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 pill users and their perceived effects on exercise performance and recovery time post training'.

3

#### 4 ABSTRACT

This study examined the type, frequency, and severity of symptoms experienced by naturally 5 menstruating women and combined, monophasic, oral contraceptive pill (mOCP) users and 6 their perceived effects on exercise performance and recovery time post training. Forty-two 7 recreationally active women; 21 naturally menstruating and 21 mOCP users participated in the 8 study. Data were collected using two approaches: 1) an online 54-part retrospective survey; 9 and 2) a daily questionnaire. 'Total number of symptoms', 'symptom index [Si] score', 10 'average symptom severity', and 'Si × severity score' were calculated from the retrospective 11 12 dataset. Real-time symptom data (i.e., 'symptom frequency per phase' and 'phase symptom frequency  $\times$  severity score') were calculated across pre-defined cycle *phases* from the daily 13 questionnaire. The retrospective survey showed that symptoms were commonly reported by 14 15 recreationally active women, but there were no differences in symptomology between the groups (P > 0.113). The daily questionnaire showed both groups experienced a greater 16 frequency and severity of symptoms whilst bleeding ( $P \le 0.001$ ), which was associated with 17 perceived reductions in exercise performance (odds ratio [OR] = 1.04 - 1.07) and a perceived 18 19 longer recovery time post-training (OR = 1.03 - 1.04). The results from this study show that 20 cycle related symptoms were commonly reported by a group of recreationally active women, with no difference in symptomology between naturally menstruating women and mOCP users. 21 The magnitude of symptoms was greater whilst bleeding, which was associated with a 22 perceived reduction in exercise performance and a longer recovery time post-training. 23

24

## 25 **1.0 INTRODUCTION**

There are complex interactions between endogenous and exogenous sex hormones and various aspects of health, well-being, exercise performance, and training (Constantini *et al.*, 2005, Elliott-Sale *et al.*, 2020, Lebrun *et al.*, 1994, McNulty *et al.*, 2020). It has been reported that between 36 to 93% of active women perceive that their menstrual cycle (MC) or hormonal contraceptive (HC) use influences their ability to perform or train (Armour *et al.*, 2020, 31 Bruinvels et al., 2021, Findlay et al., 2020, Heather et al., 2021, Martin et al., 2018, Read et al., 2021, Solli et al., 2020). At present, the specific mechanisms behind these performance and 32 training effects are not well-understood, however one plausible reason is the impact of cycle 33 related symptoms. Specifically, the cyclic fluctuations in endogenous sex hormones across the 34 MC have been associated with a variety of physical and psychological symptoms (Ferries-35 Rowe et al., 2020, Yonkers et al., 2008), which are commonly reported within the general 36 population and often impact negatively on the quality of life (Schoep et al., 2019). In contrast, 37 the oral contraceptive pill (OCP) is often prescribed to women to reduce negative MC related 38 39 symptoms within general and athletic populations (Yonkers et al., 2008, Wong et al., 2009). From a sporting perspective, cycle related symptoms are prevalent in recreationally active and 40 elite sportswomen and are perceived to impact an individual's ability to perform and train, as 41 well as general health and well-being (Armour et al., 2020, Brown et al., 2020, Bruinvels et 42 al., 2021, Clarke et al., 2021, Findlay et al., 2020, Heather et al., 2021, Martin et al., 2018, 43 Nolan et al., 2022, Oxfeldt et al., 2020, Parker et al., 2020, Read et al., 2021, Solli et al., 2020). 44 Despite these potential effects, little is known about the type, frequency, and severity of cycle 45 related symptoms and how the symptoms experienced by naturally menstruating women and 46 47 OCP users are perceived to influence exercise performance and training.

There are a range of suggested mechanisms by which the cyclical fluctuations in oestrogen and 48 progesterone across the MC might affect exercise performance (McNulty et al., 2020) and 49 50 training (Thompson et al., 2020), however the potential indirect effects of cyclical hormonal changes, such as the influence of cycle related symptoms, are often overlooked (Bruinvels et 51 52 al., 2022). In active women, common negative symptoms are likely antagonistic with optimal performance and training if not managed (Armour et al., 2020, Brown et al., 2020, Bruinvels 53 et al., 2021, Findlay et al., 2020, Heather et al., 2021, Martin et al., 2018, Read et al., 2021, 54 55 Solli et al., 2020). For instance, research by Armour et al. (2020), Brown et al. (2020), Findlay et al. (2020) and Martin et al. (2018) showed that MC related symptoms, both physical and 56 57 psychological, are prevalent in sportswomen, and most women perceive that these symptoms 58 compromise their exercise participation as well as performance and training, particularly during or just prior to menstruation. Recently, Bruinvels et al. (2021) used a novel approach 59 (Menstrual Symptom index [MSi]) that purports to quantify the type, number, and frequency 60 of cycle related symptoms. The authors demonstrated that symptoms are commonly reported 61 by regularly exercising women, and that a greater prevalence and frequency of symptoms (*i.e.*, 62 a higher MSi score) was correlated with an increased likelihood of negative outcomes, such as 63

64 missing training or competition. It is important to note, however that all previous studies have relied on retrospective self-reported data and therefore are potentially limited by memory 65 recall. Additionally, to date all studies have presented a general overview of symptoms 66 throughout the entity of the MC, as such key timepoints where specific symptoms might be 67 experienced were not examined in real-time, only retrospectively. Moreover, the tool 68 developed by Bruinvels et al. (2021) did not capture the severity of symptoms, which could 69 70 theoretically influence outcomes in addition to the type and frequency of symptoms experienced. For example, an individual might only experience one symptom per MC however 71 72 the severity of this symptom could be severe and therefore have a greater impact on the likes of performance and training. As a result, the full extent of symptoms experienced by naturally 73 74 menstruating women, and their potential impact on exercise performance and training, have yet to be examined. 75

