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Racial differences in body composition and cardiometabolic risk during the menopause transition: a prospective, observational cohort study

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1 **Racial differences in body composition and cardiometabolic risk during the**
2 **menopause transition: a prospective, observational cohort study**

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44

45 **CONDENSATION:** During the menopause transition, White women had greater gains in
46 abdominal adiposity and increased cardiometabolic risk compared to Black women.

47

48 **SHORT TITLE:** Racial disparity during the menopause transition

49

50 **AJOG AT A GLANCE:**

51 **A. Why was this study conducted?**

52 To assess longitudinal changes in body composition and cardiometabolic risk among
53 Black and White women during the menopause transition.

54 **B. What are the key findings?**

55 White women gained more abdominal adiposity during the menopause transition
56 compared to Black women, which may be due in part to differences in the pattern of
57 sex steroid hormone changes between women of different racial backgrounds.

58 **C. What does this study add to what is already known?**

59 This study demonstrates that Black women may not gain as much abdominal
60 adiposity across the menopause transition due to both higher abdominal adiposity
61 and smaller fluctuations in sex steroid hormones in the years leading up to
62 menopause.

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69 **ABSTRACT**

70 **Background.** Obesity disproportionately affects more women than men. The loss of
71 ovarian function during the menopause transition coincides with weight gain, increases
72 in abdominal adiposity, and impaired metabolic health. Racial differences in obesity
73 prevalence that results from the menopause transition are not well understood.

74 **Objectives.** To assess longitudinal changes in body composition and cardiometabolic
75 risk among Black and White women during the menopausal transition. **Study Design.**

76 In a secondary analysis of a prospective, observational cohort study—the Healthy
77 Transitions study—161 women aged 43 years and older with body mass index between
78 20 and 40 kg/m² and who had not yet transitioned through menopause were enrolled at
79 Pennington Biomedical Research Center. Women were seen annually for body
80 composition by dual-energy X-ray absorptiometry; abdominal adipose tissue distribution
81 by computed tomography; sex steroid hormones; and cardiometabolic risk factors
82 including fasting glucose, insulin, and lipids. Surrogate measures of insulin sensitivity
83 were also calculated. **Results.** Ninety-four women (25 Black, 69 White) transitioned
84 through menopause and were included within the analyses. At menopause onset, Black
85 women weighed more (77.8±3.0 vs. 70.8±1.8 kg), and had higher systolic (125±16 vs.
86 118±14 mmHg) and diastolic (80±8 vs. 74±7 mmHg) blood pressure compared to White
87 women (all p≤0.05). No other differences in body composition, sex steroid hormones, or
88 cardiometabolic risk factors were observed at menopause onset. Before menopause,
89 White women gained significant weight (+3 kg), total body adiposity (+6% percent body
90 fat, +9% fat mass, +12% trunk fat mass), and abdominal adipose tissue (+19%

91 subcutaneous fat, +15% visceral fat, +19% total adipose tissue) which coincided with
92 significant decreases in estradiol, sex hormone-binding globulin, and estrone sulfate, as
93 well as increases in follicle-stimulating hormone, total cholesterol, and low-density
94 lipoprotein cholesterol. Conversely, Black women had more abdominal adipose tissue
95 before menopause, which was maintained across the menopause transition. Black
96 women also had significant decreases in estrone sulfate and total testosterone, as well
97 as increases in follicle-stimulating hormone before menopause. In the postmenopausal
98 years, abdominal subcutaneous adipose tissue, total adipose tissue, follicle-stimulating
99 hormone, total cholesterol, and low-density and high-density lipoprotein cholesterol
100 increased only in White women. **Conclusions.** White women gained more abdominal
101 adiposity during the menopause transition compared to Black women, which may be
102 due in part to differences in the pattern of sex steroid hormone changes between
103 women of different racial backgrounds. The gains in abdominal adiposity in White
104 women were observed in tandem with increased cardiometabolic risk factors. Future
105 studies should consider comprehensive lifestyle approaches to target these increased
106 gains in abdominal adiposity (i.e., nutrition and physical activity coaching), while also
107 taking into account the potential interactions of race, body adiposity, sex steroid
108 hormones, and their influence on cardiometabolic risk.

109

110 **Key Words:** abdominal fat; adipose tissue; hormones; menopause; race; visceral fat

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116 **INTRODUCTION**

117 Obesity increases significantly in women after 40 years of age in the United
118 States, with the prevalence reaching 45% between 40 and 59 years, and 43% over the
119 age of 60.^{1,2} Rapid increases in body weight (adiposity) occurs in the years leading up
120 to menopause—known as the menopause transition (or perimenopause)—when sex
121 steroid hormones, energy balance, and body fat distribution are in flux.³ There is
122 substantial evidence that the menopause transition is associated with a redistribution of
123 subcutaneous fat from the gluteal/femoral depot to the abdominal depot³⁻⁷ which is
124 commensurate with the loss of ovarian function and decreases in physical activity,
125 energy expenditure, and fat oxidation.³ Undoubtedly, these changes predispose the
126 estimated 2 million women that reach menopause annually in the United States to
127 increased cardiometabolic risk including insulin resistance, type 2 diabetes, and
128 cardiovascular disease.⁸⁻¹⁰ These observations have even led some experts to suggest
129 that a BMI greater than 24.9 kg/m² (rather than 30 kg/m²) may be more appropriate to
130 denote obesity in midlife women.^{11,12}

131 This growing body of research, however, lacks an understanding of the potential
132 racial disparity in obesity prevalence across the menopause transition. In a cross-
133 sectional analysis of women prior to menopause,¹³ we observed that sleeping energy
134 expenditure, as well as consumption of protein, fiber, and other dietary nutrients, were
135 lower in Black compared to White women. Prior to menopause, Black women also had
136 significantly more abdominal subcutaneous adipose tissue and slightly less visceral
137 adipose tissue compared to White women.¹⁴ Longitudinal data from the Study of
138 Women's Health Across the Nation (SWAN) revealed that Black and White women

139 actually experience similar changes in body composition during the menopause
140 transition.⁴ We confirmed these findings in a previously published analyses of 51
141 women taking part in the Healthy Transitions study and who transitioned through
142 menopause.³ Previous studies, however, have not investigated whether changes in
143 body composition affect cardiometabolic risk differently among Black and White women
144 during the menopause transition.

145 A better understanding of how race may affect changes in abdominal adiposity is
146 important so that clinicians can target care to help women minimize the cardiometabolic
147 burdens observed with menopause. We hypothesize that Black women would have
148 similar increases in abdominal adiposity (particularly abdominal subcutaneous adipose
149 tissue and visceral adipose tissue) compared to White women, but that Black women
150 will experience disproportionate increases in cardiometabolic risk factors (e.g., glucose,
151 insulin, lipids, and insulin resistance) which would ultimately increase risk for developing
152 type 2 diabetes.

153

154 **MATERIALS & METHODS**

155 **Study Design**

156 Healthy Transitions was a 4-year prospective, observational cohort study that
157 investigated the effect of the menopause transition on obesity, energy expenditure, and
158 insulin sensitivity [*clinicaltrials.gov* identifier: NCT00412269] at the Pennington
159 Biomedical Research Center (PBRC) in Baton Rouge, Louisiana from 1998 to 2002.
160 The study was approved by the PBRC Institutional Review Board, and participants
161 provided written informed consent before participation. Women who had not yet

162 transitioned through menopause were enrolled and completed annual visits during the
163 years before menopause (premenopause and/or perimenopause) as well as during the
164 years after menopause (postmenopause). The study was extended for an additional 3
165 years to continue annual visits for those women who did not transition through
166 menopause from 2003 to 2006. Study outcomes included changes in body weight and
167 body composition by dual-energy X-ray absorptiometry (DXA) and computed
168 tomography (CT); sex steroid hormones; and cardiometabolic risk factors including
169 fasting glucose, insulin, and lipids.

170 A subset of 80 women (40 Black, 40 White) were targeted for additional outcome
171 measures of 24-hour energy expenditure (by respiratory chamber) at baseline, 4 years,
172 and 6 years post-enrollment, as well as insulin sensitivity (by frequently sampled
173 intravenous glucose tolerance test) at baseline, 4 years, and 8 years post-enrollment.
174 Due to the small sample size and unequal race distribution of women who transitioned
175 through menopause who had both premenopause and postmenopause measures of 24-
176 hour energy expenditure (n=25; 4 Black, 21 White), we were unable to sufficiently
177 explore how changes in energy expenditure differed by race. While frequently sampled
178 intravenous glucose tolerance test data were also only available in 19 women (2 Black,
179 17 White), we applied commonly used surrogate measures of insulin sensitivity to our
180 cohort.

