability in the type and severity of symptoms experienced during the MC as well as the possible negative and positive effects of OCs and other HCs should be considered.

4.2. Strengths and limitations

The available studies analyzing the possible effect of endogenous and exogenous female steroid hormones on exercise performance are very heterogenous and the outcome varies considerably across studies. In order to provide a meaningful conclusion, we have narrowed the sample selection and the dependent variable. With the selection of the studies, we limited the qualitative heterogeneity so that little statistical heterogeneity was observed within our meta-analyses, as shown by the small I^2 values (Figs. 2–6).

We only examined physically active women in order to minimize the risk of potential changes in the outcome measures of the performance test due to the training effect. Physically active women can push their performance limits more consistently and tend to show less variation in their test performance within themselves. A change in exercise performance in less active women might be more strongly affected by the ongoing training.

As a limitation, we have to mention that we considered the mean $\dot{V}O_{2max}$ value of the study population as inclusion criteria and not the individual values of the participants. Therefore, it is possible that women with a lower value were also included. However, 85% of the included studies considered the training history of the women for inclusion and described them as "moderately" [31], "recreationally" [27], "habitually" [23,28], "highly" [11], "physically" [30,40] active/trained [33], as "exercising women" [38], or "athletes" [26,32,34,36,37,39,41].

As the dependent variable, we chose $\dot{V}O_{2max}$, which is widely used as an indicator of cardiorespiratory fitness and reflects endurance capacity in exercise performance [9]. However, other parameters should be taken into account in the evaluation of cardiorespiratory fitness and endurance performance to be able to assess a possible influence conclusively. For example, the simultaneous measurement of minute ventilation ($\dot{V}_E$) and carbon dioxide production ($\dot{V}_{CO2}$) by cardiopulmonary exercise testing allows for the more comprehensive assessment of other clinically significant variables like the $\dot{V}_E/\ \dot{V}_{CO2}$ slope, which is a key indicator of ventilatory efficiency [9]. Submaximal exercise tests can also provide valuable information but are less precise than peak exercise testing in quantitating cardiorespiratory fitness [9]. In elite female athletes, even very small effects due to OC of MC can be meaningful [10], thus competition performances should be examined.

Furthermore, caution needs to be applied when interpreting the findings of the current data on the potential impact of the phases of the MC and the use of OCs on cardiorespiratory fitness and physical performance in general [4]. Overall, 86% of the studies included in this meta-analysis were classified as at moderate to high risk of bias, partially due to methodological heterogeneity in the determination of the different MC phases or insufficient accuracy in consideration of different characteristics of the OCs used in the trials. Thus, the current meta-analysis could not make any statement regarding the late follicular estrogen peak because most of the available studies did not consider this phase. In studies examining the influence of OCs on $\dot{V}O_{2max}$, it has to be considered that most of the OCs used did not correspond to current standard formulations.

4.3. Recommendation for future research

4.3.1. More attention to highly trained women

Further research focusing on well-trained female athletes is needed. It is remarkable that the studies including highly trained women with a $\dot{V}O_{2max} > 53$ ml/kg/min are the most precise with the smallest standard deviation [32–34]. Thus, with athletes more sensitive analysis could be performed. Furthermore, for female athletes even a small change in $\dot{V}O_{2max}$ could be relevant to the optimization of training practices and competition. For illustration, a study examining endurance athletes participating in Olympic Games/World Championships detected a difference in $\dot{V}O_{2max}$ of 3.2 ml/kg/min between female medalists and non-medalists in cross-country skiing [44].

The mean $\dot{V}O_{2max}$ of women aged 20–29 years is 37.6±10.2 ml/kg/min and 30.9±8.0 ml/kg/min for ages 30–39 years, respectively [45]. We examined physically active women with a $\dot{V}O_{2max}$ equal to or greater than 40 ml/min/kg, while highly endurance trained women have a $\dot{V}O_{2max} > 53$ ml/kg/min [15]. While just three studies [32–34] were found investigating this population, our results cannot be generalized to female athletes, which is why additional studies are needed.

