1 The relationship between gestational weight gain, maternal upper-body subcutaneous fat

2 changes and infant birth size: a pilot observational study amongst women with obesity.

3 Abstract

4 Background: It is widely acknowledged that maternal obesity and excessive gestational weight gain

5 (GWG) are associated with increased risk of fetal macrosomia and recent studies have suggested a role

- 6 for the timing and composition of GWG.
- 7 Aims: To examine the effect of the rate of change in GWG and maternal upper-body subcutaneous fat on
- 8 neonatal anthropometric outcomes in a pilot observational study amongst women with obesity.

9 Study design: Expectant women with a body mass index (BMI) > 30 kg/m² at first antenatal appointment

- 10 were recruited at 12 weeks gestation. Maternal height, weight and skinfold thickness (SFT)
- 11 measurements were collected at baseline and repeated at 28 and 36 weeks gestation. Following delivery,
- 12 World Health Organisation (WHO)-UK infant birthweight z-scores were calculated, and infant
- 13 anthropometric measurements were obtained.
- 14 Results: The sum of upper body SFT measurements increased in mid-pregnancy (0.08 ± 0.71 mm/week)
- 15 and decreased in late pregnancy (-0.04 ± 1.17 mm/week). After adjustment for maternal age, BMI and
- 16 parity, mid- but not late- pregnancy GWG was positively associated with infant birthweight z-score
- 17 (p<0.05), while mid- but not late-pregnancy changes in the sum of SFT were inversely associated with
- 18 infant birthweight z-score (p<0.01).
- 19 Conclusions: The present study suggests that mid- rather than late-pregnancy changes in weight and
- 20 upper-body subcutaneous fat are associated with infant birthweight. Further research is required in
- 21 larger, more diverse populations to explore whether pregnancy interventions aiming to improve maternal
- and offspring health can be personalised beyond BMI and GWG.

23 Key words: Pregnancy, maternal obesity, body composition, skinfold thickness, birthweight.

- 25 Abbreviations: BMI body mass index; GWG gestational weight gain; UK United Kingdom; UME -
- 26 upper arm muscle area estimate; UFE upper arm fat area estimate; FM fat mass; FFM fat free mass.

27 Introduction

28 Obesity has become a worldwide epidemic, and in the United Kingdom (UK), it is estimated that half 29 of women of childbearing age are living with overweight or obesity [1] with the prevalence of 30 maternal obesity increasing, as defined by trimester one body mass index (BMI) [2]. It is well 31 documented that maternal obesity has significant health implications for both mother and baby, 32 increasing the risk of complications during pregnancy and labour [3]. Offspring of mothers with 33 obesity are also more likely to be born large for gestational age or macrosomic [3-5] which 34 predisposes infants to adiposity and obesity during infancy and childhood [6,7]. Excessive gestational weight gain (GWG) carries similar risks to maternal obesity for both maternal and neonatal 35 36 outcomes [8,9], and postpartum weight retention increases the risk that women will enter their next 37 pregnancy with obesity [10].

38 Due to the lack of evidence-based guidelines, the National Institute for Health and Care 39 Excellence does not currently make recommendations for GWG amongst the UK population [11]. In 40 the United States (US), the Institute of Medicine (IOM) has published recommendations for GWG, which were updated in 2009 to include BMI-specific guidelines [12]. Although the IOM 41 42 recommendations were designed for the US population, the recommendations are largely based on 43 evidence derived from the US and Europe, thus, the IOM recommendations have been adopted in many other countries worldwide and are widely reported in the literature [13,14]. As well as total 44 GWG, the IOM recommend "normal" weekly rates of GWG for the second and third trimesters. 45