181

182 **Study Participants**

183 Women were recruited by print and radio advertisement, as well as targeted
184 mailings and word of mouth from the Baton Rouge, Louisiana area. Women were

185 required to be healthy, 43 years or older, with body mass index (BMI) between 20 and
186 40 kg/m², and premenopausal (i.e., have had at least 5 menstrual cycles in the last 6
187 months and have confirmed follicle-stimulating hormone (FSH) <30 mIU/mL¹⁵). Women
188 were ineligible if they were taking regular medication (including oral contraceptives or
189 other hormones), were not having regular menstrual cycles, or had clinically abnormal
190 results on laboratory tests or physical examination including diagnosed hypertension,
191 hypercholesterolemia, diabetes, or cardiovascular disease. Women self-reported their
192 race and ethnic background. Potential confounders of changes in body adiposity across
193 the menopause transition included age, as well as highest level of education and
194 smoking status (self-reported).

195 A total of 161 premenopausal women (55 Black, 102 White, 2 Asian/Asian-
196 Indian, and 2 biracial) enrolled in the study.³ Of the 157 women who were self-reported
197 as Black or White, 94 (or 60%; 25 Black, 69 White) transitioned through menopause at
198 some point during the study and, therefore, were included within the analyses. Of the 63
199 women who did not transition and were excluded from the analyses, 28 (12 Black, 16
200 White) dropped from the study and 35 (17 Black, 18 White) did not transition (see
201 **Supplemental Figure 1**). Women were classified retrospectively as having transitioned
202 through menopause (indicated as Year 0, or 'menopause onset') at the annual visit
203 where both an absence of menstrual cycles for 1-year was reported with an FSH>30
204 mIU/mL. None of the women self-reported being non-Hispanic or Latino.

205

206 **Study Procedures**

207 **Body composition and abdominal adipose tissue distribution.** Weight was
208 measured in the morning after an overnight fast (Scale-Tronix 5200; Scale-Tronix Inc.)
209 while the subject wore a surgical gown, which was subtracted from the total weight.
210 Body composition was measured by DXA (QDR 2000; Hologic, Waltham, MA) in the
211 morning following an overnight fast. Within-subject precision of the DXA, which is
212 considered the gold standard for quantifying body adiposity in adults,¹⁶ was excellent
213 (coefficient of variation for percent body fat was 1.5% [SD=0.51]). Estimates of percent
214 body fat, fat mass, and fat-free mass were measured in ~10-15 minutes while subject
215 wore a surgical gown. Abdominal adipose tissue distribution, including abdominal
216 subcutaneous adipose tissue (SAT), deep subcutaneous adipose tissue (deep SAT),¹⁷
217 superficial subcutaneous adipose tissue (superficial SAT), visceral adipose tissue
218 (VAT), and abdominal total adipose tissue (TAT) was measured by a single 10-mm slice
219 at the level of the interspace between the L4-L5 vertebrae by computed tomography
220 (GE High Speed Advantage; GE Medical Systems, Milwaukee, WI) as previously
221 described.¹⁸

222 **Sex steroid hormones.** Hormone measurements were conducted on serum
223 following an overnight fast. Estradiol, FSH, and sex hormone-binding globulin (SHBG)
224 were measured using immunoassay with chemiluminescent detection (Siemens;
225 Immulite 2000). Estrone sulfate was measured using radioimmunoassay (Siemens;
226 Diagnostic Systems Laboratories) and total testosterone was measured using
227 radioimmunoassay (Siemens; Diagnostic Products Corporation). All sex steroid
228 hormones were measured once during a single cycle.

229 **Cardiometabolic risk factors.** Systolic and diastolic blood pressure were

230 measured in triplicate at rest. Total cholesterol, high-density lipoprotein (HDL)
231 cholesterol, and triglyceride levels were measured in an overnight fasted blood sample
232 using a Beckman Synchron CX5 autoanalyzer. Low-density lipoprotein (LDL)
233 cholesterol was calculated using the Friedewald equation, assuming triglycerides were
234 within normal limits. Glucose (Beckman Synchron CX7, Beckman; Brea, CA, USA) and
235 insulin (Abbott IMx analyzer, Abbott Laboratories; Abbott Park, IL, USA) were
236 measured, and the homeostatic model assessment-insulin resistance (HOMA-IR) and
237 quantitative insulin sensitivity check index (QUICKI) were calculated as previously
238 described.^{19,20} Higher HOMA-IR and lower QUICKI are indicative of increased insulin
239 resistance. Presence (or absence) of the metabolic syndrome was also determined and
240 classified dichotomously.²¹

241

242 **Statistical Analysis**

243 The primary outcome of the original cohort study was VAT, while key secondary
244 outcomes included abdominal SAT, fat mass, and fat-free mass. We conservatively
245 estimated that 160 women (80 Black, 80 White) would need to be enrolled in our
246 longitudinal cohort study to ensure detectable differences in VAT in women of different
247 racial backgrounds (Black vs. White), as well as differences between women who and
248 did not transition through menopause, would be feasible. With this sample size, along
249 with a conservative assumption that possibly only one-third of the 160 women (or 53
250 women) would transition through menopause, we calculated >95% power to detect
251 differences in both main effects (race and menopause status) and ~60% power to
252 detect their interactions (race*menopause status) for a difference in VAT of 25 cm².

253 All analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC,
254 USA) with a significance level set at $\alpha=0.05$. All characteristics at menopause onset
255 (Year 0) are expressed as raw (unadjusted) means with 95% confidence intervals.
256 Between-race comparisons were made using a two-sample t-test. A linear mixed effect
257 repeated measure model, with a compound symmetric covariance matrix, was used to
258 estimate the percent change from menopause onset (Year 0) across all years. Fixed
259 effects in the model included race, time (as a categorical variable), and race*time
260 interaction, while only a subject random effect was used. Both between-race and within-
261 race comparisons were calculated using two-sample t-tests constructed from estimates
262 of least squares means \pm standard error of the mean (SEM) from the linear
263 model. Similarly, repeated measures models were used to estimate the associations
264 between body composition measures and hormones levels between Black and White
265 women leading up to menopause using slope estimates and t-tests. Age was not
266 adjusted for within the linear models due to the lack of difference at menopause onset
267 (Year 0) between Black and White women. Highest level of education and smoking
268 status was also not adjusted for within the linear models due to the lack of difference at
269 screening between Black and White women.

270

271 **RESULTS**

272 **Characteristics at menopause onset**

273 Ninety-four women (25 Black, 69 White) transitioned through menopause. Participant
274 characteristics at menopause onset (Year 0) are displayed in **Table 1**. At menopause
275 onset, Black women weighed more and had higher systolic and diastolic blood pressure

276 compared to White women (all $p \leq 0.05$). No other differences in body fatness, sex
277 steroid hormones, or cardiometabolic risk factors were observed between Black and
278 White women. Importantly, the 94 women who transitioned through menopause (as well
279 as within each racial group) were not different from those that did not transition through
280 menopause in terms of percent body fat and adipose tissue distributions (abdominal
281 SAT, VAT, and TAT) at baseline.

282 **Changes in body composition and abdominal adipose tissue distribution**

283 **Before menopause:** In the 2 to 6 years before menopause onset (**Figure 1**),
284 White women gained significant weight (+3 kg) and significantly more total body
285 adiposity (+6% percent body fat, +9% fat mass, +12% trunk fat mass) and abdominal
286 adipose tissue (+19% abdominal SAT, +19% abdominal TAT, +15% VAT). Conversely,
287 Black women maintained body composition and abdominal adiposity across
288 menopause. Similar trends in waist circumference, deep SAT, and superficial SAT were
289 observed in both Black and White women (see **Supplemental Table 1**). Fat-free mass
290 was maintained in both Black and White women.

291 **Postmenopause:** Both Black and White women tended to maintain total body
292 adiposity and abdominal adipose tissue achieved at the time of menopause onset into
293 their postmenopausal years. However, abdominal TAT did increase among White
294 women in years 2, 4, and 5, as well as abdominal SAT in years 2 and 5, and VAT in
295 year 4 after menopause.

296

297 **Changes in sex steroid hormones**

298 **Before menopause:** In the 1 to 6 years before menopause, White women had

299 significant decreases in estradiol and SHBG, while Black women had significant
300 decreases in total testosterone but no changes in estradiol or SHBG concentrations
301 (see **Supplemental Table 2**). Importantly, for every 1% decrease in total testosterone,
302 VAT mass decreased 0.05% in White women and increased 0.05% in Black women
303 (between-race $p=0.03$). Both Black and White women had significant decreases in
304 estrone sulfate and increases in FSH. We separated both Black and White women into
305 tertiles based on FSH levels to determine if racial differences occur within each tertile
306 (lowest, moderate, and highest percent changes in FSH). White women with the largest
307 percent increases in FSH had the greatest percent increases in abdominal SAT.
308 Specifically, the largest FSH tertile had significant abdominal SAT differences between
309 Black and White women ($p=0.004$). Conversely, there was no relationship between the
310 percent changes in FSH tertiles and abdominal SAT among Black women (**Figure 2**).

