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#### 16 Abstract

17 Physical activity and exercise training are especially important for reproductive-aged females 18 as exercise-induced health benefits can also affect their infants. However, levels of physical 19 inactivity remain high among females in this age group, before, during, and after pregnancy. 20 There is a great need for practical and feasible exercise modes to increase adherence to 21 exercise in this population, and interval training may be a time-efficient training modality. 22 Interval training is a form of exercise involving intermittent bouts of intense effort 23 interspersed with recovery periods of rest or lower-intensity exercise. A substantial amount 24 of research indicates that interval training induces superior cardiometabolic health benefits 25 compared with iso-energetic moderate-intensity continuous exercise. This review provides a 26 comprehensive overview of research on interval training interventions in reproductive-aged 27 females across various life stages, focusing on the cardiometabolic health benefits. We 28 discuss the potential role of interval training in premenopausal females with 29 overweight/obesity, polycystic ovary syndrome, and subfertility, as well as the potential 30 influence of oral contraceptives on cardiometabolic adaptations to interval training. Furthermore, this review also highlights recent findings supporting the beneficial role of high-31 32 intensity interval training for cardiometabolic health outcomes during pregnancy. In 33 summary, the existing evidence suggests that interval training can improve several 34 cardiometabolic and reproductive outcomes in females spanning different life stages. 35 However, more research is needed to further strengthen the evidence-base for physical 36 activity recommendations for females in their reproductive years of life.

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Keywords: Body composition, aerobic exercise, resistance exercise, exercise intensity,
 exercise metabolism, insulin resistance, obesity, reproduction, bone health, dyslipidemia

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#### 42 Introduction

43 Physical activity is established as a critical component of female health during preconception, 44 pregnancy, and postpartum. For reproductive-aged females, the benefits of exercise training 45 may not only affect their own health but also the health of their infants, since obesity and 46 insulin resistance affect egg cell quality and the intrauterine environment (Moholdt and 47 Hawley, 2020). Yet the majority of adolescent girls worldwide are insufficiently active 48 (Guthold et al., 2020) and only 4-15% of pregnant individuals meet the current 49 recommendations of 150 min of moderate-intensity physical activity per week (Santo et al., 50 2017, Gjestland et al., 2013, Tornquist et al., 2023). Furthermore, postpartum physical activity 51 and exercise volumes generally remain lower than pre-pregnancy levels (Hesketh et al., 2018, 52 Tornquist et al., 2023), and females who have given birth have lower cardiorespiratory fitness 53 than their age-matched counterparts (Rogers et al., 2020). Practical, enjoyable approaches 54 are clearly needed to improve adherence to exercise before, during, and after pregnancy.

55 Herein we review and discuss the potential of interval training, including high-intensity 56 interval training (HIIT) and sprint interval training (SIT), as an exercise modality to improve 57 cardiometabolic health and pregnancy outcomes in reproductive-aged females. Our aim was 58 not to contrast the effects of interval training with those of other types of exercise, such as 59 moderate-intensity continuous training (MICT) or strength training, rather to draw attention 60 to interval training as an alternative exercise option in this population. However, some of the 61 studies we discuss have made comparisons between adaptations after interval training and 62 other forms of exercise. The interval training terminology usually differentiates between two basic types of interval training at high exercise intensities: HIIT and SIT. HIIT, can be defined 63 as 'near maximal' efforts performed at intensities that elicits  $\geq$  80% (but often 85-95%) of 64 65 heart rate maximum (HRmax), whereas SIT is characterised by efforts performed at intensities 66 at or above the workload that would elicit peak oxygen uptake (VO<sub>2</sub>peak) (MacInnis and 67 Gibala, 2017). Both HIIT and SIT induce similar, and at times greater, improvements in 68 cardiometabolic health outcomes when compared with moderate-intensity continuous 69 training (MICT) (Jelleyman et al., 2015, Campbell et al., 2019, Sabag et al., 2022).