Recent studies conducted amongst women have tended to observe stronger positive associations between GWG in the second trimester [15,16] or early GWG (before the end of the second trimester) and infant birth size outcomes [17–19]. Studies examining the relationship between maternal body composition assessed via bioelectrical impedance analysis and infant birthweight have tended to observe a positive association between maternal fat-free mass (FFM), but not maternal fat mass (FM) [19–21]. With the exception of one study [17], these studies were conducted amongst women across all BMI ranges and tend to report estimates of FM or FFM at 53 single time-points rather than changes during pregnancy, which makes it difficult to establish 54 trimester-specific recommendations, particularly for women with obesity. A 2020 National Academy 55 of Medicine discussion paper focusing on GWG amongst women with obesity highlights that many 56 studies report total GWG over pregnancy, rather than patterns of GWG and correlations between 57 GWG and fetal growth [22]. A recent study conducted amongst 72 women with obesity observed 58 that individual differences in total GWG were predominantly explained by changes in FM, as assessed by air displacement plethysmography, with gains in FM significantly lower amongst women 59 60 with Class III obesity, than amongst those with Class I and II [23]. In addition, when examined by 61 trimester, FM was found to increase in the second trimester, and decrease in the third, whilst GWG 62 in the third trimester was attributed to FFM accumulation and fetal growth. However, this study did 63 not examine the relationship between these patterns of GWG, FM and FFM accrual and infant birth 64 size and there appears to be a lack of observational studies conducted amongst women with obesity 65 that examine these associations. The time periods examined also vary considerably between studies, with some looking at early versus late pregnancy, and others looking at trimesters, which makes 66 67 comparison difficult. Studies examining rates of GWG at frequent assessments are therefore useful 68 in order to increase our understanding of the importance of GWG during different stages of 69 pregnancy, facilitate comparison of GWG amongst pregnancies or varying durations, and to enable 70 the development of transferable recommendations.

71 The aim of the present study was therefore to identify whether there is a relationship 72 between trimester-specific rates of GWG or upper-body skinfold thickness (SFT) measurements and 73 infant birthweight and anthropometrics at birth. SFT measurements were chosen to assess 74 subcutaneous fat stores, which traditionally accumulate up to the end of the second trimester and 75 are subsequently mobilised in the third trimester to support maternal metabolism and rapid fetal 76 growth. In addition, callipers are a simple, quick, portable and cost-effective tool that could be used 77 in addition to weighing scales by health professionals caring for pregnant women, enabling 78 personalised care beyond BMI [24]. SFT measurements could also be used as an additional outcome

79 measure to assess the success of future pregnancy interventions aiming to reduce GWG and infant 80 macrosomia if a relationship is observed between changes in maternal upper body subcutaneous fat 81 and infant outcomes. As women with obesity are at increased risk of delivering a LGA or macrosomic 82 baby, but at lower risk of multiple pregnancy complications than women with Class III obesity [3], 83 the study focuses on women with Class I and Class II obesity (pre-pregnancy BMI \ge 30 kg/m² and <40 84 kg/m^2). To our knowledge, this is the first study to report the association between GWG, changes to maternal upper-body SFT and infant birth size amongst women with obesity in the UK. It is 85 86 therefore difficult to form a hypothesis in terms of how changes in maternal upper-body SFT will 87 affect infant birth size, however, based on previous work examining changes in maternal weight, FM 88 and FFM in women of all weights, we hypothesise that mid-pregnancy GWG will be more strongly 89 associated with infant birthweight than late-pregnancy GWG, and that we will observe reductions in 90 upper body subcutaneous fat in late pregnancy.

91 Methodology

92 Recruitment of women

Women aged between 18 and 40 years of age, with a BMI ≥ 30 and <40 kg/m² at booking and pregnant with a singleton pregnancy were eligible to take part in the study. Women meeting inclusion criteria were identified from their antenatal booking notes and approached by the researcher at their 12 week dating scan. Ethical approval was obtained from the NHS Health Research Authority National Research Ethics Service and local Research and Development approval was obtained from University Hospitals Plymouth NHS Trust.