311 **Postmenopause:** Concentrations of estradiol, estrone sulfate, SHBG, and total
312 testosterone were maintained postmenopause in both races. Conversely, FSH
313 continued to increase among White women, whereas FSH concentrations increased
314 among Black women only in years 2 and 5 postmenopause.

315

316 **Changes in cardiometabolic risk factors**

317 **Before menopause:** In the 2 to 6 years before menopause, a significant
318 increase in total cholesterol and a significant decrease in insulin sensitivity (measured
319 by QUICKI) was observed among White women (see **Supplemental Table 3**). White
320 woman also had a significant increase in LDL cholesterol in years 4 and 6 only. All other
321 cardiometabolic risk factors, including HOMA-IR and prevalence of the metabolic

322 syndrome, remained relatively unchanged before menopause among White women.
323 Conversely, no consistent changes in cardiometabolic risk factors were observed
324 among Black women before menopause.

325 Pronounced differences in the association between the changes in body
326 composition and changes in cardiometabolic risk leading up to menopause were
327 observed. Specifically, for every 1% increase in abdominal SAT: (1) total cholesterol
328 increased 0.36% in White women and decreased 0.04% in Black women (between-race
329 $p < 0.0001$) (**Figure 2**); and (2) LDL cholesterol increased 0.44% in White women and
330 0.02% in Black women (between-race $p < 0.01$). Additionally, for every 1% increase in
331 VAT mass: (1) total cholesterol increased 0.21% in White women and decreased 0.06%
332 in Black women (between-race $p < 0.0001$); and (2) LDL cholesterol increased 0.27% in
333 White women and decreased 0.04% in Black women (between-race $p = 0.0002$). And
334 finally, for every 1% increase in fat mass, glucose increased 0.04% in White women
335 compared to 0.20% in Black women (between-race $p = 0.03$) (**Figure 2**).

336 **Postmenopause:** In the 2 to 5 years postmenopause, White women had
337 significant increases in HDL cholesterol, as well as increases in total cholesterol and
338 LDL cholesterol (both in the 2 to 3 years postmenopause). No consistent changes in
339 other cardiometabolic risk factors or prevalence of the metabolic syndrome were
340 observed among White women. Conversely, no changes in cardiometabolic risk factors
341 were observed among Black women postmenopause.

342

343 **COMMENT**

344 **Principal Findings.** White women gained significantly more weight in the years
345 leading up to menopause, which was primarily due to significant increases in abdominal
346 adiposity. Commensurate with these increases in abdominal adiposity, White women
347 had more dynamic changes in sex steroid hormones and increases in cardiometabolic
348 risk, including increased total cholesterol and LDL cholesterol. In contrast, Black women
349 had more abdominal adiposity prior to menopause yet maintained these adiposity levels
350 and overall cardiometabolic health profile across the menopause transition.

351 **Results.** Our current findings are contrary to our original hypothesis that Black
352 women would have disproportionate increases in cardiometabolic risk compared to
353 White women despite similarly proposed increases in abdominal adiposity. This
354 hypothesis was supported by the combined analysis of three longitudinal cohorts (ARIC,
355 CARDIA, and Framingham Heart Study) that found for a given level of weight gain
356 among middle-age adults ages 45 to 60 years, diabetes incidence is higher in Black
357 compared to White individuals.²² Black individuals also have less visceral adiposity and
358 intrahepatic lipid,²³⁻²⁵ higher HDL cholesterol,²⁶ lower triglycerides^{23,26} and prevalence
359 of hepatic steatosis,²⁷ yet are paradoxically more insulin resistant compared to White
360 individuals.²⁸⁻³⁰ These findings demonstrate that Black women may be more susceptible
361 to increased cardiometabolic risk in response to weight gain because of
362 menopause.^{31,32} Recent findings further support the notion that Black women may have
363 greater insulin response and lower insulin clearance in response to glucose
364 administration and, therefore, may suffer more detrimental effects of weight gain during
365 the menopause transition.^{33,34} Our findings in this completed sample (n=94) are also in
366 contrast with our preliminary analysis (n=51) where we reported that Black and White

367 women had similar changes in body adiposity and sex steroid hormones across
368 menopause.³ To our knowledge, no longitudinal studies have examined whether Black
369 and White women differ in response to gains in abdominal adiposity across the
370 menopause transition using such robust measures of abdominal adiposity.

371 There are several possible explanations for why White women gained more
372 weight and abdominal adiposity—and caught up to Black women. First, Black women
373 had borderline obesity prior to menopause and lacked the hallmark increases in FSH
374 and decreases in estradiol and SHBG throughout the menopause transition which may
375 have contributed to the absence of gains in abdominal adiposity. These observations
376 were not the same among White women. Whether changes in body adiposity precludes
377 changes in sex steroid hormones (rather than vice versa) remains unclear. In SWAN,
378 obesity status was both an important predictor of sex steroid hormone levels as well as
379 the degree in which these sex steroids change across the menopause transition.^{35,36}
380 Specifically, women with obesity—especially Black women—often maintain estradiol
381 concentrations and have smaller increases in FSH.³⁵ These observations are important
382 since more mechanistic studies in both animals and humans have shown that blocking
383 FSH³⁷ and gonadal suppression with estradiol add-on³⁸ limits any gain in adiposity.
384 While further investigation is warranted, the gains in abdominal adiposity observed
385 among White women in our study are likely due in part to the interaction between both
386 obesity status and sex steroid hormones. Furthermore, we cannot understate the
387 complex interactions that exist between whole-body metabolism, sex steroid hormones,
388 genetics, and environmental factors, as well as our inability to evaluate all of these

389 factors within the present analyses, in the worsening of adiposity and cardiometabolic
390 health in midlife women.

391 One interesting finding was that Black women had a significant decrease in
392 testosterone in the years prior to menopause, which was not observed among White
393 women. It has been previously reported that testosterone concentrations are positively
394 associated with body size^{39,40} with some reporting that Black women have lower
395 testosterone levels than White women after adjusting for body size.⁴¹ In the present
396 study, Black women had greater levels of adiposity and higher (yet declining)
397 testosterone levels during the menopause transition. Thus, the maintenance of estradiol
398 combined with decreasing testosterone among Black women may have contributed to
399 the absence of increased adiposity.

400 **Clinical Implications.** Our study supports increased attention towards potential
401 race-specific dynamics in how obesity status before menopause may affect sex steroid
402 hormones and thus subsequent changes in abdominal adiposity. While the present
403 study did not find any increases in cardiometabolic risk or abdominal adiposity among
404 Black women, our observations do not indicate that Black women are less likely to
405 develop type 2 diabetes and metabolic syndrome as they age. Indeed, gains in
406 abdominal adiposity may progress at a slower rate and into the postmenopausal years
407 creating a lag in the development of cardiometabolic disease.³⁹ In addition, we observed
408 that Black women had greater increases in fasting glucose level for each small increase
409 in total fat mass, suggesting potentially greater metabolic vulnerability to excess weight
410 gain. Furthermore, we feel there is a potential opportunity for physicians to consider
411 more comprehensive risk profiling of women during the menopause transition as part of

412 their routine clinic visits. Specific assessments may include standardized waist
413 circumference measurements, as well as a more complex lipid panel and fasting
414 glucose level so that changes in cardiometabolic risk can be evaluated over time.

415 **Research Implications.** More studies are needed to disentangle which women
416 are more susceptible to weight gain and increased cardiometabolic risk during the
417 menopause transition. While interventions targeting body weight change during
418 perimenopause are scarce,^{42,43} future studies should consider more comprehensive
419 lifestyle approaches to target these increased in abdominal adiposity, including nutrition
420 and physical activity coaching.⁴⁴ Future treatment approaches for midlife women should
421 also consider the interactions of race, body adiposity, sex steroid hormones, and their
422 influence on cardiometabolic risk.

423 **Strengths and Limitations.** The strengths of our study include the relatively
424 large sample size of women with robust longitudinal measurements of body composition
425 and regional adiposity. First, existing longitudinal cohort studies in menopause often use
426 simple outcome measures like BMI and waist circumference^{4,36,39} or body composition
427 by bioelectrical impedance analysis (BIA)⁴ to assess abdominal adiposity. While
428 important epidemiologic studies benefit from the simplicity of these tools to estimate
429 body adiposity (i.e., accessible, ease of transport), BMI, waist circumference, and skin
430 calipers simply do not accurately quantify body composition to the precision that is
431 required.⁴⁵ The accuracy and reliability of BIA for quantifying body adiposity is also
432 limited, in part because of the issue of fluctuating hydration status and also because
433 many BIA instruments perform poorly on individuals with larger body sizes.⁴⁵ Having
434 more robust measures of regional (upper versus lower) adiposity is important. Indeed,

435 upper-body (abdominal) adiposity is associated with more obesity-related disorders,^{8–}
436 ^{10,46–48} while lower-body (femoral) adiposity may be more metabolically protective.^{48–52}
437 To our knowledge, only a few longitudinal studies have used more robust measures
438 such as DXA or CT to quantify changes in body adiposity across the menopause
439 transition^{5,6} in addition to our longitudinal cohort.³ Neither of those studies,^{5,6} however,
440 examined racial disparities across menopause. Indeed, longitudinal studies that
441 undertake comprehensive metabolic phenotyping in large sample sizes across the
442 menopause transition are difficult to execute due to both poor retention rates and the
443 inherent variability in the length of the menopause transition.