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HIIT, especially low-volume protocols, is a time-efficient exercise strategy that could counter
 the perceived 'time constraints' barrier to physical activity in the reproductive years (Coll et

al., 2017). Studies also suggest that women perceive greater enjoyment during HIIT compared
with during MICT, both when pregnant and not (Li et al., 2022, Wowdzia et al., 2022, Ong et
al., 2016)

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## 78 Interval training and cardiometabolic health in premenopausal females

79 Obesity and insulin resistance are associated with infertility and pregnancy complications 80 (reviewed by (Muhammad et al., 2023)). Maternal cardiometabolic health at the beginning of 81 pregnancy can also have a life-long influence on the health of the offspring (Moholdt and 82 Hawley, 2020). For females who are planning a pregnancy, interval training can be a means 83 to increase cardiorespiratory fitness, improve insulin sensitivity and reduce fat mass. Higgins 84 and colleagues showed that 6 weeks with three weekly sessions of 30-sec 'all-out' sprints, 85 repeated 5-7 times interspersed with 4 min low-intensity recovery, reduced total fat mass 86 and increased VO<sub>2</sub>peak more than MICT of equal estimated energy expenditure in young (~20 87 years old) women with overweight/obesity (Higgins et al., 2016). Similarly, Zhang and 88 colleagues showed greater visceral fat reductions after three weekly sessions of interval 89 training for 12 weeks (three separate protocols; two of which were isoenergetic to MICT) than 90 after MICT in young women with obesity (Zhang et al., 2021). HIIT has also been shown to be 91 equally effective as MICT in improving VO<sub>2</sub>peak in women aged 18-30 years with obesity, even 92 when the energy expenditure is markedly lower (~50%) and the time spent training is less 93 than half that of MICT (Kong et al., 2016).

94 Interval training can improve insulin sensitivity, which is important pre-pregnancy 95 since fasting blood glucose, blood insulin concentrations, and insulin resistance are 96 independent pre-pregnancy predictors of gestational diabetes (GDM) (Alwash et al., 2023). 97 Twelve weeks of interval training, both as SIT (80 x 6-sec cycling sprints interspersed with 9 98 sec rest), and HIIT (9 x 4-min cycling at 90% of VO<sub>2</sub>peak interspersed with 3 min rest) were 99 more effective than MICT in improving insulin sensitivity in young women with 100 overweight/obesity (Sun et al., 2019b). However, fasting glucose levels decreased only after 101 MICT. Another study showed 23% greater clamp-derived insulin sensitivity after a 10-week 102 HIIT programme, with two weekly sessions of 4 x 4 min work-bouts at 85-95% of HRmax and 103 one weekly session of 10 x 1 min with maximum effort, in women with overweight/obesity 104 referred to assisted fertilisation (Kiel et al., 2018). In summary, interval training can be a time-105 efficient exercise option to increase pre-pregnancy insulin sensitivity in females with 106 overweight/obesity, but continued research is needed to establish the effectiveness of107 interval training on insulin sensitivity in premenopausal females outside laboratory settings.

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#### 109 Interval training combined with dietary interventions

Combining interval training with dietary interventions is probably more advantageous for 110 111 cardiometabolic health benefits than either strategy alone. Indeed, the combination of HIIT 112 and time-restricted eating for 7 weeks induced greater reductions in body weight, fat mass, 113 and visceral fat area than each of these interventions on their own in reproductive-aged 114 women with body mass index  $\geq$  27 kg/m<sup>2</sup> (Haganes et al., 2022). The adherence to the HIIT 115 protocol, which was identical to the protocol in (Kiel et al., 2018), was > 90% of the scheduled 116 sessions for both the isolated HIIT group and the combined HIIT and time-restricted eating 117 group. These results indicate that HIIT, either as a sole intervention or combined with time-118 restricted eating, is a feasible and efficient lifestyle intervention to improve cardiometabolic 119 health in premenopausal females. However, a study from China reported improved VO<sub>2</sub>peak 120 but no additional effect of either MICT or HIIT added to a 4-week low-carbohydrate diet on 121 body weight, fasting glucose, or lipid concentrations in young females with 122 overweight/obesity (Sun et al., 2019a). Of note, the volume of HIIT in that study was very low, 123 with each session comprising only 2.5 min of exercise (10 x 6 sec work-bouts interspersed with 9-sec rest periods). Still, HIIT induced a ~15% improvement in VO<sub>2</sub>peak. The 124 125 corresponding improvement after MICT (comprising 30 min at 50-60% of VO<sub>2</sub>peak) was ~17%, 126 again showing the time-efficiency of HIIT for comparable improvements in cardiorespiratory 127 fitness (Sun et al., 2019a).