99 Following recruitment, verbal and written informed consent were obtained from women, 100 and the first study visit occurred between 12 and 14 weeks gestation. Further visits occurred at the 101 end of the second trimester at approximately week 28 of gestation (visit 2), and at the end of the 102 third trimester at approximately week 36 of gestation (visit 3). A single researcher performed all 103 measurements at all study visits in order to reduce inter-observer error.

104 Maternal anthropometric measurements

105 In order to examine GWG throughout pregnancy, maternal weight was measured at each visit using 106 the same digital scales for each woman throughout the duration of the study. GWG was recorded as 107 a simple difference between weight at each study visit to give a crude value for GWG in each 108 trimester and a 'total' GWG for the study duration.

109 Weekly rates of GWG were calculated for each woman, based on the difference in weight between 110 study visits, divided by the number of weeks (and days) between visits. Reporting GWG in this way 111 accounts for gestation, and facilitates comparison against the IOM guidelines (Table 1). Rates of GWG were calculated for the second trimester (between visits 1 and 2, defined as mid-pregnancy 112 GWG), the third trimester (between visits 2 and 3, defined as late pregnancy GWG) and over the 113 114 study duration (between visits 1 and 3, defined as total pregnancy). Women were further classified 115 as achieving 'insufficient', 'adequate' or 'excessive' GWG according to their rate of GWG between 116 each of these time points according to IOM guidelines (Table 1) [12].

Range in kg	Mean (range) in kg / week
12.5 – 18.0	0.51 (0.44-0.58)
11.5 – 16.0	0.42 (0.35–0.50)
7.0 – 11.5	0.28 (0.23-0.33)
5.0 - 9.0	0.22 (0.17-0.27)
	12.5 – 18.0 11.5 – 16.0 7.0 – 11.5

117 Table 1 IOM recommendations for total and rate of weight gain during pregnancy, by pre-pregnancy BMI

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119 Maternal upper-body SFT of the biceps, triceps and subscapular were assessed at each 120 anthropometric visit according to the methods described by Kannieappan et al. [25] and the 121 International Society for the Advancement of Kinanthropometry (ISAK) [26] using Harpenden 122 callipers (British Indicators, Sussex, England) by a single researcher in order to minimise inter123 observer error. A full set of all three SFT measurements was completed in order to reduce the 124 effects of skinfold compressibility prior to repeating a second measurement at each site. If the 125 difference was greater than 7.5%, a third measurement was taken according to ISAK 126 recommendations. SFT for each site was reported in mm as the mean of two measurements, or the 127 median of three measurements [26]. In addition, SFT measurements were reported as the sum of all 128 three measurements rather than entered into an equation as recommended by numerous authors 129 to assess changes in body composition over time and to reduce systematic error associated with 130 equations, which are particularly difficult to validate in a pregnant population [27,28]. Rate of 131 change to the sum of these three SFT measurements over the study duration, as well as in mid-132 pregnancy and late-pregnancy were calculated (in mm/week) to adjust for length of gestation for 133 each woman.

134 Infant outcomes

135 Information about the infants was collected from hospital notes, or through measurements made by 136 the researcher. This included gestational age at delivery, method of delivery, the incidence of any 137 complications, infant gender, birthweight and head circumference. Birthweight and head circumference were used to calculate the z-scores from UK-WHO reference values for term infants 138 139 [29,30] using the LMS method [31] (LMS Growth Programme v2.77, Medical Research Council, UK) 140 which adjusted for infant gender. Crown-heel length was measured by the researcher using a mobile 141 measuring mat (Seca 210, Hamburg, Germany). This measurement was taken as soon after delivery 142 as possible and recorded to the nearest 5 mm. Length z-scores were also calculated from UK-WHO reference values for term infants [29,30] using LMS software and were adjusted for infant gender 143 144 and age at assessment.