444 Our study has several limitations. First, we were unable to evaluate the influence
445 of menopause stage or length of perimenopause on our study outcomes due to the
446 absence of cycle variability data. We were also unable to quantify predictors of diabetes
447 incidence since only two of the women that transitioned through menopause actually
448 developed type 2 diabetes. Instead, we quantified presence or absence of the metabolic
449 syndrome (≥ 3 conditions indicative of presence) as a surrogate marker of metabolic
450 health. While our large sample size is indeed a strength of the study, we still lacked a
451 truly equal race distribution of women who transitioned through menopause, which likely
452 accounts for some of the larger standard deviations/errors observed among Black
453 women. Furthermore, we did not time our measurement of sex steroid hormones due to
454 logistical concerns and the complexities that a larger sample size would entail. We also
455 did not routinely measure changes in thyroid hormones—particularly thyroid stimulating
456 hormone (TSH), triiodothyronine (T_3), and thyroxine (T_4)—which are responsible for
457 regulating metabolism. Additionally, our follow-up period after menopause onset may

458 not be sufficient in length to capture all potential increases in cardiometabolic risk that
459 arise in the postmenopausal years. Some longitudinal studies have reported that Black
460 women may have a slower trajectory to develop the metabolic syndrome and type 2
461 diabetes despite higher levels of body adiposity at baseline.³⁹ Differences in physical
462 activity and dietary intake (and diet quality) may also have contributed to the observed
463 changes in body adiposity and cardiometabolic risk.⁵³⁻⁵⁶ Despite our preliminary findings
464 that physical activity and dietary intake decreases in the years before menopause,³ we
465 were unable to evaluate racial differences in physical activity and dietary changes due
466 to the discontinued collection of these data during the 3-year extension of the study.

467 **Conclusions.** To our knowledge, our study is the first to examine whether
468 women of different racial backgrounds differ in response to gains in abdominal adiposity
469 across the menopause transition using robust measures of abdominal adiposity. We
470 found that White women gained more abdominal adiposity during the menopause
471 transition compared to Black women, which may be due in part to differences in the
472 pattern of sex steroid hormone changes between women of different racial
473 backgrounds. Future studies should evaluate which women are more susceptible to
474 weight gain and increased cardiometabolic risk during the menopause transition.

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490 data, and drafted majority of the manuscript; LMR interpreted data and edited the
491 manuscript; RAB performed statistical analyses; SRS designed and conducted the
492 study, and edited the manuscript; CMC conducted the study and edited the manuscript;
493 FY, collected and assembled data for statistical analyses, and edited the manuscript;
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| Table 1. Characteristics of Women by Race at Menopause Onset (Year 0)[†] | | | | | |
|--|----------------------------|-------------------------|-------------------------|---------------------|----------------|
| | Everyone (n=94) | Black (n=25) | White (n=69) | Difference | p-value |
| Age, years | 53 (52, 53) | 52 (51, 53) | 53 (52, 53) | -1 (-2, 0) | 0.23 |
| Weight, kg | 72.7 (69.6, 75.8) | 77.8 (71.9, 83.8) | 70.8 (67.2, 74.4) | 7.0 (0.1, 13.9) | 0.05 |
| BMI, kg/m ² | 27.0 (25.8, 28.2) | 28.8 (26.5, 31.0) | 26.3 (24.9, 27.7) | 2.4 (-0.2, 5.1) | 0.07 |
| Waist Circumference, cm | 83.7 (80.8, 86.6) | 86.6 (81.0, 92.2) | 82.6 (79.3, 86.0) | 4.0 (-2.6, 10.5) | 0.23 |
| Waist-to-Hip Ratio | 0.80 (0.79, 0.82) | 0.81 (0.77, 0.84) | 0.80 (0.78, 0.82) | 0.01 (-0.03, 0.04) | 0.79 |
| Sex Steroid Hormones | | | | | |
| Estradiol, pg/mL | 68.6 (46.5, 90.6) | 76.3 (29.8, 122.9) | 66.3 (41.0, 91.6) | 10.0 (-42.9, 63.0) | 0.71 |
| Estrone Sulfate, ng/mL | 3.1 (2.0, 4.2) | 3.7 (1.6, 5.8) | 2.9 (1.6, 4.2) | 0.8 (-1.7, 3.2) | 0.54 |
| FSH, mIU/mL | 63.9 (55.9, 71.9) | 75.0 (59.6, 90.4) | 59.9 (50.6, 69.2) | 15.1 (-2.9, 33.1) | 0.10 |
| SHBG, nmol/L | 63.6 (54.6, 72.7) | 61.4 (43.7, 79.2) | 64.4 (53.8, 75.1) | -3.0 (-23.7, 17.7) | 0.77 |
| Total Testosterone, ng/dL | 25.8 (24.5, 27.1) | 24.8 (22.2, 27.3) | 26.2 (24.6, 27.7) | -1.4 (-4.4, 1.5) | 0.34 |
| Cardiometabolic Risk Factors | | | | | |
| Systolic Blood Pressure, mmHg | 120 (117, 123) | 125 (119, 130) | 118 (115, 122) | 7 (0, 13) | 0.04 |
| Diastolic Blood Pressure, mmHg | 76 (74, 78) | 80 (78, 83) | 74 (72, 76) | 6 (3, 10) | <0.001 |
| Heart Rate, bpm | 56 (53, 60) | 57 (51, 63) | 56 (53, 60) | 1 (-7, 8) | 0.90 |
| Total Cholesterol, mg/dL | 211 (204, 219) | 221 (207, 236) | 208 (199, 216) | 13 (-3, 30) | 0.11 |
| HDL Cholesterol, mg/dL | 66 (63, 69) | 67 (60, 73) | 66 (63, 70) | 0 (-7, 7) | 0.94 |
| LDL Cholesterol, mg/dL | 123 (116, 130) | 133 (121, 146) | 119 (112, 127) | 14 (-0, 29) | 0.06 |
| Triglycerides, mg/dL | 110 (95, 125) | 107 (78, 136) | 111 (94, 129) | -4 (-38, 30) | 0.80 |
| Glucose, mg/dL | 95 (93, 96) | 94 (91, 97) | 95 (93, 97) | -1 (-5, 3) | 0.70 |
| Insulin, mU/mL | 8.8 (7.7, 9.9) | 10.0 (7.9, 12.1) | 8.4 (7.1, 9.6) | 1.7 (-0.8, 4.1) | 0.19 |
| HOMA-IR | 2.1 (1.8, 2.4) | 2.4 (1.9, 3.0) | 2.0 (1.7, 2.3) | 0.4 (-0.2, 1.1) | 0.21 |
| QUICKI | 0.35 (0.35, 0.36) | 0.35 (0.33, 0.36) | 0.36 (0.35, 0.37) | -0.01 (-0.03, 0.00) | 0.14 |
| Body Composition by DXA | | | | | |
| Percent Body Fat, % | 41.0 (39.2, 42.9) | 42.3 (38.7, 45.9) | 40.6 (38.4, 42.7) | 1.7 (-2.5, 5.9) | 0.43 |
| Fat Mass, kg | 30.8 (28.1, 33.5) | 34.1 (28.9, 39.3) | 29.7 (26.6, 32.8) | 4.4 (-1.7, 10.5) | 0.15 |
| Fat-Free Mass, kg | 41.7 (40.7, 42.8) | 43.3 (41.2, 45.3) | 41.2 (40, 42.4) | 2.0 (-0.3, 4.4) | 0.09 |
| Trunk Fat Mass, kg | 13.3 (11.6, 14.9) | 14.4 (11.2, 17.6) | 12.8 (10.9, 14.7) | 1.6 (-2.1, 5.3) | 0.40 |
| Body Composition by CT | | | | | |
| Abdominal SAT, cm ² | 350 (322, 378) | 377 (320, 433) | 341 (309, 374) | 36 (-30, 101) | 0.28 |
| VAT, cm ² | 100 (86, 114) | 96 (68, 125) | 101 (85, 118) | -5 (-38, 28) | 0.77 |

| | | | | | |
|----------------------------------|----------------|----------------|----------------|---------------|------|
| Abdominal TAT, cm ² | 449 (411, 487) | 470 (393, 546) | 443 (399, 486) | 27 (-61, 115) | 0.54 |
| Deep SAT, cm ² | 181 (166, 197) | 192 (160, 223) | 178 (160, 196) | 14 (-23, 51) | 0.45 |
| Superficial SAT, cm ² | 163 (144, 182) | 162 (124, 200) | 163 (141, 185) | -1 (-45, 43) | 0.97 |

Abbreviations: BMI, body mass index; FSH, follicle-stimulating hormone; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment-insulin resistance; LDL, low-density lipoprotein; QUICKI, quantitative insulin sensitivity check index; SAT, subcutaneous adipose tissue; SHBG, sex hormone-binding globulin; TAT, total adipose tissue; VAT, visceral adipose tissue.