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# 129 Interval training and bone health

130 HIIT can also improve bone metabolism in young females, who constitute a critical 131 osteoporosis-prevention population. (Lu et al., 2022) showed that total bone mineral density 132 increased by 8.5% after 8 weeks of HIIT (versus 5.5% after MICT) among sedentary but 133 otherwise healthy females and that HIIT elicited greater changes in markers of bone metabolism (1,25-dihydroxyvitamin D<sub>3</sub>, calcaneus broadband ultrasound attenuation, and 134 135 calcaneus stiffness index). The HIIT programme consisted of three weekly sessions of 136 treadmill running, including 6 x 3-min bouts of running at 80-90% of VO<sub>2</sub>max, separated by 2-137 min active recovery at 30-40% of VO<sub>2</sub>max (Lu et al., 2022). The reason for the superior

osteogenic effect of HIIT is probably that impact force is a relevant element in the stimulationof bone metabolism (Santos et al., 2017).

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141 The influence of oral contraceptives on adaptations to interval training

142 Women taking oral contraceptives may not get the same cardiometabolic adaptations to 143 interval training, compared with women experiencing regular natural menstruation 144 (Schaumberg et al., 2017, Schaumberg et al., 2020). An observational study showed that oral contraceptive users had lesser VO<sub>2</sub>peak and peak cardiac output adaptations after a 4-week 145 146 SIT programme, compared with women with normal menstruation (Schaumberg et al., 2017). 147 The SIT protocol included three weekly cycling sessions of 10 x 1 min sprints at 100-120% of 148 peak power output interspersed by 2 min of passive recovery. Although VO<sub>2</sub>peak increased in 149 both groups (8.5% in the oral contraceptive users and 13% in those with normal 150 menstruation), the results indicated that oral contraceptives dampened physiological 151 adaptations to SIT. As such, exogenous ovarian hormones may limit central adaptations of 152 oxygen delivery, which has been demonstrated by a lesser improvement in pulmonary oxygen 153 uptake kinetics during a square-wave step-transition cycle protocol in oral contraceptive 154 users (Schaumberg et al., 2020). Interestingly, after a 4-week follow-up (detraining period), 155 the oral contraceptive users had a lower decline in physiological and performance 156 adaptations, compared with normal menstruating women (Schaumberg et al., 2017). The 157 knowledge about how the menstrual cycle and hormonal contraceptives affect physical 158 performance and adaptations to exercise training is still incomplete.

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## 160 Interval training in polycystic ovary syndrome

161 Interval training has also been shown to improve some cardiometabolic health outcomes in 162 individuals with polycystic ovary syndrome (PCOS). PCOS is the leading cause of anovulatory 163 infertility and menstrual disorders, and individuals with PCOS are at an increased risk of 164 obesity, insulin resistance, type 2 diabetes, dyslipidaemia, and cardiovascular diseases (Teede 165 et al., 2018, Hoeger et al., 2021, Fazleen et al., 2018, Melo et al., 2015). PCOS is characterised by excess androgen production by the ovaries as well as the adrenal glands contributing to 166 167 hyperandrogenism which presents as hirsutism, acne, androgenic alopecia, and/or increased 168 amount of testosterone, menstrual irregularities, oligo/anovulation, and insulin resistance. 169 Abnormal steroid metabolism resulting in increased cortisol production is also a feature of PCOS (Tsilchorozidou et al., 2003, Rosenfield and Ehrmann, 2016). Lifestyle modification,
including exercise and diet, is regarded as a cornerstone in PCOS management (Teede et al.,
2018), with the evidence to date suggesting that HIIT at least can provide short-term benefits
for symptom management (Santos et al., 2021, Patten et al., 2020).