145 Infant anthropometric measurements were taken as close to birth as possible, in most 146 instances within 72 hours of delivery. Where this was not possible, for example, for infants who 147 spent longer than this on the neonatal intensive care, or transitional care units, measurements were

used after adjusting them for age. A model that calculated an infant upper arm fat area estimate
(UFE) and upper arm muscle area estimate (UME) was used. The equations are based on mid-upper
arm circumference and triceps skinfold, and has been previously validated against magnetic
resonance imaging in children [32]:

152 TUA = $C^2 / (4\pi)$

153 UFE = C x (TS/2)

- 154 **UME = TUA UFE**
- 155 TUA = total upper arm area; UFE = upper arm fat area estimate; UME = upper arm muscle area
 156 estimate; C = mid upper arm circumference, TS = triceps skinfold (mm).

157 Statistical analysis

All data was entered into and analysed using SPSS (Statistics Package for the Social Sciences) for Windows version 21 (IBM, Chicago USA). The level of significance was set to a probability p < 0.05 for all statistical tests performed, and unless otherwise stated, data were presented as means \pm standard deviation (SD).

162 Continuous outcome measures were inspected for normality and if this assumption was met, parametric tests were performed. Pearson's correlation coefficients (r) were run to assess the 163 164 relationships between maternal changes in upper body subcutaneous fat and GWG. Multiple regression was used to evaluate the extent to which maternal rates of GWG and SFT changes over 165 166 pregnancy influence infant birthweight z-scores, UFE and UME after adjustment for maternal age, 167 booking BMI and parity, and in the case of UFE and UME, also adjusted for infant sex and gestational age. For all models there was independence of residuals, as assessed by a Durbin-Watson statistic of 168 169 approximately 2.0, homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values and there was no evidence of multicollinearity, as 170 171 assessed by tolerance values greater than 0.1. As the current study is the first, to the author's 172 knowledge, to examine the effect of the rate of change in upper body SFT measurements on birthweight and infant body composition, there was no data on which to base an *a priori* power calculation. However, posthoc power calculations show that the large effect sizes observed for the multiple regression analyses reached 99% power, and thus, statistical analysis was adequately powered.

177 Results

A total of 75 women gave their consent to participate in the study, which was 31% of women
approached. All women in the study identified their ethnicity as White Caucasian.

Data was collected for 75 women at visit one (12-14 weeks gestation), 65 women at visit two (28 weeks gestation), and 59 women at visit three (36 weeks gestation), with a total of 16 women lost to follow up between the first and last study visit. Womens' ages ranged from 19 years to 40 years, with a mean age of 29.8 \pm 4.8 years and mean BMI was 33.0 \pm 1.9 kg/m². There were no significant differences in maternal descriptive characteristics nor birth outcomes obtained from notes between women completing the study and those who were lost to follow up, data not shown.

186 Anthropometric measurements collected at each study visit are shown in Table 2.

	Visit 1 (n=75)	Visit 2 (n=65)	Visit 3 (n=59)
Weight (kg)	89.7 ± 8.7	95.1 ± 9.2	97.0 ± 9.9
Trimester-specific rate of GWG (kg/week)	-	0.3 ± 0.2	0.3 ± 0.4
Total pregnancy rate of GWG (kg/week)	-	-	0.3 ± 0.3
Proportion of women gaining in excess of IOM guidelines, n (%)	-	38 (59)	31 (54)
Arm circumference (cm)	35.2 ± 2.7	34.8 ± 2.8	34.3 ± 3.0
Triceps SFT (mm)	29.6 ± 5.2	30.4 ± 5.9	28.5 ± 5.7
Biceps SFT (mm)	$18.9\left\{ 17.6-20.3 ight\} ^{ op}$	19.1 ± 6.0	18.0 ± 6.4
Subscapular SFT (mm)	34.2 ± 7.5	35.4 ± 9.0	34.5 ± 8.5
Sum of SFT (mm)	83.7 ± 13.6	85.0 ± 15.0	81.0 ± 17.1
Trimester-specific rate of change in SFT (mm/week)	-	0.1 ± 0.7	-0.1 ± 1.2
Total pregnancy rate of change in SFT (mm/week)	-	-	-0.1 ± 0.7
Data are mean ± SD unless otherwi †Mean calculated by back-transfor			

187 Table 2 Maternal anthropometric measurements

Gestational weight gain (GWG), Institute of Medicine (IOM), Skinfold thickness (SFT).