4.3.2. Standardization of menstrual cycle research

There is a need for agreement on the terminology and methodological approaches within exercise science with women as participants to improve the quality of future research [4]. It is hypothesized that methodical differences play a major role in the contradictory results of recent evidence on exercise performance and the MC [22]. In order to provide a foundation for future high-quality MC research, a combination of three methods to verify MC phases is recommended: the calendar-based counting method combined with urinary luteinizing hormone surge testing as well as the measurement of serum estrogen and progesterone concentrations. Measurement of serum estrogen and progesterone in a resting state prior to the performance test is also important since potential effects of the MC on exercise performance are expected to be a consequence of the female steroid hormone levels [22].

4.3.3. Consideration of the different hormonal contraceptive formulations

With regard to studies investigating the influence of OCs on exercise performances, further research with the current standard formulations (20–30 mcg EE) is needed. Four intervention-based studies utilized an OC with a dosage of 35 mcg EE [25,26,28,38]. Interestingly, three of them [26,28,38] observed a possible adverse effect of the OC due to $\dot{V}O_{2max}$, while those studies using a dosage of 20–30 mcg EE showed no effect [37,39]. Furthermore, the varying dose and type of progestin in OC formulations confer distinct pharmacokinetic properties, potentially resulting in substantially different physiological effects [46]. Different properties of synthetic progestins were not considered in any study. Estranes and gonanes are related to testosterone and are associated with more androgenic side effects including also altered carbohydrate and lipid metabolism [42]. The 19-norpregnanes, including nestorone, nomogestrol acetate and trimegestone are related to progesterone with a high specificity to bind the progesterone receptors. They have no to little interaction with other steroid receptors. Newer progestins, like dienogest and drospirenone have partial antiandrogenic effects, while drospirenone offers additional anti-mineralocorticoid properties [47].

Moreover, research on the potential effect of the use of continuous cycle OCs as well as progestin-only pills and other HC on exercise performance is needed. Despite an extensive search strategy, no studies evaluating the effect on $\dot{V}O_{2max}$ were identified including HCs that did not qualify as OCs.

5. Conclusions

Our meta-analyses could not demonstrate any relevant effects of the MC, considering the early follicular and luteal phase, or the OCs on $\dot{V}O_{2max}$.

Due to the methodical issues, there is a lack of reliable, evidence-based data on the potential impact of the MC and the use of OCs on $\dot{V}O_{2max}$ and physical performance in general. There is a need for agreement on the terminology and methodological approaches within research in exercise science with women as participants. More high-quality studies with larger sample sizes focusing on well-trained women are needed. Further research should address the late follicular estrogen peak, and the different properties of OCs should be considered more accurately. Studies of OCs with the current standard formulations and studies comparing the influence of different progestins on cardiorespiratory fitness are needed, as well as studies on the use of continuous cycle OCs and progestin-only contraceptives.

Author contribution statement

Lea Franziska Schumpf, Christian Braun, Adriana Peric, Michael Johannes Schmid, Dirk Lehnick, Corina Christmann-Schmid, Christine Brambs: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

Data included in article/supplementary material/referenced in article.

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Attestation statements

Data regarding this meta-analysis has not been previously published. Data will be made available to the editors of the journal for review or query upon request.

Registration

Prospero CRD42021291213. Date of registration: December 14, 2021.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e17049.

References

[1] K.J. Elliott-Sale, K.L. McNulty, P. Ansdell, S. Goodall, K.M. Hick, K. Thomas, et al., The effects of oral contraceptives on exercise performance in women: a systematic review and meta-analysis, Sports Med. 50 (2020) 1785–1812, https://doi.org/10.1007/s40279-020-01317-5.

[2] K.L. McNulty, K. Elliott-Sale, E. Dolan, P.A. Swinton, P. Ansdell, S. Goodall, et al., The effects of menstrual cycle phase on exercise performance in eumenorrheic women: a systematic review and meta-analysis, Sports Med. 50 (2020) 1813–1827, https://doi.org/10.1007/s40279-020-01319-3.

[3] B. Thompson, A. Almarjawi, D. Sculley, X. Janse de Jonge, The effect of the menstrual cycle and oral contraceptives on acute responses and chronic adaptations to resistance training: a systematic review of the literature, Sports Med. 50 (2020) 171–185.