174 (Mohammadi et al., 2023) reported that an 8-week interval training programme 175 consisting of three weekly sessions of 4 sets of 4-6 x 30-sec sprints at maximal aerobic velocity, 176 resulted in significant reductions in body weight, fat percentage, insulin resistance (HOMA-177 IR), LDL, and total cholesterol levels, as well as increased estimated VO<sub>2</sub>max. The 30-sec 178 sprints were interspersed with 30 sec of moderate-intensity recovery, while the sets of four 179 sprints were interspersed with 5 min passive recovery. In this study, testosterone and cortisol 180 levels decreased significantly after SIT, compared with a no-exercise control group. In another 181 study, 10 weeks of three weekly sessions of HIIT (two 4 x 4 min at 90-95% of HRmax and one 182 10 x 1 min at maximal intensity) improved insulin sensitivity (HOMA-IR) and VO<sub>2</sub>peak 183 (Almenning et al., 2015). Of note, these beneficial changes were evident without any 184 significant changes in body weight, body composition, or reproductive hormones, compared 185 with the no-exercise control group. However, a 16-week HIIT intervention, with two separate 186 HIIT groups, one performing the  $4 \times 4$  min protocol as described above and the other the 10 187 x 1 min protocol, did not induce any improvements in insulin sensitivity, body composition, 188 VO<sub>2</sub>peak, fat oxidation, endothelial function, or reproductive hormones (Kiel et al., 2022b, 189 Kiel et al., 2022a, Lionett et al., 2021). The most likely reason for no effects of HIIT in this 190 study was low adherence to the exercise protocol, with on average two sessions per week 191 during the 16-week intervention period.

192 HIIT can also lead to added cardiometabolic benefits to alleviate PCOS symptoms on 193 top of metformin therapy. (Samadi et al., 2019) showed that a 12-week aquatic 'Tabata-style' 194 interval training programme accompanied by oral metformin improved body composition, 195 estimated VO<sub>2</sub>max, insulin resistance (HOMA-IR), hirsutism severity, and several sexhormones relevant in PCOS pathology, compared with a control group of metformin only 196 197 therapy. The training protocol in this study consisted of three weekly sessions with four 4-min 198 bouts, each comprising eight rounds of 20-sec maximal effort work interspersed with 10 sec 199 of rest. However, there were no added effect of HIIT on menstrual frequency, compared with 200 the metformin-only control group.

201 Some randomised controlled trials (RCTs) have compared the effects of interval 202 training with those of MICT on cardiometabolic outcomes in PCOS (Nasiri et al., 2022, Ribeiro 203 et al., 2020, Patten et al., 2022). (Nasiri et al., 2022) reported similar improvements in body 204 composition after 8 weeks of three weekly sessions of either HIIT or a combination of MICT 205 and resistance training, but a greater increase in estimated VO<sub>2</sub>max after HIIT. Their HIIT 206 protocol was the same as in the study by (Mohammadi et al., 2023) above. The combination 207 group undertook 25-40 min treadmill running at 60-70% of HR reserve, in addition to 30-40 208 min resistance training. In line with this, (Ribeiro et al., 2020) reported similar reductions in 209 waist circumference without any change in body weight or testosterone levels after 16 weeks 210 with three weekly sessions of progressive MICT or HIIT. The adherence was higher to HIIT 211 (97%), which involved six to ten 2-min work-bouts progressing from 70% to 90% of HRmax, 212 compared with MICT (85%), involving 30-50 min continuous walking/running at 65-80% of 213 HRmax.

214 In contrast, (Patten et al., 2022) showed greater improvements in cardiometabolic and 215 reproductive outcomes after 12 weeks of HIIT than after MICT. The HIIT protocol in this study 216 consisted of twice weekly sessions of 12 x 1-min work bouts at 90-100% of HRpeak 217 interspersed with 2 min low-intensity recovery and one weekly session of 8 x 4 min at 90-95% 218 HRpeak interspersed with 2 min low-intensity recovery. The exercise protocols in this study 219 were designed to match the minimum exercise recommendations, and the MICT consisted of 220 three weekly sessions of 45 min continuous cycling at 60-75% of HRpeak. VO<sub>2</sub>peak increased 221 after both exercise protocols, but significantly more after HIIT than MICT (5.8 ml/kg/min 222 versus 3.2 ml/kg/min), and only HIIT improved insulin sensitivity (Patten et al., 2022). 223 Furthermore, menstrual cycle regulation improved after HIIT, independent of changes in body 224 weight, fat mass or fat distribution.

In summary, HIIT has positive effects on several cardiometabolic and reproductive outcomes in PCOS, but with inconsistent evidence for effects on body composition, and metabolic and reproductive outcomes (hormone levels, menstrual cycle regulation). These inconsistencies can probably be attributed to the different phenotypes of PCOS and their response to exercise interventions. Differences in the duration and intensity of exercise, study sample size, and adherence rate may also contribute to varying outcomes.