188 189	Table 2 shows that mean rate of GWG in mid-pregnancy, late pregnancy, and in total over
190	pregnancy was 0.33 \pm 0.23, 0.29 \pm 0.40 and 0.32 \pm 0.26 kg/week, respectively. The proportion of
191	women gaining in excess of IOM guidelines was 59 and 54% in mid- and late-pregnancy, respectively.
192	In addition, Table 3 shows GWG class of obesity, and the proportion of women gaining weight in
193	excess of the IOM guidelines. Mid-pregnancy GWG and rate of GWG were significantly higher
194	amongst women in Class I (5.5 \pm 0.5 kg and 0.4 \pm 0.1 kg/week) than amongst women in Class II (2.8 \pm
195	1.2 kg; p = 0.026 and 0.2 \pm 0.1 kg/week; p=0.024), whereas GWG in late-pregnancy and over total
196	pregnancy were not significantly different between women in the two classes of obesity (P>0.05).

197 Table 3 Gestational weight gain by obesity class.

	Class I Obesity (n=46)	Class II Obesity (n=11)
Mid-pregnancy GWG (kg)	5.5 ± 0.5	2.8 ± 1.2
Mid-pregnancy rate of GWG	0.4 ± 0.1	0.2 ± 0.1
(kg/week)		
Proportion of women gaining in	31.0 (67.4)	4.0 (36.4)
excess of IOM guidelines in mid-		
pregnancy, n (%)		
Late-pregnancy GWG (kg)	2.4 ± 0.5	2.1 ± 1.0
Late-pregnancy rate of GWG	0.3 ± 0.1	0.3 ± 0.1
(kg/week)		
Proportion of women gaining in	26.0 (56.5)	5.0 (45.5)
excess of IOM guidelines in late-		
pregnancy, n (%)		
Total GWG (kg)	8.1 ± 1.0	4.9 ± 1.9
Total pregnancy rate of GWG	0.3 ± 0.1	0.2 ± 0.1
(kg/week)		
Proportion of women gaining in	28.0 (60.1)	5.0 (45.5)
excess of IOM guidelines over total		
pregnancy, n (%)		
Data are mean ± SD unless otherwise sta	ited.	
Gestational weight gain (GWG), Institute	of Medicine (IOM), Skinfold	thickness (SFT).

198

The rate of GWG was significantly and positively associated with the rate of SFT changes in mid-pregnancy (r=0.467), late-pregnancy (r=0.478) and over total pregnancy (r=0.609; all p<0.01). Changes in SFT were highly variable over pregnancy for the study population with an overall trend for a reduction in upper body subcutaneous fat between early and late pregnancy, although this did

203 not reach statistical significance (p=0.071).

204 Information concerning the delivery of infants, was available for 74 infants, of which three 205 were pre-term (<37 weeks gestation) and excluded from analysis. Infant anthropometric 206 measurements acquired from hospital notes and from the researcher's home visit are shown in 207 Table 4.

208 Table 4 Infant outcomes (n=71)

	n	Mean	SD
Gestation length (days) ⁺	71	275.0	13.0
Infant gender male, n (%)	71	41 (58)	-
Vaginal delivery, n (%)	71	45 (63)	-
Birthweight, g	71	3497.0	461.0
Birthweight, z-score	71	0.1	0.9
Head circumference, cm ⁺	55	35.0	2.0
Head circumference, z-score	55	0.4	1.3
Crown-heel length, cm	56	50.8	2.1
Crown-heel length, z-score	56	0.1	1.0
Infant arm circumference, cm ⁺	56	10.0	1.5
Triceps skinfold thickness, mm	56	6.7	1.8
UME, cm ²	56	445.5	105.1
UFE, cm ²	56	334.4	108.2
†Median (IQR)			

Standard deviation (SD), upper arm area muscle estimate (UME), upper arm area fat estimate (UFE).