¹Values are expressed as raw means (95% confidence intervals) at menopause onset (Year 0).

FIGURE LEGENDS

Figure 1. Percent Change in Body Composition & Adipose Tissue Distribution

Percent change in percent body fat (%), fat mass (kg), abdominal subcutaneous adipose tissue (SAT; cm²), and visceral adipose tissue (VAT; cm²) are displayed across the menopause transition in years. Menopause onset is denoted as Year 0, with negative years implying years before menopause onset and positive years implying years after menopause onset. Data are displayed as means with 95% confidence intervals for each race. Closed circles (●) indicate data from Black women, and open circles (○) indicate data from White women.

Figure 2. Percent Change in Body Composition & Adipose Tissue Distribution

Percent change in body composition (fat mass and abdominal subcutaneous adipose tissue (SAT)) are plotted against changes in cardiometabolic risk and sex steroid status including glucose, total cholesterol, and follicle-stimulating hormone (FSH). Individual data are provided for each race. Closed circles (●) or black bars indicate individual data from Black women, and open circles (○) or white bars indicate data from White women. Solid lines (—) and dashed lines (- - -) are indicative of overall trends for Black and White women, respectively. Respective equations, R-squared value, and/or p-value are provided for (or between) each race.

Figure 1. Percent Change in Body Composition & Adipose Tissue Distribution

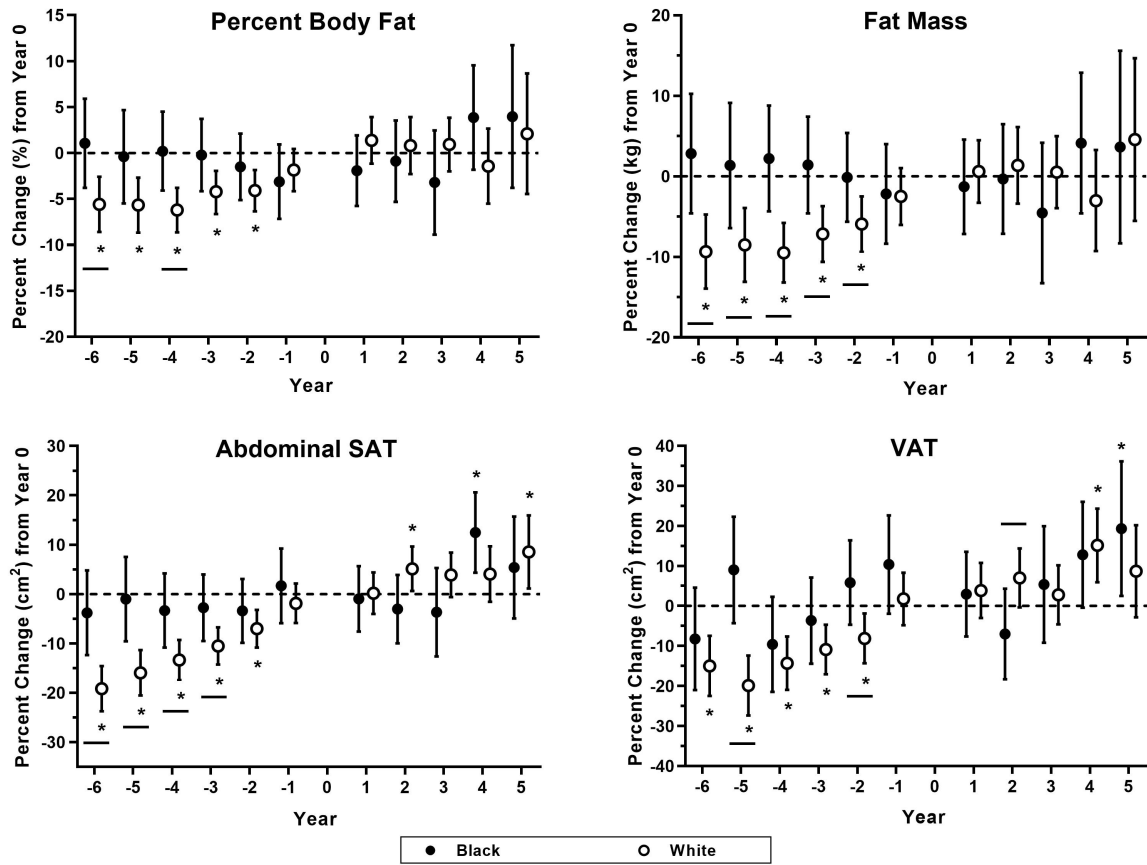
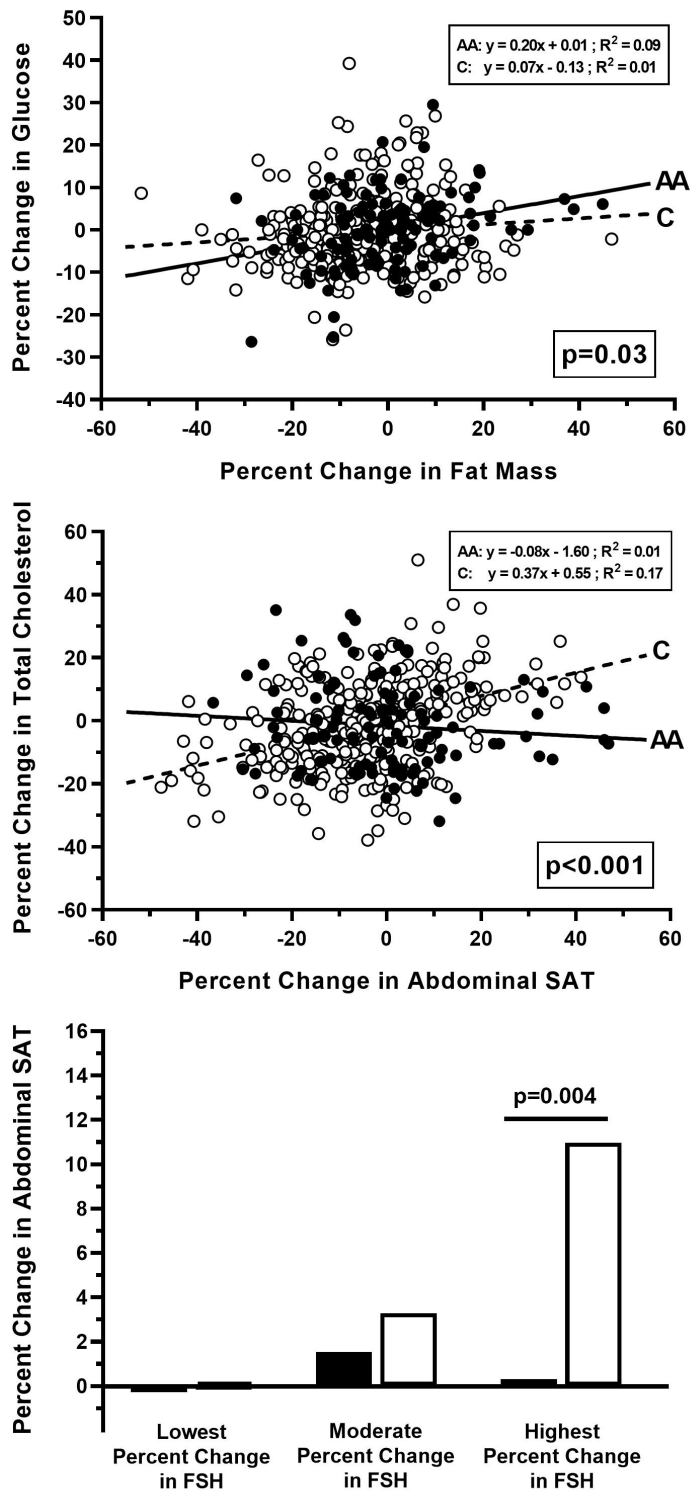


Figure 2. Relationship Between Changes in Body Composition, Hormones, and Cardiometabolic Risk Factors



Supplemental Figure 1.
Online Supporting Material

161 Women Enrolled (Total)

4 Were Excluded from Analyses (2 Asian/Asian-Indian, 2 Biracial)



157 were Black or White

63 Did Not Transition Through Menopause

- 28 dropped (12 Black, 16 White)
- 35 did not transition (17 Black, 18 White)