The naturally occurring MC is susceptible to external perturbations; around 50% of 76 77 sportswomen use some form of HC, with the OCP the most prevalent type (Heather et al., 2021, Martin et al., 2018). Whilst there are various types of OCPs each with different 78 79 compositions, potencies, and androgenicity, most are combined, monophasic, OCPs (mOCPs) that contain ethinyl oestradiol and a type of progestin delivered in a fixed amount for 21 pill-80 taking days, followed by seven pill-free days (Elliott-Sale et al., 2020). These exogenous 81 oestrogens and progestins act to suppress the hypothalamic-pituitary-ovarian (HPO) axis, 82 83 which results in low endogenous levels of sex hormones (Elliott-Sale et al., 2020). Specifically, mOCP use results in four distinct hormonal environments: 1) a downregulated endogenous 84 oestradiol profile during the 21 pill-taking days that rises during the seven pill-free days; 2) a 85 chronically downregulated endogenous progesterone profile; 3) a daily surge of synthetic 86 oestrogen and progestin during pill-taking days; and 4) seven exogenous hormone-free days 87 88 (Rechichi et al., 2009). In addition to its use as a birth control method, OCPs are commonly prescribed by medical professionals to ameliorate cycle related symptoms experienced across 89 the naturally occurring MC (Yonkers et al., 2008, Wong et al., 2009). However, recent research 90 91 highlights that some users still experience negative symptoms related to their OCP use, which might also affect performance and training (Clarke et al., 2021, Heather et al., 2021, Martin et 92 al., 2018, Nolan et al., 2022, Parker et al., 2020). Indeed, it has been reported that exogenous 93 ethinyl oestradiol has a higher oestrogen receptor affinity and is several times more potent than 94 endogenous oestradiol (Bennink et al., 2005), which might play a role in the aetiology of cycle 95 related symptoms during the pill-taking days. Additionally, it could be theorised that the 96

97 downregulation of endogenous sex hormones and sudden withdrawal of exogenous sex 98 hormones might play a role in the aetiology of cycle related symptoms during the pill-free days 99 (Sulak *et al.*, 2000). Despite this, few studies have investigated the experience of cycle related 100 symptoms in OCP users and their potential impact on perceived exercise performance and 101 training outcomes in active women.

Overall, given that sportswomen (irrespective of reproductive hormonal profile) might be 102 affected by cycle related symptoms, and that these symptoms have the potential to influence 103 104 aspects of exercise performance and training, it is important to gain a better understanding of symptoms in this population. Therefore, the purpose of this study was to: 1) retrospectively 105 describe and compare the type, frequency, and severity of symptoms experienced by naturally 106 menstruating women and mOCP users; 2) investigate in real-time the effect of MC and mOCP 107 108 phases on the type, frequency, and severity of symptoms; and 3) determine whether the symptoms experienced by naturally menstruating women and mOCP users during pre-defined 109 110 MC and mOCP phases are associated with perceived exercise performance and recovery time post-training. 111

112

#### **113 2.0 METHODS**

#### 114 **2.1 Participants**

In total, 42 women volunteered to take part. The sample included 21 naturally menstruating 115 (mean  $\pm$  standard deviation [SD]: age, 29  $\pm$  5 years; stature, 164.9  $\pm$  5.7 cm; mass, 63.7  $\pm$  9.1 116 kg) and 21 mOCP users (age 28  $\pm$  4 years; stature 165.2  $\pm$  7.1 cm; mass 60.9  $\pm$  11.6 kg). 117 Naturally menstruating participants self-reported having a regular MC between 21 and 35 days 118 in length for at least one year prior to participation. Additionally, all naturally menstruating 119 participants were not taking any form of HC for a minimum of three-months prior to the 120 investigation, and self-reported being free from other medication (i.e., hormonal replacement 121 therapy), MC related irregularities (e.g., amenorrhea), or conditions (e.g., polycystic ovarian 122 syndrome, endometriosis, pregnancy) known to affect the HPO axis. To employ a homogenous 123 124 design, all participants in the mOCP group reported taking a mOCP containing ethinyl oestradiol and progestin (Supplementary File 1) for 21 days, followed by a seven-day pill free interval (or 125 taken for 28 days, inclusive of a seven-day inactive/placebo pill interval) for a minimum of 126 three-months prior to the study (Elliott-Sale et al., 2013). All participants were deemed at least 127

recreationally active (McKay et al., 2022). Participants also reported taking part in multiple 128 sports/forms of activity (i.e., 'Running', 'Cycling', 'Swimming', 'Gym-based classes', and 129 'Weight training'). A small percentage (19%) of participants were classified as trained (McKay 130 et al., 2022). All participants were healthy, were not taking any form of medication, and were 131 free from any injury in the past six months. Full ethical approval was granted, and the study 132 was conducted in accordance with the Declaration of Helsinki. Written, informed consent was 133 obtained from all participants prior to participation. This study uses the term 'woman' for 134 people who self-report identifying with the sex they were assigned with at birth (Robinson et 135 136 al., 2022).

#### 137 **2.2 Design**

138 Data were collected for this study using two approaches. Firstly, an initial 54-part online survey was created (Online Surveys, Jisc, UK) and distributed to all participants via email. The survey 139 retrospectively assessed reproductive status, the type, frequency, and severity of symptoms 140 typically experienced, and the perceived effects of the MC and mOCP use on aspects of exercise 141 performance and training. Information gathered from the initial 54-part online survey was used 142 to ensure all participants met the *a priori* inclusion and exclusion criteria, and to answer aim 143 one, and partly answer aim three of the present study. Secondly, following a virtual pre-testing 144 session to habituate participants to all procedures, participants tracked cycle related data (i.e., 145 day of MC or mOCP cycle, blood flow amount during period or withdrawal bleed, as well as 146 ovulation tracking in naturally menstruating participants), and their symptoms daily to further 147 quantify symptom type, frequency, and severity across pre-defined MC and mOCP phases. To 148 do this, each participant received a unique link to an online form (Google Forms, Google, UK), 149 consisting of 12 questions, which they completed daily, at a similar time of day (± two-hours), 150 to minimise the effects of diurnal variation. Recording of daily cycle related data and symptom 151 tracking began on day one of menses in naturally menstruating women, or day one of pill-152 withdrawal in mOCP users and continued for the duration of one full MC (*i.e.*, until the onset 153 of the next menses) or mOCP cycle (i.e., until day 21 of pill-consumption). A daily text reminder 154 was sent at the same time each day to all participants to ensure compliance. Results from this 155 daily cycle related data, and symptom tracking were used to answer aim two, and partly answer 156 aim three in the present study. 157