[4] K.J. Elliott-Sale, C.L. Minahan, X.A.K. Janse de Jonge, K.E. Ackerman, S. Sipilä, et al., Methodological considerations for studies in sport and exercise science with women as participants: a working guide for standards of practice for research on women, Sports Med. 51 (2021) 843–861, https://doi.org/10.1007/s40279-021-01435-8.

[5] M.L. Dombovy, H.W. Bonekat, T.J. Williams, B.A. Staats, Exercise performance and ventilatory response in the menstrual cycle, Med. Sci. Sports Exerc. 19 (1987) 111–117.

[6] R.B. Schoene, H.T. Robertson, D.J. Pierson, A.P. Peterson, Respiratory drives and exercise in menstrual cycles of athletic and nonathletic women, J. Appl. Physiol. Respir. Environ. Exerc. Physiol. 50 (1981) 1300–1305, https://doi.org/10.1152/jappl.1981.50.6.1300.

[7] S.E. Campbell, D.J. Angus, M.A. Febbraio, Glucose kinetics and exercise performance during phases of the menstrual cycle: effect of glucose ingestion, Am. J. Physiol. Endocrinol. Metab. 281 (2001) E817–E825.

[8] T.W. Zderic, A.R. Coggan, B.C. Ruby, Glucose kinetics and substrate oxidation during exercise in the follicular and luteal phases, J. Appl. Physiol. 90 (2001) 447–453.

[9] R. Ross, S.N. Blair, R. Arena, A.S. Church, J.P. Despreés, B.A. Frankling, et al., Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American heart association, Circulation 134 (2016) e653–e699, https://doi.org/10.1161/cir.0000000000000461.

[10] M. Burrows, C.E. Peters, The influence of oral contraceptives on athletic performance in female athletes, Sports Med. 37 (2007) 557–574, https://doi.org/10.2165/00007256-200737070-00001.

[11] A.T. Mattu, D. Iannetta, M.J. Maclnnis, P.K. Doyle-Baker, J.M. Murias, Menstrual and oral contraceptive cycle phases do not affect submaximal and maximal exercise responses, Scand. J. Med. Sci. Sports 30 (2020) 472–484, https://doi.org/10.1111/sms.13590.

[12] J. Mäestu, J. Jürimäe, T. Jürimäe, Monitoring of performance and training in rowing, Sports Med. 35 (2005) 597–617, https://doi.org/10.2165/00007256-200535070-00005.

[13] D.C. Poole, A.M. Jones, Measurement of the maximum oxygen uptake VO2max: VO2peak is no longer acceptable, J. Appl. Physiol. 122 (2017) 997–1002, https://doi.org/10.1152/japplphysiol.01063.2016.

[14] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al., The PRISMA 2020 statement: an updated guideline for reporting systematic reviews, BMJ 372 (2021) n71, https://doi.org/10.1136/bmj.n71.

[15] L. Decroix, K. de Pauw, C. Forster, R. Meeusen, Guidelines to classify female subject groups in sport-science research, Int. J. Sports Physiol. Perform. 11 (2016) 204–213.

[16] T. Muka, M. Glisic, J. Milic, S. Verhoog, J. Bohlius, W. Bramer, et al., A 24-step guide on how to design, conduct, and successfully publish a systematic review and meta-analysis in medical research, Eur. J. Epidemiol. 35 (2020) 49–60, https://doi.org/10.1007/s10654-019-00576-5.

[17] W.M. Bramer, M. Rethlefsen, J. Kleijnen, O.H. Franco, Optimal database combinations for literature searches in systematic reviews: a prospective exploratory study, Syst. Rev. 6 (2017) 245, https://doi.org/10.1186/s13643-017-0644-y.

[18] M. Ouzzani, H. Hammady, Z. Fedorowicz, A. Elmagarmid, Rayyan - a web and mobile app for systematic reviews, Syst. Rev. 5 (2016) 210, https://doi.org/10.1186/s13643-016-0384-4.

[19] L.M. Redman, G.C. Scroop, R.J. Norman, Impact of menstrual cycle phase on the exercise status of young, sedentary women, Eur. J. Appl. Physiol. 90 (2003) 505–513, https://doi.org/10.1007/s00421-003-0889-0.