94 Transitioned Through Menopause & Included in Analyses

- 25 Black
- 69 White

| Supplemental Table 1. Percent Change in Body Composition from Menopause Onset in Women Who Transitioned Through Menopause¹ | | | | | | | | | | | | |
|--|--------------------|--------------------|--------------------|--------------------|-------------------|------------------|----------------|-----------|------------------|------------|-------------------|-------------------|
| Year | -6 | -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
| Weight, kg | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 29 | 9 / 29 | 14 / 42 | 17 / 51 | 20 / 52 | 14 / 43 | 25 / 68 | 18 / 37 | 16 / 31 | 7 / 33 | 11 / 17 | 5 / 10 |
| Black | -0.7(1.8) | -0.4(1.8) | 0.2(1.5) | 0(1.4) | 0.2(1.3) | 0.4(1.5) | 77.8(3) | 0(1.4) | -0.3(1.4) | -1.3(2) | 0.2(1.7) | 0.6(2.4) |
| White | -4.3(1)* | -3.3(1)* | -3.8(0.9)* | -3.2(0.8)* | -2.1(0.8)* | -1.7(0.9) | 70.8(1.8) | -0.3(0.9) | 0.2(1) | -0.5(1) | 0(1.3) | 1.3(1.7) |
| Difference | 3.6(2) | 3(2.1) | 4(1.8)* | 3.2(1.6) | 2.3(1.6) | 2.1(1.8) | 7(3.5)* | 0.3(1.7) | -0.5(1.8) | -0.8(2.3) | 0.2(2.1) | -0.8(2.9) |
| BMI, kg/m² | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 29 | 9 / 29 | 14 / 42 | 17 / 51 | 20 / 52 | 14 / 43 | 25 / 68 | 18 / 37 | 16 / 31 | 7 / 33 | 11 / 17 | 5 / 10 |
| Black | -0.7(1.8) | -0.4(1.8) | 0.2(1.5) | 0(1.4) | 0.2(1.3) | 0.4(1.5) | 28.8(1.2) | 0(1.4) | -0.3(1.4) | -1.3(2) | 0.2(1.7) | 0.6(2.4) |
| White | -4.3(1)* | -3.3(1)* | -3.8(0.9)* | -3.2(0.8)* | -2.1(0.8)* | -1.7(0.9) | 26.3(0.7) | -0.3(0.9) | 0.2(1) | -0.5(1) | 0(1.3) | 1.3(1.7) |
| Difference | 3.6(2) | 3(2.1) | 4(1.8)* | 3.2(1.6) | 2.3(1.6) | 2.1(1.8) | 2.4(1.3) | 0.3(1.7) | -0.5(1.8) | -0.8(2.3) | 0.2(2.1) | -0.8(2.9) |
| Waist Circumference, cm | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 29 | 9 / 25 | 14 / 43 | 17 / 48 | 20 / 52 | 13 / 44 | 25 / 69 | 18 / 37 | 16 / 31 | 7 / 33 | 11 / 17 | 5 / 10 |
| Black | -2.2(2.2) | -1.3(2.3) | -0.1(2) | -0.7(1.8) | 2(1.7) | 1.7(2) | 86.6(2.8) | 0.6(1.8) | -0.4(1.9) | -0.2(2.6) | 0.8(2.1) | 2.5(3) |
| White | -6.3(1.3)* | -5.8(1.4)* | -5.4(1.1)* | -4.1(1.1)* | -1.3(1) | 0.4(1.1) | 82.7(1.7) | -0.6(1.2) | 1.4(1.3) | 1.9(1.3) | 1.8(1.6) | 3.3(2.1) |
| Difference | 4.1(2.6) | 4.5(2.7) | 5.3(2.3)* | 3.4(2.1) | 3.3(2) | 1.3(2.3) | 4(3.3) | 1.2(2.1) | -1.7(2.3) | -2.1(2.9) | -1(2.7) | -0.8(3.7) |
| Percent Body Fat, % | | | | | | | | | | | | |
| <i>n</i> (B/W) | 9 / 23 | 8 / 23 | 12 / 39 | 15 / 47 | 19 / 47 | 14 / 44 | 22 / 62 | 16 / 34 | 11 / 21 | 6 / 24 | 6 / 11 | 3 / 4 |
| Black | 1.1(2.5) | -0.4(2.6) | 0.2(2.18) | -0.22(2) | -1.5(1.8) | -3.1(2.1) | 42.3(1.8) | -1.9(2) | -0.9(2.3) | -3.2(2.9) | 3.9(2.9) | 4(4) |
| White | -5.6(1.5)* | -5.7(1.5)* | -6.2(1.2)* | -4.2(1.2)* | -4.1(1.2)* | -1.9(1.2) | 40.6(1.1) | 1.4(1.3) | 0.8(1.6) | 0.9(1.5) | -1.4(2.1) | 2.1(3.3) |
| Difference | 6.6(2.9)* | 5.3(3) | 6.4(2.5)* | 4(2.3) | 2.6(2.2) | -1.3(2.4) | 1.7(2.1) | -3.3(2.3) | -1.7(2.8) | -4.1(3.3) | 5.3(3.6) | 1.9(5.2) |
| Fat Mass, kg | | | | | | | | | | | | |
| <i>n</i> (B/W) | 9 / 23 | 8 / 23 | 12 / 39 | 15 / 46 | 19 / 46 | 13 / 43 | 22 / 62 | 16 / 34 | 10 / 20 | 6 / 24 | 6 / 11 | 3 / 4 |
| Black | 1.8(3.9) | 0.7(4.1) | 1.6(3.4) | 0.6(3.1) | -0.6(2.9) | -2.3(3.3) | 34.1(2.6) | -1.3(3) | 2.4(3.7) | -4(4.6) | 4.6(4.6) | 4.8(6.3) |
| White | -9.6(2.4)* | -8.9(2.4)* | -9.8(1.9)* | -7.3(1.8)* | -5.9(1.8)* | -3.4(1.8) | 29.7(1.6) | 1.1(2) | 1.6(2.5) | 1.2(2.3) | -2.8(3.3) | 4.4(5.3) |
| Difference | 11.4(4.5)* | 9.6(4.7)* | 11.4(3.9)* | 7.8(3.6)* | 5.2(3.4) | 1.1(3.8) | 4.4(3.1) | -2.4(3.6) | 0.8(4.5) | -5.3(5.1) | 7.4(5.6) | 0.4(8.2) |
| Fat-Free Mass, kg | | | | | | | | | | | | |
| <i>n</i> (B/W) | 9 / 23 | 8 / 23 | 12 / 39 | 15 / 46 | 19 / 46 | 13 / 43 | 22 / 62 | 16 / 34 | 10 / 20 | 6 / 24 | 6 / 11 | 3 / 4 |
| Black | -0.7(1.5) | 1(1.6) | 1.4(1.3) | 0.7(1.2) | 1.4(1.1) | 2.6(1.3)* | 43.3(1) | 0.7(1.2) | 0.5(1.4) | -1.6(1.8) | -1.7(1.8) | -0.4(2.5) |
| White | -0.8(0.9) | 0.1(0.9) | 0.1(0.8) | -0.4(0.7) | 0.4(0.7) | -0.4(0.7) | 41.2(0.6) | -1(0.8) | 0.1(1) | -0.6(0.9) | -1.4(1.3) | 0.1(2.2) |
| Difference | 0.2(1.8) | 0.9(1.9) | 1.4(1.5) | 1.1(1.4) | 0.9(1.3) | 3(1.5)* | 2(1.2) | 1.7(1.4) | 0.4(1.8) | -1.1(2) | -0.4(2.2) | -0.5(3.3) |
| Trunk Fat Mass, kg | | | | | | | | | | | | |
| <i>n</i> (B/W) | 9 / 23 | 8 / 23 | 12 / 39 | 16 / 47 | 19 / 47 | 13 / 44 | 22 / 62 | 16 / 34 | 10 / 21 | 6 / 24 | 6 / 11 | 3 / 4 |
| Black | 7.5(5.8) | 5.9(6.1) | 1.4(5.1) | 4(4.7) | 3.2(4.3) | -2.7(4.8) | 14.4(1.6) | -2.8(4.6) | 0(5.3) | -6.9(6.8) | 2.3(6.9) | 10(9.4) |
| White | -12.3(3.6)* | -11.6(3.6)* | -13.5(2.9)* | -9.9(2.7)* | -8.1(2.7)* | -3.2(2.8) | 12.8(1) | 5(3) | 2.5(3.7) | 3.5(3.5) | 0.2(4.9) | 12.6(8) |
| Difference | 19.8(6.8)* | 17.5(7.1)* | 14.9(5.9)* | 13.9(5.4)* | 11.3(5.1)* | 0.4(5.6) | 1.6(1.9) | -7.7(5.5) | -2.5(6.5) | -10.4(7.7) | 2.1(8.4) | -2.6(12.3) |
| Abdominal SAT, cm² | | | | | | | | | | | | |
| <i>n</i> (B/W) | 8 / 29 | 8 / 29 | 11 / 40 | 15 / 50 | 17 / 48 | 11 / 42 | 23 / 67 | 16 / 36 | 14 / 30 | 7 / 30 | 9 / 17 | 5 / 9 |
| Black | -3.8(4.4) | -1(4.4) | -3.3(3.8) | -2.8(3.4) | -3.4(3.3) | 1.7(3.8) | 360(29) | -1(3.4) | -3(3.5) | -3.7(4.6) | 12.5(4.1)* | 5.4(5.3) |
| White | -19.2(2.3)* | -15.9(2.3)* | -13.4(2.1)* | -10.5(1.9)* | -7(1.9)* | -1.9(2) | 341(17) | 0.2(2.1) | 5.1(2.3)* | 3.9(2.3) | 4.1(2.9) | 8.5(3.8)* |
| Difference | 15.4(4.9)* | 14.9(4.9)* | 10(4.4)* | 7.7(3.9)* | 3.6(3.8) | 3.5(4.3) | 19(33) | -1.1(4) | -8.2(4.2) | -7.6(5.1) | 8.4(5) | -3.2(6.5) |
| VAT, cm² | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 29 | 9 / 29 | 12 / 40 | 16 / 50 | 17 / 49 | 11 / 42 | 23 / 67 | 17 / 36 | 14 / 30 | 7 / 30 | 9 / 17 | 5 / 10 |
| Black | -8.2(6.5) | 9(6.8) | -9.6(6) | -3.6(5.5) | 5.8(5.4) | 10.4(6.3) | 96(14) | 3(5.4) | -7(5.7) | 5.4(7.4) | 12.8(6.7) | 19.4(8.6)* |