158 **2.3 Methodology** 

Data gathered from the initial 54-part online survey included: 1) demographic data (i.e., age 160 and sex); 2) current MC and HC status (i.e., MC length, period duration, type of HC used and 161 duration of use); 3) type, frequency, and severity of cycle related symptoms; 4) training history; 162 5) respective cycle monitoring and tracking; 6) perceived effects of the MC and mOCP use on 163 aspects of performance and training; and 7) previous education on the MC and HC use 164 (Supplementary File 2). All survey questions were either multiple choice check boxes, short/ 165 long text answers, a matrix, or a linear scale. Free text answers were also requested where 166 'Other' was applicable. The 54-part online survey was adapted specifically for this study based 167 168 on previous research in this area (Bruinvels et al., 2021). The survey was piloted with five researchers and five participants for language, comprehension, and compliance. To help 169 170 content and face validity, as well as general clarity around questions, minor edits were made to the survey wording based on their feedback. To ensure a uniform understanding of the pre-171 defined MC and mOCP phases and to assist in the answering of questions an idealised four-172 phase lay definition (and diagram) was provided to participants within the survey. Although 173 174 only three pre-defined *phases* were used within the study for those in the naturally menstruating group, a four-phase lay diagram was provided to help participant understanding 175 176 (Supplementary File 3). The survey was designed to take approximately 20 minutes to 177 complete.

#### 178 2.3.2 Daily cycle related data and symptom tracking

Data gathered from the daily cycle and symptom tracking form included: 1) day of MC or 179 mOCP cycle; 2) blood flow amount during period or withdrawal bleed; and 3) symptom type, 180 presence, and severity with 18 possible symptoms listed based on previous work (Bruinvels et 181 al., 2021), with the addition of symptom severity questions enhancing the form and the novelty 182 of the current study. Additionally, to identify MC phases participants in the naturally 183 menstruating group were asked to track ovulation using urinary ovulation detection kits 184 (Advanced Digital Ovulation Test, Clearblue, Switzerland) and basal body temperature (BBT) 185 using a digital thermometer (One Step Digital Basal Thermometer, Home Health Ltd, UK). 186 Specifically, beginning on a predetermined day (depending on each participant's typical cycle 187 length), using the start of menses as day one, participants in the naturally menstruating group 188 used the ovulation detection kits once daily (at the same time each day with first urine void 189 190 after their longest sleep), until a positive ovulation test was achieved. The urinary ovulation

detection kit tracked changes in oestrogen and luteinizing hormone (LH) concentration (greater 191 than 40 mIU·mL<sup>-1</sup>) and provided participants with a static smiley face when the 'LH surge' 192 was detected. The urinary ovulation detection kit used had 99% accuracy in detecting the 'LH 193 surge', as determined by the manufacturer. Participants were asked to record the status of the 194 smiley face within the daily form. For BBT, participants were instructed to take this measure 195 orally every morning before rising and record the value in °C, to two decimal places, within 196 the daily form. Further information pertaining to cervical fluid was also collected but was not 197 198 used to confirm ovulation and/or classify phases. All questions in the form were either multiple choice check boxes, short text answers, a matrix, or a linear scale. The form was designed to 199 take approximately five minutes to complete. 200

## 201 2.3.3 Menstrual cycle and combined, monophasic, oral contraceptive pill phase classification

The MC and mOCP cycle, were separated into pre-defined phases (Supplementary File 4). 202 Specifically, the MC was classified into three *phases* which were selected as those theoretically 203 coinciding with low concentrations of oestrogen and progesterone (phase one, 'early follicular 204 phase'), rising/high oestrogen and low progesterone (phase two, 'mid- to late 205 follicular/ovulatory phase'), and high oestrogen and progesterone (phase three, 'mid-luteal 206 phase'). Menstrual cycle phases were calculated based on the first day of menstruation. Phase 207 one was defined as the first five days of the cycle from the onset of self-reported menstruation. 208 Phase two was defined as four days prior to a positive ovulation test and the day of the positive 209 ovulation test (Stricker et al., 2006). Phase three was classified as the time between five to nine 210 211 days post a positive ovulation test and was also indicated by BBT (i.e., a significant rise in BBT [approximately 0.25 to 0.50 of a degree] following ovulation, that remains relatively 212 constant for 10 to 16 days; Thompson et al., 2019). Participants that did not report a positive 213 ovulation test or a biphasic rise in BBT were subsequently excluded from the analysis. As such, 214 215 our confidence in the hormonal profiles captured during phase one and phase two of the MC in the present study is high, however phase three of the MC is estimated rather than confirmed, 216 thus our confidence in the hormonal profile of phase three is limited. To ensure an equal 217 number of days were used for each *phase* the mOCP cycle was classified into four *phases*: phase 218 one ('mOCP withdrawal', days 1 to 7 of pill-free days), phase two ('mOCP consumption, days 219 220 1 to 7'), phase three ('mOCP consumption, days 8 to 14'), and phase four ('mOCP consumption, days 15 to 21). The *phases* of the mOCP cycle were defined using counting from either the first 221 day of the mOCP free *phase* or the mOCP taking *phase*. It is important to acknowledge that 222

these profiles, reflecting  ${}_{m}OCP$  consumption and withdrawal, are pseudo-phases as they are 'artificial' *phases* in comparison with the phases of the MC, but for the purposes of this study will be referred to as *phases*.

### 226 **2.4 Data analysis**

## 227 2.4.1 54-part online survey

The raw data from the 54-part online survey were exported from Online Surveys directly to 228 Microsoft Excel software for Windows. The sum of the number of symptoms reported was 229 calculated to create the 'total number of symptoms', with a maximum value of 18. The average 230 frequency of the symptoms reported, was then calculated using a Likert scale, based on 231 previous research (Bruinvels et al., 2021). Specifically, the following numerical value was 232 attached to the Likert, 'often' = 3 points, 'sometimes' = 2 points, 'rarely' = 1 point, and 'never' 233 = 0 points for each of the 18 symptoms reported. The 'symptom index (Si) score' was then 234 calculated by totalling the frequency score (0-3) for each symptom (0-18) reported, with total 235 scores ranging from 0 (minimum) to 54 (reporting every symptom, often). 'Average symptom 236 237 severity score' was assessed using a Likert scale, with the following numerical values attached to the Likert, 'absent' = 1, 'mild' = 2, 'moderate' = 3 and 'severe' = 4. The 'Si score' was then 238 239 multiplied by the 'average symptom severity score' to provide an overall 'Si × severity score'.