210	A multiple regression was used to evaluate the extent to which maternal rates of GWG and
211	changes in SFT in mid- and late-pregnancy influence infant birthweight z-scores, UME and UFE after
212	adjustment for maternal age, booking BMI and parity. The models examining UFE and UME were
213	additionally adjusted for infant sex and gestational age, which were already accounted for in the
214	birthweight z-scores. The models statistically significantly predicted birthweight z-score (p=0.016)
215	and UFE (p = 0.017), but not infant UME, which didn't quite reach statistical significance (p =0.055).
216	As shown in Table 5, mid- but not late-pregnancy GWG was significantly and positively associated
217	with infant birthweight z-score, while mid- but not late-pregnancy change in the sum of SFT was

- significantly and inversely associated with infant birthweight z-score. Mid-pregnancy GWG was also
- 219 positively associated with infant UFE, however, for late pregnancy this relationship was reversed.

	Birthweight z-score (n=56)			UFE (n=53)		
	β	95% CI	р	β	95% CI	р
Mid-pregnancy GWG, kg/week	0.47	0.39 – 3.32	0.014	0.49	53.03 – 384.3	0.011
Mid-pregnancy change in the sum of SFT, mm/week	-0.50	-1.110.28	0.001	-0.28	-92.36– 3.39	0.068
Late-pregnancy GWG, kg/week	0.16	-0.39 – 1.12	0.329	-0.37	-187.6813.06	0.025
Late-pregnancy change in the sum of SFT, mm/week	-0.24	-0.45 - 0.05	0.107	0.19	-10.87– 47.71	0.212
Multiple regression adjust age* *UFE model only.	ed for ma	iternal body mas	s index, pa	arity, age,	infant sex* and ges	tational

220 Table 5 Multiple regression coefficients.

222 Discussion

This study is the first to our knowledge that has examined the impact of trimester-specific rates of GWG and changes in upper-body skinfold measurements on infant anthropometric measurements amongst women with obesity in the UK. Our findings suggest that mid- rather than late-pregnancy changes in weight and upper-body subcutaneous fat are associated with infant birthweight and upper body fat, suggesting that the second trimester may be an opportune window for pregnancy interventions aiming to improve pregnancy and infant outcomes for women with obesity.

229 Mid-pregnancy GWG was positively associated with birthweight z-score, while no 230 association was observed for late-pregnancy GWG. These observations are consistent with others in 231 the literature. For example, Farah et al. [19] observed a positive correlation between GWG before 232 the third trimester and infant birthweight, with no association reported for GWG during the third trimester in a cohort of 184 non-diabetic women in Ireland. Hivert et al [15] observed a positive 233 234 association between rate of GWG in all three trimesters and birthweight z-score amongst 979 235 mother-child pairs from the Project Viva cohort in the USA, with the largest effect size observed for 236 second trimester GWG, while Widen et al [16] observed that high rate of GWG, as defined by 237 tertiles, in the second trimester only was associated with higher infant birthweight and length 238 amongst 156 women in another USA cohort.

239 In terms of changes in maternal adiposity, there was large variation in the accumulation of 240 upper body fat amongst women in the cohort, and only mid-pregnancy changes in maternal upper-241 body skinfold measurements were associated with infant birthweight, in an inverse direction. This is 242 in contrast to findings from Dodd et al [33] who estimated maternal FM from the same three sites 243 measured in the present study amongst 1582 overweight women in South Australia, and did not 244 observe any significant associations between total GWG, maternal percentage body fat, nor 245 individual SFT measurements and infant birthweight. Hediger et al [34] observed an inverse 246 relationship between change in triceps, but not subscapular SFT and infant birthweight, but this was