| | | | | | | | | | | | | |
|--|--------------------|--------------------|--------------------|--------------------|-------------------|-----------|---------|-----------|--------------------|---------------------|-------------------|------------------|
| White | -15(3.8)* | -19.9(3.8)* | -14.3(3.4)* | -10.9(3.2)* | -8.1(3.2)* | 1.8(3.3) | 101(8) | 3.9(3.5) | 7(3.7) | 2.8(3.7) | 15.2(4.7)* | 8.7(5.9) |
| Difference | 6.7(7.5) | 28.9(7.8)* | 4.7(6.9) | 7.2(6.3) | 13.9(6.2)* | 8.6(7.1) | -5(16) | -0.9(6.4) | -14(6.9)* | 2.6(8.3) | -2.4(8.2) | 10.7(10.4) |
| Abdominal TAT, cm² | | | | | | | | | | | | |
| <i>n</i> (B/W) | 8 / 29 | 8 / 29 | 11 / 40 | 15 / 50 | 17 / 48 | 11 / 42 | 23 / 67 | 16 / 36 | 14 / 30 | 7 / 30 | 9 / 17 | 5 / 9 |
| Black | -4.6(4.4) | 0.4(4.4) | -4.6(3.9) | -3.2(3.5) | -2.2(3.3) | 3.1(3.9) | 449(39) | -0.2(3.4) | -4.1(3.6) | -2.1(4.6) | 12.2(4.2)* | 6.8(5.3) |
| White | -18.9(2.3)* | -17(2.3)* | -13.9(2.1)* | -10.9(1.9)* | -7.7(2)* | -1.4(2.1) | 443(23) | 0.8(2.2) | 5.3(2.3)* | 3.4(2.3) | 6.3(2.9)* | 8.8(3.8)* |
| Difference | 14.4(5)* | 17.4(5)* | 9.3(4.4)* | 7.8(4) | 5.6(3.9) | 4.5(4.4) | 7(45) | -1.1(4) | -9.4(4.2)* | -5.6(5.1) | 5.9(5.1) | -2(6.5) |
| Deep SAT, cm² | | | | | | | | | | | | |
| <i>n</i> (B/W) | 8 / 27 | 8 / 27 | 11 / 38 | 15 / 48 | 17 / 48 | 11 / 41 | 23 / 67 | 16 / 35 | 14 / 29 | 7 / 29 | 9 / 17 | 5 / 10 |
| Black | 1.1(5.5) | 2.2(5.5) | 0(4.8) | -0.8(4.2) | -3.9(4.1) | 3.9(4.8) | 183(16) | 0.7(4.2) | 0.2(4.4) | -4.3(5.7) | 15.2(5.2)* | 5.1(6.6) |
| White | -21(3)* | -14.9(3)* | -14.5(2.6)* | -10.9(2.4)* | -6.2(2.4)* | -1.5(2.6) | 178(9) | 2.4(2.7) | 5(2.9) | 2(2.9) | 3.6(3.6) | -3.2(4.6) |
| Difference | 22.2(6.2)* | 17(6.2)* | 14.5(5.4)* | 10.1(4.9)* | 2.3(4.7) | 5.4(5.4) | 6(19) | -1.7(5) | -4.9(5.2) | -6.3(6.4) | 11.6(6.3) | 8.3(8.1) |
| Superficial SAT, cm² | | | | | | | | | | | | |
| <i>n</i> (B/W) | | | 5 / 16 | 8 / 24 | 9 / 30 | 10 / 34 | 13 / 38 | 8 / 22 | 4 / 10 | 2 / 3 | | |
| Black | | | -12(5.7)* | -6.3(4.8) | -4(4.7) | -3.1(4.5) | 162(19) | -4(4.9) | -10(6.3) | -15.2(8.3) | | |
| White | | | -12.5(3.3)* | -13.6(2.8)* | -7.9(2.6)* | -2.4(2.5) | 163(11) | 2.8(2.9) | 4.8(3.9) | 12.8(6.6) | | |
| Difference | | | 0.5(6.6) | 7.3(5.6) | 3.9(5.3) | -0.7(5.2) | -1(22) | -6.8(5.7) | -14.8(7.3)* | -27.9(10.6)* | | |

Abbreviations: B, Black; BMI, body mass index; SAT, subcutaneous adipose tissue; TAT, total adipose tissue; VAT, visceral adipose tissue; W, White.

¹Data at menopause onset (Year 0) presented as raw mean (SEM). Significant differences in mean percent change (SEM) from Year 0 ($p < 0.05$) are denoted with an asterisk (*). Negative numbers indicate the percent that the raw value is less than Year 0.