## 240 *2.4.2 Daily cycle and symptom tracking*

The raw data from the daily cycle related data and symptom tracking form were exported from 241 Google Forms directly to Microsoft Excel software for Windows. To quantify the type, 242 frequency, and severity of symptoms across the MC and mOCP cycle, cycles were first 243 244 separated into pre-defined *phases* (see heading '2.3.3'). The number of symptoms experienced in each phase were summed to create the 'symptom frequency per phase'. The mode severity 245 (*i.e.*, 'absent' = 1, 'mild' = 2, 'moderate' = 3 and 'severe' = 4) of each of the symptoms 246 experienced per phase was then calculated to create the 'symptom severity per phase'. Finally, 247 the 'symptom frequency per *phase*' was then multiplied by the 'symptom severity per *phase*' 248 to give an overall 'phase symptom frequency × severity score'. 249

### 250 **2.5 Statistical analysis**

The statistical software package IBM SPSS Statistics (Version 24, SPSS Inc., USA) for 251 Windows was used to conduct the statistical analysis. Data are presented as mean  $\pm$  SD (for 252 normally distributed, continuous data), medians  $(Mdn) \pm$  interquartile range (IQR; for non-253 normally distributed, or ordinal data), and number and percentages (for categorial data). 254 Normal distribution of data was confirmed using the Shapiro-Wilk test. If a normality breach 255 was detected, a nonparametric Mann-Whitney U test was used. For data collected from the 256 initial 54-part online survey an independent t-test was used to assess between group 257 comparisons in the 'total number of symptoms' and the 'Si score'. As data were ordinal, a 258 259 nonparametric Mann-Whitney U test was used to assess for any between group comparison in 'average symptom severity'. Additionally, as data were not normally distributed, a 260 nonparametric Mann-Whitney U test was used to assess for any between group comparison in 261 the overall 'Si × severity score'. For data collected through daily tracking, one-way repeated 262 measures ANOVAs were used to assess for differences in 'symptom frequency per phase', and 263 the 'phase symptom frequency × severity score' across MC and mOCP 'phases' 264 (independently). Sphericity was assessed using Mauchly's test of sphericity. Where sphericity 265 was violated, a Greenhouse-Geisser correction was used. If a significant main effect was 266 observed, a post hoc Bonferroni-corrected pairwise comparison was used. As data were ordinal, 267 268 a nonparametric Friedman test was used to assess differences in 'symptom severity per phase' across MC and mOCP phases (independently). A binomial logistic regression was used to 269 270 predict changes in perceived exercise performance and recovery time post-training in specific MC and mOCP phases (from the 54-part online survey), based on the 'phase symptom 271 272 frequency  $\times$  severity score' (from the daily cycle and symptom tracking form). The odds ratio for each variable and the accompanying 95% confidence intervals (CIs) were calculated. The 273 274  $\alpha$  for all statistical tests was set at  $P \leq 0.05$ .

275

#### 276 **3.0 RESULTS**

### 277 **3.1 Participant characteristics**

Self-reported, descriptive, MC and mOCP characteristics data are displayed in Supplementary
File 5.

# 3.2 The type, frequency, and severity of cycle related symptoms from the initial 54-part online survey

- The reported type and frequency of each symptom, for each group, are shown in Figure 1. There was no difference in the 'total number of symptoms' reported (naturally menstruating:  $12 \pm 4$  symptoms; mOCP:  $11 \pm 4$  symptoms; P = 0.353), the 'Si score' (naturally menstruating:  $26 \pm 10$ ; mOCP:  $22 \pm 10$ ; P = 0.200), 'average symptom severity' (naturally menstruating: 3 'moderate' [*Mdn*]; mOCP: 2 'mild' [*Mdn*]; P = 0.145), and the overall 'Si × severity score'
- 287 (naturally menstruating: 68 [*Mdn*]  $\pm$  90 [*IQR*]; mOCP: 50 [*Mdn*]  $\pm$  56 [*IQR*]; *P* = 0.113) between
- 288 naturally menstruating women and <sub>m</sub>OCP users.

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

Two naturally menstruating women were excluded from this analysis because one exhibited a short luteal phase defect (defined by not having a luteal phase long enough to meet mid-luteal analysis classification in the present study), and one was identified as anovulatory (defined by a lack of a positive ovulation test and no biphasic response in BBT). The different types of symptoms experienced across MC and mOCP *phases*, for each group, are shown in Figure 2.

There was a difference in 'symptom frequency per *phase*' across MC *phases* (P = 0.001; Figure 296 3, Panel A), whereby naturally menstruating women experienced a greater frequency of 297 symptoms during phase one ( $28 \pm 18$  symptoms) of the MC compared to phases two ( $13 \pm 13$ ) 298 symptoms; P = 0.006 [95% CI 4 to 27]), and three (16 ± 12 symptoms; P = 0.010 [95% CI 3 299 to 22]), whereas there was no difference between phases two and three (P = 0.611). There was 300 no difference in 'symptom severity per *phase*' across MC *phases* (phase one: *Mdn* = 2 ['mild'], 301 phase two: Mdn = 2 ['mild'], and phase three: Mdn = 2 ['mild']; P = 0.084). The 'phase 302 symptom frequency  $\times$  severity score' differed across MC *phases* (P < 0.001; Figure 3, Panel 303 304 B), whereby the '*phase* symptom frequency  $\times$  severity score' was greater during phase one (62)  $\pm$  43 Au) of the MC compared to phases two (26  $\pm$  25 Au; *P* = 0.005 [95% CI 10 to 62]) and 305 three  $(37 \pm 27 \text{ Au}; P = 0.026 [95\% \text{ CI } 3 \text{ to } 48])$ , but there was no difference between the phases 306 two and three (P = 0.287). 307