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# 232 Interval training and female fertility

The effect of exercise on fertility outcomes, especially in females undergoing artificial 233 234 reproductive techniques (ART) has been a disputable topic among researchers. A population-235 based cohort study reported that exercising for 4 hours or more per week before ART was 236 negatively associated with live births compared with females not regularly engaged in physical activity (Morris et al., 2006). In line with this, some earlier epidemiological 237 238 investigations showed that higher intensity and frequency of exercise increased risks of 239 subfertility and infertility (Gudmundsdottir et al., 2009) and delayed time to spontaneous 240 pregnancy (Wise et al., 2012). In contrast, others reported that physical activity before IVF 241 had no effect (Gaskins et al., 2016) or beneficial effects (Kucuk et al., 2010, Rich-Edwards et 242 al., 2002, Chavarro et al., 2007) on reproductive outcomes. The conflicting results across the 243 studies regarding the effect of physical activity on fertility outcomes can perhaps be 244 attributable to the type of infertility, classification system of exercise levels, recall bias of 245 reporting lifetime exercise, and other confounders such as dietary habits and individual 246 variabilities.

247 Several recent systematic reviews and meta-analyses concluded that physical activity 248 before ART is associated with increased rates of clinical pregnancy and live births (Rao et al., 249 2018, Hakimi and Cameron, 2017, Mussawar et al., 2023). In an observational cohort study 250 by (Palomba et al., 2014), physical activity before ART was associated with a 3-fold increase 251 in clinical pregnancy and live births. They also showed that a minimum of 30 min of vigorous 252 exercise 3 times per week significantly increased the chance of conception in females with 253 obesity and PCOS (Palomba et al., 2008). However, data on the effect of HIIT on fertility 254 outcomes are scarce. In a pilot RCT conducted by (Kiel et al., 2018), 3 weekly HIT sessions for 255 10 weeks improved cardiometabolic outcomes in females undergoing ART, but without any 256 significant differences in fertility outcomes. Interestingly, in the trial on HIIT in PCOS 257 mentioned above (Kiel et al., 2022b), eight participants (~20%) in the two HIIT groups, versus 258 none in the control group, became pregnant during the 16-week intervention period or the 259 follow-up at 12 months from baseline. Keeping the individual differences and the confounders 260 in mind, more studies need to be performed on the role of HIIT on reproductive outcomes in 261 females.

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## 263 Interval training during pregnancy

264 Regular physical activity in pregnancy is well established to be safe and effective in improving 265 health outcomes for both mother and baby (da Silva et al., 2017). Further, vigorous-intensity 266 exercise, typically prescribed at intensities up to 85% of maternal HRmax (MHRmax), in the 267 third trimester of pregnancy appears to be safe for most healthy pregnancies (Beetham et al., 268 2019). The upper limit of exercise intensity recommended during pregnancy has historically 269 been increasing. It was generally accepted that bed rest or 'confinement' was appropriate in 270 early 20th-century prenatal care. In 1985, the American College of Obstetricians and 271 Gynecologists (ACOG) issued the first guidelines for physical activity during pregnancy, in 272 which they warned pregnant individuals to keep MHR below 140 beats/min and not to 273 exercise for more than 15 min at a time (ACOG, 1985). In 1994, the HR-based 274 recommendation was removed, and women were advised to base their workouts on 275 subjective feelings of tiredness (ACOG, 1994). From around 2003, there were several physical 276 activity guidelines for pregnancy around the world, all of which agreed that moderate-277 intensity exercise appeared to be safe (ACOG, 2003, Davies et al., 2003). Finally, recent 278 guidelines suggest either high-intensity exercise only in a monitored environment (Mottola et 279 al., 2018) or only for those who have previously engaged in vigorous exercise (Bull et al., 280 2020). As such, HIIT has only been investigated in recent years by a handful of studies.

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# 282 Acute effects of interval training during pregnancy