[20] G. Wells, B. Shea, D. O'Connell, J. Peterson, V. Welch, M. Losos, P. Tugwell, The Newcastle–Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

[21] J.P.T. Higgins, P.C. Gotzsche, P. Jüni, D. Moher, A.D. Oxman, J. Savovic, et al., The Cochrane Collaboration's tool for assessing risk of bias in randomised trials, BMJ 343 (2011) d5928, https://doi.org/10.1136/bmj.d5928.

[22] X. Janse de Jonge, B. Thompson, A. Han, Methodological recommendations for menstrual cycle research in sports and exercise, Med. Sci. Sports Exerc. 51 (2019) 2610–2617, https://doi.org/10.1249/mss.0000000000002073.

[23] T.M. Dean, L. Perreault, R.S. Mazzeo, T.J. Horton, No effect of menstrual cycle phase on lactate threshold, J. Appl. Physiol. 95 (2003) 2537–2543, https://doi.org/10.1152/japplphysiol.00672.2003.

[24] J. Frandsen, N. Pistoljevic, J.P. Quesada, F.J. Amaro-Gahete, C. Ritz, S. Larsen, et al., Menstrual cycle phase does not affect whole body peak fat oxidation rate during a graded exercise test, J. Appl. Physiol. 128 (2020) 681–687, https://doi.org/10.1152/japplphysiol.00774.2019.

[25] R.W. Bryner, R.C. Toffle, I.H. Ullrich, R.A. Yeater, Effect of low dose oral contraceptives on exercise performance, Br. J. Sports Med. 30 (1996) 36–40.

[26] C.M. Lebrun, M.A. Petit, D.C. McKenzie, J.E. Taunton, J.C. Prior, Decreased maximal aerobic capacity with use of a triphasic oral contraceptive in highly active women: a randomised controlled trial, Br. J. Sports Med. 37 (2003) 315–320, https://doi.org/10.1136/bjsm.37.4.315.

[27] K.M. Quinn, F. Billaut, A.C. Bulmer, C.L. Minahan, Cerebral oxygenation declines but does not impair peak oxygen uptake during incremental cycling in women using oral contraceptives, Eur. J. Appl. Physiol. 118 (2018) 2417–2427, https://doi.org/10.1007/s00421-018-3968-y.

[28] G.A. Casazza, S.H. Suh, B.F. Miller, F.M. Navazio, G.A. Brooks, Effects of oral contraceptives on peak exercise capacity, J. Appl. Physiol. 93 (2002) 1698–1702, https://doi.org/10.1152/japplphysiol.00622.2002.

[29] J.R. Day, H.B. Rossiter, E.M. Coats, A. Skasick, B.J. Whipp, The maximally attainable VO_2 during exercise in humans: the peak vs. maximum issue, J. Appl. Physiol. 95 (2003) 1901–1907, https://doi.org/10.1152/japplphysiol.00024.2003.

[30] B.A. Beidleman, P.B. Rock, S.R. Muza, C.S. Fulco, V.A. Forte Jr., A. Cymerman, Exercise VE and physical performance at altitude are not affected by menstrual cycle phase, J. Appl. Physiol. 86 (1999) 1519–1526, https://doi.org/10.1152/jappl.1999.86.5.1519.

[31] D.A. Bemben, P.C. Salm, A.J. Salm, Ventilatory and blood lactate responses to maximal treadmill exercise during the menstrual cycle, J. Sports Med. Phys. Fit. 35 (1995) 257–262.

[32] M.J. De Souza, M.S. Maguire, K.R. Rubin, C.M. Maresh, Effects of menstrual phase and amenorrhea on exercise performance in runners, Med. Sci. Sports Exerc. 22 (1990) 575–580, https://doi.org/10.1249/00005768-199010000-00006.

[33] E. Goldsmith, M. Glaister, The effect of the menstrual cycle on running economy, J. Sports Med. Phys. Fit. 60 (2020) 610–617, https://doi.org/10.23736/s0022-4707.20.10229-9.