There was a difference in 'symptom frequency per *phase*' across mOCP *phases* (P < 0.001; Figure 4, Panel A), whereby pill users experienced a greater frequency of symptoms during phase one ( $35 \pm 24$  symptoms) compared with all other mOCP *phases* (phase two:  $18 \pm 20$ symptoms, P = 0.001 [95% CI 6 to 28]; phase three:  $13 \pm 17$  symptoms, P < 0.001 [95% CI 9 to 34]; phase four:  $19 \pm 21$  symptoms P < 0.003 [95% CI 5 to 27], respectively), but there was no difference between any of the mOCP consumption *phases* (P = 0.079, P = 1.000, and P =

0.376, respectively). There was no difference in 'symptom severity per phase' across mOCP 314 *phases* (phase one: Mdn = 2 ['mild']; phase two: Mdn = 2 ['mild']; phase three: Mdn = 2315 ['mild']; and phase four: Mdn = 2 ['mild']; P = 0.702). The 'phase symptom frequency x 316 severity score' differed across  $_{\rm m}$ OCP *phases* (P < 0.001; Figure 4, Panel B), whereby the '*phase* 317 symptom frequency  $\times$  severity score' was greater during phase one (73 ± 55 Au) of the mOCP 318 *cycle* compared with all other mOCP *phases* (phase two:  $36 \pm 39$  Au, P = 0.002 [95% CI 11 to 319 61]; phase three:  $30 \pm 46$  Au, P = 0.005 [95% CI 11 to 75]; phase four:  $42 \pm 51$  Au, P = 0.022320 [95% CI 4 to 59], respectively), however there was no difference between any of the mOCP 321 consumption *phases* (P = 0.981, P = 1.000, and P = 0.477, respectively). 322

# 323 3.4 Perceived effect of menstrual cycle and combined, monophasic, oral contraceptive pill 324 *phase* on aspects of exercise performance and training

325 The perceived effect of MC and mOCP phases on aspects of exercise performance and training in naturally menstruating women and mOCP users as determined from the initial 54-part online 326 survey is shown in Table 1. Specifically, 67% of naturally menstruating women reported a 327 perceived improvement in their exercise performance during phase two of the MC, whilst 38% 328 reported a perceived decrease in exercise performance during phase one of the MC. Most 329 naturally menstruating women reported that their perceived recovery time following a training 330 session took longer during phase one (48%), whereas the majority perceived their recovery 331 time following a training session to be quicker in phase two (67%). Fifty-seven percent of 332 mOCP users reported a perceived improvement in their exercise performance during pill-taking 333 days, whilst 57% reported a perceived decrement in exercise performance during pill-free days. 334 Most mOCP users reported no differences in perceived recovery time following a training 335 336 session across mOCP *phases* (57% and 71%, respectively).

## 337 3.5 Association between perceived exercise performance and recovery time post-training 338 and the experience of cycle related symptoms

The effect of '*phase* symptom frequency × severity score' on the probability of perceived reduced/improved exercise performance or longer/quicker recovery time post-training across MC *phases* in naturally menstruating women and across  $_{m}OCP$  *phases* in pill users is shown in Table 2 (as determined from both the initial 54-part online survey and daily tracking data). The odds ratios for the '*phase* symptom frequency × severity score' provide an estimate of the change in odds for the corresponding response variable per unit increase in '*phase* symptom frequency × severity score'. A higher '*phase* symptom frequency × severity score' was

associated with a perceived reduction in exercise performance and a longer recovery time post-346 training during phase one of the MC in naturally menstruating women, and during pill-free 347 days in <sub>m</sub>OCP users. Specifically, it is estimated that the odds of perceiving performance as 348 reduced in phase one of the MC/ pill-free days are multiplied by 1.07 and 1.04 per unit increase 349 in '*phase* symptom frequency × severity score', respectively. Likewise, it is estimated that the 350 odds of perceiving recovery time to take longer post-training during phase one of the MC/ pill-351 free days are multiplied by 1.04 and 1.03 per unit increase in '*phase* symptom frequency  $\times$ 352 severity score', respectively. 353

354

## 355 4.0 DISCUSSION

The purpose of this study was to examine the type, frequency, and severity of symptoms 356 experienced by naturally menstruating women and mOCP users, and their perceived effect on 357 exercise performance and recovery time post training. Two approaches were used to answer 358 these aims, firstly an initial retrospective 54-part online survey, and secondly a cycle and 359 symptom form completed daily across one MC or mOCP cycle. Data from the initial 360 retrospective survey showed that cycle related symptoms were commonly reported by a group 361 of recreationally active women, and there appears to be no differences in symptomology 362 between naturally menstruating women and mOCP users. As such, these results emphasise the 363 need for active women, and those working with them, to consider regular and consistent 364 365 monitoring of cycle related symptoms, to the same degree, irrespective of mOCP use. 366 Moreover, data from daily symptom tracking showed that the type of symptoms reported, as well as symptom frequency and severity, changed across MC and mOCP phases, whereby 367 368 participants experienced a greater magnitude of symptoms whilst bleeding (*i.e.*, during phase one of the MC in naturally menstruating women, and during the pill-free days in mOCP users) 369 370 compared to all other timepoints. Finally, experiencing a greater magnitude of symptoms 371 (higher '*phase* symptom frequency × severity score'), was associated with a greater likelihood of perceived negative outcomes, including a perceived reduction in exercise performance and 372 a perceived longer recovery time post-training, whilst all participants were bleeding. Together, 373 these results highlight the importance of daily symptom mapping, as retrospective recall does 374 375 not account for the potential effect of different phases on the magnitude of cycle related symptoms, which when elevated might translate to negative implications on perceived 376 performance and recovery outcomes. Further research is required to establish whether these 377

perceived negative effects result in an actual reduction in performance and/or recovery insportswomen.