283 We are at an exciting time in exercise and pregnancy research, at which there is a growing 284 interest in examining the feasibility, safety, and efficacy of higher-intensity exercise in 285 pregnancy. Indeed, some recent investigations have assessed the acute maternal and fetal 286 responses to HIIT during pregnancy (Wowdzia et al., 2022, Wowdzia et al., 2023, Anderson et 287 al., 2021, Andersen et al., 2021). In a randomised, crossover study, Wowdzia and colleagues 288 reported that HIIT (10 x 1 min work bouts at  $\geq$  90% MHRmax, interspersed with 1 min active 289 recovery) and MICT (30 min at 64-76% of MHRmax) equally reduced post-exercise interstitial 290 glucose levels in normoglycaemic pregnant individuals (Wowdzia et al., 2022). In patients with 291 GDM, moderate-intensity postprandial interval walking, with alternating 3 min of slow and 292 fast walking for 20 min, was effective in reducing postprandial glucose excursions (Andersen 293 et al., 2021). In (non-pregnant) people with type 2 diabetes, a single session of high-intensity 294 interval walking was superior to MICT matched for oxygen consumption, time, and perceived 295 exertion in reducing postprandial blood glucose levels (Karstoft et al., 2014). Postprandial HIIT may therefore be an efficient option for improving glycaemic control in individuals with GDM,
however, the potential for HIIT to reduce blood glucose levels in pregnant people with
hyperglycaemia requires further study.

299 Blood flow is redirected to working muscles in periods of higher intensity exercise, and 300 the historically conservative prescription of exercise intensity during pregnancy stems from 301 worries about compromised well-being of the fetus at high exercise intensities. However, the 302 fetus adapts to reduced blood flow by increasing its own HR, on average by 6 bpm (Skow et 303 al., 2019). Such an increase is a beneficial adaptation which may help to optimise the fetal 304 autonomic nervous system and placental function (Kubler et al., 2022, Bauer et al., 2020). 305 Whether there is an upper limit of maternal exercise (i.e., a high volume and/or high intensity 306 of exercise) for these beneficial fetal and placental adaptations is still not known.

307 A recent study from (Wowdzia et al., 2023) showed no indications of fetal distress 308 after 10 x 1 min HIIT sessions at which the intensity was  $\geq$  90% MHRmax, with no signs of fetal 309 bradycardia or changes in umbilical blood flow measures (Wowdzia et al., 2023). In line with 310 this, a study by Anderson and colleagues demonstrated that HIIT performed as circuit-based 311 resistance training did not influence fetal HR or umbilical flow indices (Anderson et al., 2021). 312 In this study, pregnant participants in late second and early third trimesters completed 20-313 sec resistance training circuits with intensity up to 90% of MHRmax, interspersed with 60-sec 314 recovery. However, a study in pregnant Olympic-level athletes showed transient fetal 315 bradycardia and high umbilical artery pulsatility index when the participants exercised at > 316 90% of MHRmax for 5 min (Salvesen et al., 2012). The clinical significance of this finding is 317 unclear, and an earlier study suggested no adverse effects on birth weight or placenta weight 318 after a high-volume, high-intensity exercise regime during pregnancy (Kardel and Kase, 1998). 319 These conflicting findings may be due to the duration of the work-bouts, and fetal well-being 320 may be compromised during prolonged exercise at high intensity.

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# 322 *Effects of interval training interventions in pregnancy*

There are only a few RCTs of the effects of regular interval training in pregnancy on maternal and infant outcomes. Halse and colleagues conducted an RCT comparing the effects of supervised interval training on a cycle ergometer, combined with unsupervised steady-state exercise, with a usual care group in pregnant participants with diet-controlled GDM (Halse et al., 2014, Halse et al., 2015). This study found that 6 weeks of three weekly interval training 328 sessions of up to 45 min, including 15-60 sec bouts at 75-85% of age-predicted MHRmax 329 interspersed with 2-min moderate-intensity recovery periods, improved aerobic fitness 330 (Halse et al., 2015) and postprandial glucose concentrations (Halse et al., 2014) compared 331 with a usual care group. No adverse events were reported in this study. Furthermore, Wang 332 and colleagues showed that three weekly sessions of cycling SIT reduced the incidence of 333 GDM for individuals with overweight/obesity (22% in the exercise group versus 41% in the 334 control group) (Wang et al., 2017). The cycling exercise programme consisted of 3-5 repetitions of 30-sec sprints interspersed with 2 min recovery, was initiated in the first 335 336 trimester, and continued until gestational week 37. In the latter study, the frequency of 337 potential adverse events, such as miscarriage and fetal death did not differ between the 338 exercise and control groups.