247 in late pregnancy, in contrast to the findings in the current study, where late pregnancy changes in 248 SFT did not contribute to the regression model. The study by Hediger et al. [34] was conducted in 249 608 women of all weights, and is more consistent with previous literature that suggests pregnant 250 women accrue subcutaneous fat in early and mid-pregnancy, and tend to experience a decrease in 251 SFT measurements in trimester three, when fat stores are mobilised to support rapid fetal growth 252 [35,36]. However, studies conducted amongst women with obesity suggest that subcutaneous fat 253 gains tend to be less than for women with a lower BMI [37,38]. A recent study conducted by Most et 254 al. [23] found individual differences in GWG amongst 54 women with obesity to be largely explained 255 by changes in maternal FM, with gains in FM significantly higher for women with Class I and II obesity 256 (who gained FM) compared with women with Class III obesity (who lost FM). Straughen and 257 colleagues [39] observed that subcutaneous fat declines measured by ultrasound in women with 258 overweight or obesity were more rapid from early through to late pregnancy than amongst women 259 with a healthy BMI. In a study conducted by Misra and Trudeau (2011), circulating leptin 260 concentration at the start of pregnancy was 1.8 times higher for women with obesity compared with 261 healthy weight women, but by the end of pregnancy it was just 1.2 times higher. These findings 262 suggest that metabolic adaptions to pregnancy amongst women with obesity are different to those 263 observed amongst healthy weight women and may explain our observation of an inverse 264 relationship between mid-pregnancy subcutaneous fat changes and infant birth size, despite 265 observing a positive relationship between mid-pregnancy GWG and infant birthweight. As already 266 discussed women tend to experience a decrease in subcutaneous fat in the final trimester, but based 267 on the observations from the present study, in combination with observations form the literature 268 examining women with obesity discussed above, it is possible that fat stores are perhaps mobilised 269 earlier, thus perhaps explaining, in part, the observations in the present study. In addition, the 270 positive relationship between mid-pregnancy GWG and birthweight may be driven by changes to 271 weight that exclude upper-body subcutaneous fat. For example increases in FFM, which would

incorporate TBW, the foetus, placenta and amniotic fluid, or changes to maternal FM at other
locations, such as visceral adipose tissue and breast tissue.

274 It is also important to acknowledge, that although it was a strength of the current study that 275 one researcher took all SFT measurements to reduce inter-observer error, this would not be the case 276 in clinical practice, if multiple health professionals were taking measurements, nor in larger research 277 studies, with multiple researchers. Further studies using methods of assessment that are able to 278 distinguish between the maternal and fetal unit are warranted, although achievement of this is likely 279 to require the use of four-compartment models, which is not generally feasible in larger cohort 280 studies. Widen and Gallagher [24] suggest further validation of portable methods such as BIA is 281 required with revised equations for use in pregnancy to account for changes in TBW and FFM 282 hydration during pregnancy, that can be effectively used in women from pre- to post-partum.

283 With regards to infant adiposity, higher mid-pregnancy GWG predicted infant UFE, while in 284 late pregnancy, an inverse relationship was observed between GWG and UFE. The model did not 285 significantly predict infant UME. These findings agree with others in the literature to an extent, with 286 one study reporting that women gaining 'excessive' weight in early pregnancy gave birth to babies 287 with significantly greater fat mass assessed via total body electrical conductivity, than those born to 288 women gaining 'excessive' GWG in late pregnancy [18]. In keeping with the present study, the 289 Norwegian STORK study used SFT measurements to assess infant subcutaneous fat and observed 290 that mid-pregnancy rate of GWG (15-28 weeks gestation) was the strongest independent predictor 291 of infant sum of SFT [40]. However, unlike the present study, no proxy for infant FFM was used, and 292 late-pregnancy GWG was not reported.

Although findings from the current study and previous work suggest that infant birth size outcomes may be driven by changes in maternal weight and body composition, it is not clear whether advising women to adhere to IOM recommendations will positively influence infant birth size, particularly amongst women with obesity. This could explain why lifestyle interventions that successfully reduce GWG do not tend to observe significant reductions in infant birthweight [41,42].