380 Data from the present study showed that cycle related symptoms are prevalent in mOCP users, and that symptomology appears to be similar among naturally menstruating women and mOCP 381 users, even though OCPs are often prescribed to women with the intention of alleviating 382 symptoms associated with the MC (Yonkers et al., 2008, Wong et al., 2009). Indeed, this study 383 shows that the most reported symptoms in mOCP users are 'Mood changes/ irritability/anxiety', 384 which agrees with previous findings by Heather et al. (2021) who reported that the majority 385 (56%) of OCP users reported side effects of use, with the most common being mood 386 387 disturbances. Interestingly, results from the current study show no difference in the frequency and severity of cycle related symptoms between the naturally menstruating women and mOCP 388 389 users. This is despite 46% of pill users in the present study reporting the use of mOCPs to manage the symptoms experienced during the naturally occurring MC. Although, it is 390 391 important to note that previous experience of symptoms prior to mOCP use is unknown so this finding must be interpreted in context. In agreement with these findings, Clarke et al. (2021) 392 393 showed similarities in the symptoms experienced between HC users and naturally menstruating women, although this study extends these findings using a novel symptom monitoring tool. 394 However, regardless of the prevalence of cycle related symptoms, they might not be seen as a 395 396 deterrent from OCP use, with previous work highlighting that the reported benefits of HC use, such as its use as a birth control measure, outweigh the experience of negative symptoms 397 (Martin et al., 2018, Parker et al., 2020). Thus, it is important that sportswomen do not solely 398 make their decision to use or not use OCPs based on the cycle related symptom data reported 399 herein and all relevant factors should be considered before individuals make this decision. 400 Overall, these results indicate that with or without the intention of mOCP use to reduce cycle 401 related symptoms, there appears to be no difference in symptomology between MC and mOCP 402 403 users. Therefore, practitioners are recommended to monitor the magnitude of cycle related symptoms, and use this data to develop symptom management strategies, in all sportswomen, 404 405 irrespective of reproductive hormonal profile.

Few studies in active women have quantified the symptoms experienced across pre-defined MC and <sub>m</sub>OCP phases in real-time, and instead have focused on collecting retrospective symptom data across the entity of the MC and HC *cycle*. However, considering the different potential factors driving symptoms key timepoints for symptoms are likely to vary across

phases. Indeed, the present study shows that during phase one of the MC the frequency and 410 severity of symptoms experienced was greater when compared to all other MC phases, in 411 naturally menstruating women. Whilst the aetiology of MC symptoms is likely complex and 412 multifactorial, the changes in symptoms across MC phases might be attributable to fluctuations 413 in endogenous sex hormones (oestrogen and progesterone) across the MC. For example, the 414 magnitude of symptoms experienced in this study was greater when oestrogen and 415 progesterone were at their lowest in naturally menstruating women. Additionally, an 416 417 overproduction of prostaglandins occurring at this timepoint (i.e., during menstruation) has 418 been commonly cited to result in primary dysmenorrhea (Guo et al., 2013). Likewise, together, the changes in the release of inflammatory markers (Puder et al., 2006) and reactive oxygen 419 species (Gaskins et al., 2012) across the MC might have caused the 'period pain' and other 420 physical symptoms experienced at this time in the present study. Moreover, it is thought that 421 variations in neurobiology across the MC, such as alterations in serotonergic and gamma-422 aminobutyric acid systems (Ansdell et al., 2019), as well as dopaminergic signalling (Del Río 423 et al., 2018) could affect the prevalence and severity of psychological symptoms experienced 424 425 by naturally menstruating women across MC phases. Results from the current study also 426 revealed that, like their naturally menstruating counterparts, mOCP users also experienced 427 changes in symptom magnitude across mOCP phases, with a greater frequency and severity of symptoms reported during the pill-free days when typically, a withdrawal bleed occurs, which 428 429 agrees with previous literature (Sulak et al., 2000). Therefore, it is plausible that the action of bleeding (i.e., the mechanisms that result in the withdrawal bleed and the perceptual effects of 430 431 bleeding) during the pill-free days might play a role in the aetiology of mOCP symptoms during the pill-free days regardless of circulating hormone concentrations. In contrast, given that 432 433 exogenous ethinyl oestradiol has a higher oestrogen receptor affinity and is several times more potent than endogenous oestradiol (Bennink et al., 2005), its sudden withdrawal during the pill-434 435 free days might remove any potential positive effects on symptomology, and thus contribute to the symptoms experienced during this time. Although, it is important to gain a better 436 understanding of the aetiology of cycle related symptoms in both naturally menstruating and 437 <sub>m</sub>OCP users from future research. 438

Understanding the frequency and severity of symptoms is important as recent research has
shown that an increased number of both physical and psychological cycle related symptoms is
associated with changes in various aspects of exercise performance and training. Specifically,
Bruinvels *et al.* (2021) reported that experiencing a greater number of MC symptoms was

correlated with changing/missing training, missing a competition, as well as needing to use 443 pain medication. Although agreeing with the work by Bruinvels et al. (2021), the current study 444 extends these findings to consider the phase effect of cycle related symptoms on exercise 445 performance and recovery time post training. Indeed, the current study highlights that having 446 a higher '*phase* symptom frequency × severity score' was associated with negative outcomes, 447 such as a perceived reduction in exercise performance and a longer recovery time post-training, 448 whilst participants were bleeding. While previous work investigating the effect of the MC and 449 OCP use on performance and training has focussed on qualitative outcomes, few studies have 450 451 examined the influence of symptoms on these outcomes. Indeed, a recent systematic review and meta-analysis investigating the effect of MC phase on exercise performance (McNulty et 452 al., 2020) showed that performance might, on average, be reduced by a trivial amount during 453 the early follicular phase of the MC, compared with all other MC phases, in some individuals. 454 Whilst a mechanistic explanation was beyond the scope of the paper, it was indicated that 455 456 performance changes could be attributable to the fluctuations in endogenous sex hormones across the MC, but the potential influence of symptoms on these objective markers of 457 458 performance was not considered. However, as established from the current results, the perceived reduction in performance during phase one of the MC, in some individuals, could be 459 460 attributable to the greater magnitude of symptoms experienced at this timepoint, within those individuals. Unfortunately, within the current study it was not possible to compare time aligned 461 phase symptomology between naturally menstruating women and mOCP users, thus it is 462 unknown if the previous trivial difference in exercise performance reported between naturally 463 464 menstruating and OCP users (Elliott-Sale et al., 2020) might also be explained by group differences in symptomology during phase one, when both groups were bleeding. As such, 465 there is a need to adopt a multifaceted approach to investigating the effect of MC and mOCP 466 phase on performance and training, which considers not only the reproductive hormonal milieu, 467 but also the symptoms experienced by the individual, irrespective of whether they are naturally 468 menstruating or taking the mOCP. Future work should adopt our real-time, daily, data collection 469 processes to investigate the potential relationship between cycle related symptoms and 470 objective exercise performance and training outcomes and should build upon these data with 471 mechanistic work to fully understand the underlying processes driving this potential 472 relationship. Moreover, from a practical position, it is important for practitioners to track cycle 473 related symptom data daily, rather than retrospectively, to identify key timepoints where an 474 individual might experience a greater magnitude of symptoms which could potentially impact 475 their perception of performance and/or recovery. 476