339 A recent study showed increased VO<sub>2</sub> at the anaerobic threshold, reduced fat mass and 340 increased fat-free mass after an online 8-week HIIT intervention, compared with an 341 education-only control group (Yu et al., 2022). There is no detailed description of the HIIT 342 protocol, but the aim was that the participants exercised in work bouts with an intensity 343 greater than the anaerobic threshold for as long as they felt comfortable (Yu et al., 2022). The 344 authors did not observe any adverse effects during pregnancy, childbirth, or on neonatal 345 outcomes. Interestingly, there was a greater dropout in the education-only group compared 346 with the HIIT group (Yu et al., 2022). This finding aligns with other studies which indicate 347 greater enjoyment and therefore adherence with interval training (Li et al., 2022, Wowdzia et 348 al., 2023, Ong et al., 2016).

349 Interval training prescription during pregnancy

350 Some individuals develop medical conditions during pregnancy for which exercise, 351 particularly high-intensity exercise, is not recommended. Some countries recommend using 352 a screening tool, such as the Get Active Questionnaire for Pregnancy from Canada (Canadian 353 Society for Exercise Physiology, 2021), to screen for any absolute or relative contraindications 354 to exercise. It also seems pertinent to suggest, that until further evidence becomes available, 355 the duration of work-bouts with intensity > 90% of MHR should be  $\leq 1$  min. There are several ways intensity can be measured in pregnancy. Cardiovascular parameters change in 356 357 pregnancy, for example, resting HR increases throughout gestation. However, maximum HR 358 drops only slightly during pregnancy (~4 bpm) (Lotgering et al., 1991), and therefore using a 359 percentage of MHRmax is suitable in pregnancy. However, not all women will have access to

360 HR monitors or know their HR max, in which case rating of perceived exertion (RPE), or the 361 'talk-test', can be suitable. All these measures rate the relative intensity of the exercise, even 362 with increasing body weight and increased dyspnoea throughout gestation. As such, the 363 absolute workload may decrease as pregnancy progresses but still provides the same 364 physiological stimulus to the body. Some form of HIIT can thus continue through to the end 365 of the third trimester of pregnancy for most women.

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#### 367 Interval training in the postpartum period

368 The postpartum period, sometimes referred to as the 'fourth trimester', is the time after 369 delivery when the pregnancy-related physiologic changes are returning to the non-pregnant 370 state. The World Health Organization 2020 guidelines on physical activity and sedentary 371 behaviour recommend that postpartum females should be physically active for at least 150 372 min/week, with moderate intensity (Bull et al., 2020). According to the Physical Activity 373 Guidelines for Americans (U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, 2018), only 374 individuals who already do vigorous-intensity aerobic exercise, can continue doing so after 375 their pregnancy. The research underlying these recommendations is very limited and often 376 based on expert opinion or consensus rather than empirical evidence. Moderate-to-vigorous 377 physical activity generally declines in pregnancy and remains low postpartum (Hesketh et al., 378 2018, Borodulin et al., 2009). Consequently, cardiorespiratory fitness is lower postpartum 379 compared with age-matched females who have not given birth (Armitage and Smart, 2012, 380 Rogers et al., 2020). Since HIIT can be an efficient exercise mode for rapid improvements in 381 cardiorespiratory fitness, such training could have a place after pregnancy to prevent a 382 decline in fitness (Figure 1). We could, however, not find any studies on the effect of HIIT in 383 the postpartum period, on maternal health outcomes or breast milk composition. 384 Nevertheless, current expert opinions suggest a gradual start and subsequent progression of 385 HIIT postpartum (Bø et al., 2017, Deering et al., 2020).

There are few exercise guidelines specifically for lactating people and little knowledge about the impact of exercise on breast milk composition. Based on a few observational studies (Lovelady et al., 1990, Fly et al., 1998) and one RCT (Dewey et al., 1994), the consensus seems to be that exercise does not affect milk production, composition, or infant growth (ACOG, 2020, Bane, 2015). However, some studies indicate that there is a transient increase in lactate concentrations in breast milk after high-intensity exercise (Carey et al., 1997, Wallace and Rabin, 1991). Based on these findings, it has been discussed whether increased lactate concentrations may alter the taste of breast milk, and thus reduce the infants' acceptance of the milk after high-intensity exercise (Larson-Meyer, 2002). However, (Wright et al., 2002) showed that high-intensity exercise did not impede infant acceptance of breast milk postexercise. An ongoing RCT will determine the effect of maternal HIIT on breastmilk composition in lactating people with overweight/obesity (Moholdt et al., 2023).