298 A recent observational study, conducted in Ireland, suggests that when infant birthweight is 299 subtracted from total GWG, the positive correlation between GWG and birthweight no longer exists 300 [43]. The authors argue that modifying GWG and maternal adiposity in women with obesity during 301 pregnancy is therefore unlikely to influence the growth of the baby, and that focus should move 302 from restricting GWG to encouraging a varied, balanced diet. However, it is important to note that 303 even if modifying GWG during pregnancy cannot alter infant birthweight, excess GWG is associated 304 with increased risk of other adverse outcomes [8,44] such as postpartum weight retention, which 305 increases the risk of women entering subsequent pregnancies with obesity, as well as their risk of 306 associated chronic diseases [10].

307 The current study is not without its limitations, and the primary limitation of the study is the 308 sample size of 75 women all of white ethnicity. This is due to the location of the study hospital, 309 where 95.4% of the population identify themselves as belonging to this group [45]. Future studies 310 investigating the relationship between maternal subcutaneous body fat changes and infant birth size 311 need to be conducted in other areas of the UK amongst women with obesity to determine whether 312 similar patterns are observed amongst more diverse populations. In addition, women were recruited 313 at the end of their first trimester, at their 12 week dating scan, and therefore, we were unable to 314 collect information concerning GWG and body composition changes from conception to week 12 315 gestation. Although some studies have indicated that minimal GWG occurs in the first trimester [12], 316 physiological changes such as growth of the uterus and breast tissue and plasma volume expansion 317 begin early in pregnancy. Studies examining maternal body composition changes early in pregnancy 318 are scarce, due to the difficulties recruiting women early in their pregnancy before their pregnancy 319 has been confirmed via dating scan, which occurs in the UK at 12 weeks gestation. Therefore, 320 although the majority of published studies appear to report stronger associations between mid-late 321 pregnancy GWG and FFM, observational studies examining changes in GWG and maternal body 322 composition in cohorts of women from pre-conception through to delivery are required in larger,

323 more ethnically diverse populations in order to confirm this, particularly amongst women with 324 obesity, where relatively little is known about very early changes in maternal body composition.

325 Despite methodological differences between the studies described above and limitations of 326 the present study, maternal changes in weight and body composition appear to play an important 327 role in the predication of infant birthweight and adiposity, especially in mid-pregnancy. To our 328 knowledge, this is the first study to have examined the relationship between the rate at which 329 maternal upper body subcutaneous fat changes over pregnancy in women with obesity and 330 highlights the need for a more personalised approach beyond BMI and total GWG to optimise 331 outcomes for mother and baby, particularly in the second trimester. However, the findings from this 332 pilot study amongst women with obesity, in combination with those in the literature amongst 333 women of all weights, do not consistently support the use of SFT measurements in addition to the 334 monitoring of GWG to assess risk of adverse birth size outcomes, but it is clear that more research is 335 warranted examining the relationship between GWG and changes in maternal body composition 336 amongst women with obesity. Future studies should examine the relationship between the 337 composition of GWG and infant body composition using body composition assessment methods that 338 can distinguish between the maternal and foetal unit, that are portable, and that can be used in a 339 clinical setting throughout pregnancy at frequent intervals.

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349	Acknowledgments:
350	This research was supported by the University of Plymouth. The authors would also like to thank
351	University Hospitals Plymouth NHS Trust for hosting the study, as well as all women and their
352	families for participating. Also thank you to Debbie Egan and Jackie Bartlett for helping facilitate
353	recruitment in antenatal clinics, Dr Martha Paisi for advising on the use of child growth standards
354	and to Dr Nathaniel Clark for his constructive comments on the manuscript.
355	
356	Funding:
357	This research did not receive any specific grant from funding agencies in the public, commercial, or
358	not-for-profit sectors.
359	Competing Interests:
360	The authors declare no competing interests.
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