#### 477 **4.1 Limitations and future directions**

It is important to acknowledge that the current study has several limitations. Indeed, data was 478 collected from a small group (n = 42) of recreationally active women, therefore the average 479 response presented in this study might not be specific and meaningful to all women. As such, 480 further research using a larger sample size and investigating within different populations (*i.e.*, 481 elite woman athletes) is warranted. Data from the initial 54-part online survey are self-reported, 482 and therefore reliant on memory recall. Additionally, this study used an adapted version of the 483 MSi tool developed by Bruinvels et al. (2021), however, quantifying symptoms in this way has 484 not been formally validated. Moreover, it is important note that this study focused on three pre-485 486 defined cycle phases, as such this data disregards the late luteal phase whereby there is a swift and substantial ratio change in sex hormone concentrations. Indeed, the late luteal phase is 487 488 thought to be a key window whereby the magnitude of symptoms might be most affected which could theoretically have a greater influence on performance and training outcomes (Bruinvels 489 490 et al., 2022). Thus, in the future, studies should consider adopting a more fluid research design that allows for the investigation of multiple timepoints across the MC (i.e., inclusion of the late 491 luteal phase) or OCP use, as this will help provide a complete picture of potential effects, 492 493 allowing sportswomen to perform and train consistently across their entire respective cycle. 494 Furthermore, although the current study utilised two (*i.e.*, calendar-based counting and urinary 495 ovulation detection kits) out of the possible three recommended methods to identify MC phase and confirm an ovulatory cycle for experimental designs within this field, the methods used do 496 not provide any information regarding endogenous sex hormone concentrations (Thompson et 497 al., 2019). Since MC phase was not subsequently verified by serum for both oestrogen and 498 progesterone (due to restrictions because of the COVID-19 pandemic) it slightly reduces our 499 confidence in the accuracy of the sex hormone environment implied by the phase definitions 500 used in the present study (i.e., if the actual sex hormone concentrations matched the predicted 501 502 sex hormone concentrations; Elliott-Sale et al., 2021). Whilst we have a high degree of confidence in the determination of phase one and two, as oestrogen and progesterone need to 503 be low to menstruate, and a positive urinary ovulation test result infers the pre-ovulatory peak 504 505 in oestrogen, phase three is estimated and thus, where possible, future studies need to improve methodological quality. However, it is essential to acknowledge the real-world application of 506 507 the methods utilised in the present study. For example, it can be impractical and expensive to 508 take serum blood samples from all women to verify phase of cycle within an applied 509 environment and instead the use of non-evasive, cost-effective, and immediate methods, such

as BBT and urinary ovulation detection kits offer useful insights into potential sex hormone 510 concentrations (Hicks et al., 2022). Only naturally menstruating women and mOCP users were 511 included in the current study, however previous research shows that negative symptoms are 512 more common in progestin-only HC users (Martin et al., 2018, Parker et al., 2020). Similarly, 513 the brand, composition of synthetic oestrogen and progestin, dosage, and androgenicity of 514 mOCP used by participants in the pill group differed which could have influenced 515 symptomology. Therefore, future research should consider investigating symptoms and 516 perceived performance and training effects in active women using different forms of HC, and 517 518 where possible try to achieve a homogenous sample. It is also necessary to acknowledge that symptomology is complex, and it remains impossible to decipher whether the reported 519 symptoms were directly related to the MC or mOCP use. Further, it is important to consider the 520 individual nature of the MC and responses to mOCP use, and that physiology (McNulty et al., 521 2021) and lifestyle factors (*i.e.*, diet, exercise, sleep, and stress) might not be the same across 522 consecutive MCs or mOCPs within the same individual. As such, it is possible that symptoms 523 might differ largely between individuals and between cycles within the same individual. 524 525 Therefore, practically it is key to consider these effects on an individual level, as some women might be affected and others not, and future studies should explore variability in symptoms 526 527 within individuals from one cycle to the next to facilitate a deeper understanding of individual responses. Finally, data were collected during the COVID-19 pandemic, thus it is unknown 528 529 whether, and to what extent, this might have had an influence on the cycle related symptoms experienced during this time (Phelan et al., 2021). Despite these limitations, our dataset 530 531 provides a new insight into the symptoms experienced by some naturally menstruating women and mOCP users, which should be considered by active women and those working with them. 532

## 533 **4.2 Practical implications**

534 These findings emphasise the importance of continued awareness of cycle related symptoms and their potential impact on exercise performance and recovery time post training to inform 535 best practice. Given the similarities in symptomology between naturally menstruating and 536 mOCP users, regular screening of symptom profiles across all sportswomen (irrespective of 537 538 reproductive hormonal profile) is advised based on these results, and the use of methods provided in the present study to monitor symptoms might be considered as a suitable tool within 539 a practical setting. Moreover, given the potential perceived negative effect of symptoms on 540 exercise performance and training outcomes at different timepoints across the MC and mOCP 541

*cycle*, real-time, consistent, symptom mapping should be considered to identify and predict key 542 windows of opportunity for symptom management strategies, and thus limit any potential 543 negative effect of symptoms on performance or training outcomes. Additionally, the inter-544 individual variability in symptoms experienced and their association with perceived 545 performance and training outcomes in the present study supports an individualised approach. 546 For example, it is likely that individuals who experience a high number of symptoms and 547 perceive these symptoms to influence performance and training will report the biggest benefit 548 of symptom mapping alongside proactive symptom management. 549