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## 399 **Concluding remarks and future perspectives**

400 Although females are less likely than males to be included in exercise training studies 401 (Anderson et al., 2023), emerging evidence suggests that regular physical activity undertaken 402 as HIIT improves cardiometabolic and reproductive outcomes in reproductive-aged females 403 spanning different life stages (Graphical Abstract). As such, HIIT has been shown to be 404 beneficial in females with obesity, PCOS, diabetes, and GDM. Several guidelines suggest that 405 moderate to vigorous activity has beneficial effects in females undergoing ART, even if HIIT is 406 most often not mentioned specifically in such guidelines. Furthermore, evidence to date 407 suggests that HIIT may be a suitable option also in pregnancy, yet we need more evidence of 408 the safety of HIIT to confidently integrate it into physical activity guidelines for pregnant 409 individuals. Recent studies also show that at least some HIIT protocols are well tolerated by 410 the fetus. Additional research is needed on HIIT in pregnancy to provide reassurance and 411 support to individuals who wish to participate in this type of exercise, without fear of harming 412 themselves or their baby. Indeed, conservative advice on exercise during pregnancy may increase the fear of exercise and lead to lower levels of physical activity and reduced 413 414 psychological well-being (Coll et al., 2017). Moreover, maintaining a high level of training 415 during pregnancy may also assist with a faster return to exercise training in the postpartum 416 period. There is a particular paucity of research on HIIT in the postpartum period, and this 417 should be a fruitful topic for further studies. Finally, supervised HIIT may also provide a more 418 time-efficient and enjoyable option for women who may otherwise not meet PA guidelines.

419

## 420 Take home message

- Physical activity levels remain low in many reproductive-aged females.
- Interval training can be an alternative exercise option, that is time-efficient and
  provides multiple health benefits.

424 Recent studies indicate that high-intensity interval training is safe also during 425 pregnancy. 426 More research is needed to establish the safety and efficacy of interval training 427 during pregnancy and postpartum. 428 Funding 429 430 TM has received funding from the European Research Council (ERC) under the EU's Horizon 431 Europe Research and Innovation Programme agreement no. 101075421 and from the European Foundation for the Study of Diabetes and the Novo Nordisk Foundation 432 (NFF19SA058975). MAJS received funding from the Liaison Committee for education, 433 434 research, and innovation in Central Norway. 435 436 **Competing interests** 437 The authors declare there are no competing interests. 438 439 Data availability 440 This manuscript does not report data. 441 442 References 443 444 ACOG 1985. Technical bulletin number 87—ACOG guidelines: Exercise during pregnancy and 445 the postnatal period. *Exercise in pregnancy*, 313-319. 446 ACOG 1994. Exercise during pregnancy and the postpartum period. International Journal of 447 Gynecology & Obstetrics, 45, 65-70. 448 ACOG 2003. Exercise during pregnancy and the postpartum period. Clin Obstet Gynecol, 46, 449 496-9. 450 ACOG 2020. Physical Activity and Exercise During Pregnancy and the Postpartum Period: 451 ACOG Committee Opinion, Number 804. Obstet Gynecol, 135, e178-e188. ALMENNING, I., RIEBER-MOHN, A., LUNDGREN, K. M., SHETELIG LOVVIK, T., GARNAES, K. K. 452 453 & MOHOLDT, T. 2015. Effects of High Intensity Interval Training and Strength 454 Training on Metabolic, Cardiovascular and Hormonal Outcomes in Women with 455 Polycystic Ovary Syndrome: A Pilot Study. PLoS One, 10, e0138793. 456 ALWASH, S., MCINTYRE, D. & MAMUN, A. 2023. The pre-pregnancy fasting blood glucose, 457 glycated hemoglobin and lipid profiles as blood biomarkers for gestational diabetes mellitus: evidence from a multigenerational cohort study. J Matern Fetal Neonatal 458 459 Med, 36, 2195524. 460 ANDERSEN, M. B., FUGLSANG, J., OSTENFELD, E. B., POULSEN, C. W., DAUGAARD, M. & OVESEN, P. G. 2021. Postprandial interval walking-effect on blood glucose in 461 pregnant women with gestational diabetes. Am J Obstet Gynecol MFM, 3, 100440. 462

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762	Figure 1. The theoretical slopes of cardiorespiratory fitness during female lifespan under
763	several different conditions: Nulligravida individuals (never pregnant), primiparous (has given
764	birth once), and multiparous (has given birth more than once).
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# Time