[34] C.M. Lebrun, D.C. McKenzie, J.E. Taunton, Effects of menstrual cycle phase on athletic performance, Med. Sci. Sports Exerc. 27 (1995) 437–444.

[35] G. Smekal, S.P. von Duvillard, P. Frigo, T. Tegelhofer, R. Pokan, P. Hofman, H. Tschan, et al., Menstrual cycle: no effect on exercise cardiorespiratory variables or blood lactate concentration, Med. Sci. Sports Exerc. 39 (2007) 1098–1106, https://doi.org/10.1249/mss.0b013e31805371e7.

[36] S. Vaiksaar, J. Jürimae, J. Maestu, P. Purge, S. Kalytka, L. Shakhlina, et al., Phase of oral contraceptive cycle and endurance capacity of rowers, Percept. Mot. Skills 113 (2011) 764–772, https://doi.org/10.2466/05.06.PMS.113.6.764-772.

[37] A. Rickenlund, K. Carlström, B. Ekblom, T.B. Brismar, B. von Schoultz, A.L. Hirschberg, Effects of oral contraceptives on body composition and physical performance in female athletes, J. Clin. Endocrinol. Metab. 89 (2004) 4364–4370, https://doi.org/10.1210/jc.2003-031334.

[38] M. Notelovitz, C. Zauner, L. McKenzie, Y. Suggs, C. Fields, C. Kitchens, The effect of low-dose oral contraceptives on cardiorespiratory function, coagulation, and lipids in exercising young women: a preliminary report, Am. J. Obstet. Gynecol. 156 (1987) 591–598, https://doi.org/10.1016/0002-9378(87)90059-7.

[39] M. Nakamura, S. Nose-Ogura, Effect of administration of monophasic oral contraceptive on the body composition and aerobic and anaerobic capacities of female athletes, J. Obstet. Gynaecol. Res. 47 (2021) 792–799, https://doi.org/10.1111/jog.14613.

[40] D. Gordon, A. Scruton, R. Barnes, J. Baker, L. Prado, V. Merzbach, The effects of menstrual cycle phase on the incidence of plateau at VO_{2max} and associated cardiorespiratory dynamics, Clin. Physiol. Funct. Imag. 38 (2018) 689–698, https://doi.org/10.1111/cpf.12469.

[41] S. Vaiksaar, J. Jürimae, J. Maestu, P. Purge, Kalytka, L. Shakhlina, et al., No effect of menstrual cycle phase and oral contraceptive use on endurance performance in rowers, J. Strength Condit Res. 25 (2011) 1571–1578, https://doi.org/10.1519/JSC.0b013e3181df7fd2.

[42] M.V. Dragoman, The combined oral contraceptive pill – recent developments, risks and benefits, Best Pract. Res. Clin. Obstet. Gynaecol. 28 (2014) 825–834, https://doi.org/10.1016/j.bpobgyn.2014.06.003.

[43] K.J. Elliott, N.T. Cable, T. Reily, Does oral contraceptive use affect maximum force production in women? Br. J. Sports Med. 39 (2005) 15–19, https://doi.org/10.1136/bjsm.2003.009886.
[44] E. Tønnessen, T.A. Haugen, E. Hem, S. Leirstein, S. Seiler, Maximal aerobic capacity in the winter-Olympics endurance disciplines: Olympic-medal benchmarks for the time period 1990-2013, Int. J. Sports Physiol. Perform. 10 (2015) 835–839, https://doi.org/10.1123/ijspp.2014-0431.
[45] L.A. Kaminsky, R. Arena, J. Myers, Reference standards for cardiorespiratory fitness measured with cardiopulmonary exercise testing: data from the fitness registry and the importance of exercise national database, Mayo Clin. Proc. 90 (2015) 1515–1523, https://doi.org/10.1016/j.mayocp.2015.07.026.
[46] H. Kuhl, Pharmacokinetics of the newer progestogens and the controversy about gestodene, Contraception 56 (1997) 401–403, https://doi.org/10.1016/s0010-7824(97)00189-3.
[47] R. Sitruk-Ware, A. Nath, The use of newer progestins for contraception, Contraception 82 (2010) 410–417, https://doi.org/10.1016/j.contraception.2010.04.004.