550

### 551 5.0 CONCLUSION

This study provides an in-depth insight into the type, frequency, and severity of symptoms 552 experienced by a group of naturally menstruating women and mOCP users, across pre-defined 553 cycle *phases*, relative to their perceived impact on exercise performance and recovery time 554 post-training. Results revealed that symptoms were common in these women, but there were 555 556 no differences in symptomology between groups. The type, frequency, and severity of symptoms changed across cycle *phases*, with a greater magnitude of symptoms reported whilst 557 558 bleeding. A higher 'phase symptom frequency × severity score', was associated with reduced exercise performance and a longer recovery time post-training whilst bleeding. Practically, 559 560 these results emphasise the need for active women, and those working with them, to consider real-time monitoring of symptoms, and any associated impact on exercise performance and 561 recovery, rather than relying on retrospective data. This recommendation is applicable 562 regardless of sex hormone profile. In turn, this should be accompanied, where needed, by 563 individualised management strategies to minimise any negative effects of symptoms on 564 exercise performance and recovery, particularly around key phases where the magnitude of 565 symptoms might be greater. Further high-quality investigation is needed to understand the 566 influence of symptomology on objective markers of exercise performance and recovery. 567

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#### 689 TABLES

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

Outcome	Group	Not applicable		Phase 1		Phase 2		Phase 3		Phase 4	
		n	%	n	%	n	%	n	%	n	%
More likely to decrease the	Naturally menstruating	6	29	11	52	0	0	0	0	-	-
number of training sessions	mOCP	8	38	12	57	1	5	1	5	1	5
More likely to increase the	Naturally menstruating	8	38	1	5	10	48	7	33	-	-
number of training sessions	mOCP	9	43	0	0	12	57	12	57	12	57
More likely to miss a	Naturally menstruating	2	10	16	76	0	0	0	0	-	-
training session	mOCP	10	48	11	52	0	0	0	0	0	0
More likely to miss	Naturally menstruating (n	2	50	2	50	0	0	0	0	-	-
competition	= 4) mOCP (n = 4)	2	50	2	50	0	0	0	0	0	0
Perceive a training session	Naturally menstruating	3	14	12	57	1	5	5	24	_	-
to be harder	mOCP	5	24	16	76	0	0	0	0	0	0
Porocivo e training sossion	Naturally monstructing	6	20	2	14	11	52	Q	28		
to be easier	mOCP	10	29 48	2	14	9	43	8 9	43	- 9	43

Perceive performance to be improved	Naturally menstruating mOCP	3 8	14 38	4 1	19 5	14 12	67 57	9 12	43 57	- 12	57
Perceive performance to be reduced	Naturally menstruating mOCP	6 9	29 43	8 12	38 57	1 0	5 0	1 0	5 0	-0	- 0
Feel more fatigued prior to, during and post a training session	Naturally menstruating mOCP	1 7	5 33	11 14	52 67	0 0	0 0	3 0	14 0	- 0	- 0
Feel more energised prior to, during and post a training session	Naturally menstruating mOCP	3 13	14 62	3 2	14 10	13 7	62 33	7 7	33 33	- 7	33
Experience reduced motivation towards training	Naturally menstruating mOCP	2 8	10 38	10 13	48 62	0 0	0 0	3 0	14 0	- 0	- 0
Experience increased motivation towards training	Naturally menstruating mOCP	4 12	19 57	2 0	10 0	12 9	57 43	10 9	48 43	- 9	- 43
Perceive recovery to take longer post a training session	Naturally menstruating mOCP	4 12	19 57	10 9	48 43	0 0	0 0	1 0	5 0	- 0	- 0
Perceive recovery to be quicker post a training session	Naturally menstruating mOCP	5 15	24 71	1 1	5 5	14 5	67 24	8 5	38 24	- 5	- 24

Table 2. Estimated odds ratios and 95% confidence intervals for the effect of '*phase* symptom frequency × severity score' on perceived exercise performance and recovery time post-training across menstrual cycle *phases* (*i.e.*, phase one: 'early follicular phase'; phase two: 'late follicular/ovulatory phase'; and phase three: 'mid-luteal phase') and combined, monophasic, oral contraceptive pill ( $_{m}OCP$ ) *phases* (phase one: ' $_{m}OCP$  withdrawal', days 1 to 7 of pill-free days; phase two: ' $_{m}OCP$  consumption, days 1 to 7'; phase three: ' $_{m}OCP$  consumption, days 8 to 14'; and phase four: ' $_{m}OCP$  consumption, days 15 to 21') in naturally menstruating women (n = 19) and pill users (n = 21).

	Group	Reduced performance				Improved performance				Longer recovery				Quicker recovery			
		Phase	Phas	Phas	Phas	Phas	Phase	Phase	Phase	Phase	Phas	Phas	Phas	Phas	Phase	Phas	Phas
		1	e 2	e 3	e 4	e 1	2	3	4	1	e 2	e 3	e 4	e 1	2	e 3	e 4
<i>'Phase</i>	Naturally	n = 8	n =	n =	-	n =	n = 14	n = 9	-	n = 10	n =	n =	-	n =	n = 14	n =	-
sympto	menstruatin		1	1		4					0	1		1		8	
m	g	1.07	-	-	-	0.84	1.00	1.00	-	1.04	-	-	-	-	0.99	1.01	-
frequen		(1.01				(0.6	(0.97	(0.97		(1.00					(0.96	(0.9	
cy ×		to				6 to	to	to		to					to	7 to	
severity		$1.14)^{*}$				1.08	1.05)	1.04)		$1.07)^{*}$					1.03)	1.05	
score'						)										)	
	mOCP	n = 12	n =	n =	n =	n =	n = 12	n = 12	n = 12	n = 9	n =	n =	n =	n =	n = 5	n =	n =
			0	0	0	1					0	0	0	0		5	5
		1.04	-	-	-	-	0.99	0.99	1.00	1.03	-	-	-	-	1.01	1.00	1.00
		(1.00					(0.97	(0.96	(0.98	(1.00					(0.99	(0.9	(0.9
		to					to	to	to	to					to	8 to	9 to
		$1.08)^{*}$					1.01)	1.01)	1.02)	$1.05)^{*}$					1.03)	1.02	1.02
																)	)

Values are odd ratios (95% confidence interval). \*denotes odd ratios deemed significant ( $P \le 0.05$ ). -denotes data not available (*e.g.*, no participant reported specific variable in specific *phase*).