| Supplemental Table 2. Percent Change in Sex Steroid Hormones from Menopause Onset in Women Who Transitioned Through Menopause¹ | | | | | | | | | | | | |
|--|----------------------------------|----------------------------------|---------------------------------|---------------------------------|---------------------------------|--------------------------------|------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|-------------------------------|
| Year | -6 | -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
| Estradiol, pg/mL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 3 / 7 | 3 / 12 | 6 / 11 | 6 / 22 | 6 / 21 | 8 / 24 | 13 / 44 | 7 / 13 | 8 / 13 | 3 / 14 | 4 / 5 | 1 / 5 |
| Black | 80.2 (120.5) | 194.8 (120.5) | 121.6 (85.8) | 53 (85.7) | 57.9 (85.7) | -16.8 (75.3) | 76.3(23.2) | -5.7 (79.8) | 7.6 (75.2) | 40.5 (119.6) | -5.7 (103.8) | 3.6 (201) |
| White | 83.5 (78.3) | 211.6 (60.5)* | 134.3 (62.8)* | 146.9 (45.2)* | 235.9 (46.1)* | 123.4 (43.3)* | 66.3(12.6) | 0.9 (58.2) | -16.2 (57.7) | 20.3 (55.9) | 46.9 (91.5) | -48.3 (92.7) |
| Difference | -3.3 (143.7) | -16.8 (134.8) | -12.6 (106.3) | -93.9 (96.9) | -178 (97.3) | -140.3 (86.9) | 10(26.4) | -6.6 (98.8) | 23.7 (94.8) | 20.2 (132) | -52.5 (138.4) | 51.9 (221.4) |
| FSH, mIU/mL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 14 | 8 / 30 | 13 / 30 | 16 / 41 | 19 / 45 | 13 / 43 | 25 / 69 | 18 / 37 | 17 / 31 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | -76.5 (26.1)* | -73.7 (24.7)* | -61.2 (20.2)* | -38.9 (18.6)* | -45.8 (17.5)* | -4.0 (20.2) | 75(7.8) | 30.6 (17.9) | 42.1 (18.3)* | 17.8 (25.9) | 69.3 (20.8)* | 23.7 (30.1) |
| White | -85.4 (18.1)* | -73.0 (13.2)* | -73.6 (13.1)* | -56.7 (11.6)* | -37.7 (11.2)* | -1.5 (11.4)* | 59.9(4.7) | 30.4 (12.0)* | 45.7 (12.9)* | 66.7 (12.6)* | 99.0 (16.6)* | 93.1 (21.0)* |
| Difference | 8.9 (31.8) | -0.8 (28.0) | 12.4 (24.1) | 17.8 (22.0) | -8.1 (20.8) | -2.4 (23.1) | 15.1(9.1) | 0.1 (21.5) | -3.7 (22.3) | -48.9 (28.8) | -29.7 (26.6) | -69.4 (36.7) |
| SHBG, nmol/L | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 15 | 8 / 29 | 13 / 30 | 15 / 42 | 18 / 45 | 14 / 43 | 25 / 69 | 17 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | 10(24.5) | 10.2(23) | 5.6(18.3) | 30.6(17.1) | 2.8(15.7) | -2.1(17.7) | 61.4(8.9) | 7(16.2) | 5.3(16.2) | -1.4(24.3) | -9(19) | -8(28.7) |
| White | 41.1 (16.6)* | 40.4 (12.2)* | 92 (12)* | 75.3 (10.3)* | 49 (9.9)* | 12.9 (10.1) | 64.5(5.4) | 8.4 (10.8) | -10.3 (11.6) | -11.7 (11.4) | -2.9 (15.6) | -15.1 (20.2) |
| Difference | -31.1 (29.6) | -30.2 (26) | -86.3 (21.8)* | -44.7 (19.9)* | -46.1 (18.6)* | -15 (20.4) | -3(10.4) | -1.4 (19.5) | 15.6 (19.9) | 10.3 (26.9) | -6.1 (24.6) | 7.1 (35) |
| Total Testosterone, pg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 14 | 9 / 27 | 13 / 26 | 16 / 40 | 19 / 42 | 14 / 42 | 25 / 66 | 18 / 34 | 16 / 29 | 6 / 29 | 11 / 14 | 5 / 8 |
| Black | 157.9 (14.7)* | 4.9(13) | 53 (10.9)* | 20.8 (9.9)* | 28.6 (9.2)* | 6.5(10.6) | 24.8(1.3) | 6.9(9.4) | 6.7(9.9) | -0.5(15.7) | 15.3(11.8) | 18.3(17.2) |
| White | 8.6(10.3) | 14.2(7.6) | 14.3(7.7) | 4(6.3) | 9.4(6.1) | 7(6.1) | 26.2(0.8) | 2.3(6.8) | 6.6(7.3) | 7.9(7.3) | 4.9(10.3) | 13.2(13.5) |
| Difference | 149.3 (18)* | -9.4 (15.1) | 38.8 (13.4)* | 16.8 (11.8) | 19.2 (11) | -0.5 (12.2) | -1.4(1.5) | 4.6 (11.6) | 0.1 (12.3) | -8.4 (17.3) | 10.4 (15.7) | 5.1 (21.9) |
| Estrone Sulfate, ng/mL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 15 | 8 / 29 | 13 / 30 | 15 / 41 | 17 / 43 | 13 / 42 | 25 / 68 | 18 / 37 | 17 / 31 | 7 / 32 | 12 / 17 | 5 / 9 |
| Black | 1269.8 (286.1)* | 1682.1 (267.7)* | 729.5 (210.4)* | 396.8 (196)* | 203.8 (184.2) | 122.4 (210.4) | 3.7(1.1) | 21.9 (179.1) | 52.5 (184.3) | -16.2 (285.7) | -33.3 (218.9) | -39.5 (337.8) |
| White | 326 (195.2) | 678.6 (140.8)* | 1068 (138.5)* | 553.7 (118.6)* | 433.2 (115.8)* | 185.1 (117.2) | 2.9(0.6) | 11.4 (124.72) | -50.4 (136.1) | -45.5 (134) | -32.4 (183.4) | -124.3 (251.6) |
| Difference | 943.7 (346.3)* | 1003.5 (302.5)* | -338.5 (251.8) | -156.8 (229.1) | -229.3 (217.6) | -62.7 (240.8) | 0.8(1.2) | 10.5 (218.28) | 102.9 (229.1) | 29.2 (315.5) | -1 (285.5) | 84.9 (421.2) |

Abbreviations: B, Black; FSH, follicle-stimulating hormone; SHBG, sex hormone-binding globulin; W, White.

¹Data at menopause onset (Year 0) presented as raw mean (SEM). Significant differences in mean percent change (SEM) from Year 0 ($p < 0.05$) are denoted with an asterisk (*). Negative numbers indicate the percent that the raw value is less than Year 0.

| Supplemental Table 3. Percent Change in Cardiometabolic Risk Factors from Menopause Onset in Women Who Transitioned Through Menopause ¹ | | | | | | | | | | | | |
|--|--------------------|-------------------|--------------------|----------------|-------------------|---------------------|----------|-------------|-------------------|------------------|--------------------|------------------|
| Year | -6 | -5 | -4 | -3 | -2 | -1 | 0 | 1 | 2 | 3 | 4 | 5 |
| Total Cholesterol, mg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 15 | 9 / 30 | 13 / 30 | 16 / 42 | 19 / 45 | 14 / 43 | 25 / 69 | 18 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | -4.5(4.6) | -6.7(4.1) | -1.2(3.5) | -2.1(3.2) | -2.1(3) | 0(3.4) | 221(7) | -1(3) | 1.3(3.1) | 7.6(4.6) | 2.4(3.6) | -4.3(5.4) |
| White | -11.6(3.1)* | -6.9(2.3)* | -8.5(2.3)* | -3.7(2) | -4.3(1.9)* | -1.7(2) | 208(4) | 2.5(2.1) | 7.1(2.2)* | 6.1(2.2)* | 5.5(2.9) | 5.9(3.8) |
| Difference | 7(5.6) | 0.2(4.7) | 7.3(4.2) | 1.7(3.8) | 2.2(3.5) | 1.7(3.9) | 13(8) | -3.5(3.7) | -5.8(3.8) | 1.5(5.1) | -3.1(4.7) | -10.2(6.5) |
| HDL Cholesterol, mg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 15 | 9 / 30 | 13 / 30 | 16 / 42 | 19 / 45 | 14 / 43 | 25 / 69 | 18 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | -6.1(4.6) | -6.17(4.2) | -4.7(3.7) | -4.1(3.4) | -5.3(3.2) | -2.2(3.6) | 66(3) | -2.4(3.3) | 3.4(3.3) | 4.9(4.6) | 1.5(3.8) | 0.4(5.3) |
| White | -7.7(3.1)* | -2.7(2.4) | -1.6(2.4) | 2.1(2.1) | 1(2) | -0.3(2.1) | 66(2) | 3.2(2.2) | 7.6(2.3)* | 8.8(2.3)* | 7.4(2.9)* | 8.3(3.7)* |
| Difference | 1.7(5.6) | -3.5(4.8) | -3.1(4.4) | -6.2(4) | -6.2(3.8) | -2(4.1) | 0(4) | -5.6(3.9) | -4.1(4.1) | -3.9(5.1) | -5.9(4.8) | -8(6.5) |
| LDL Cholesterol, mg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 7 / 15 | 9 / 30 | 13 / 30 | 16 / 41 | 19 / 45 | 14 / 43 | 25 / 68 | 18 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | 2.3(6.7) | -4.5(6) | 4.1(5) | 1.9(4.6) | 3(4.3) | 2.1(4.9) | 133(6) | 1.1(4.4) | 2(4.5) | 12.4(6.6) | 7(5.2) | -3.5(7.8) |
| White | -9.1(4.5)* | -5.2(3.3) | -11.3(3.3)* | -5(2.9) | -4.4(2.8) | -1.4(2.8) | 119(4) | 2.7(3) | 10.5(3.2)* | 8.8(3.1)* | 6.3(4.3) | 8.8(5.5) |
| Difference | 11.4(8.1) | 0.7(6.8) | 15.4(6)* | 6.8(5.4) | 7.4(5.1) | 3.4(5.6) | 14(7) | -1.6(5.3) | -8.4(5.5) | 3.5(7.3) | 0.6(6.7) | -12.2(9.5) |
| Triglycerides, mg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 30 | 9 / 30 | 14 / 42 | 17 / 52 | 19 / 52 | 15 / 45 | 25 / 69 | 18 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | -1.1(11.9) | -6.9(12.4) | -16.5(10) | -3.9(9.7) | -11.5(9.3) | 3.8(10.2) | 107(15) | -1.4(9.5) | -0.8(9.7) | 5.2(13.7) | -9.1(11) | -5.1(15.9) |
| White | -12.7(6.9) | -11.2(6.9) | -0.1(6.1) | 4.5(5.6) | -3(5.6) | 3.9(5.9) | 111(9) | 9.1(6.4) | 3.5(6.7) | -3.5(6.6) | 10.4(8.7) | 18.2(11) |
| Difference | 11.6(13.8) | 4.3(14.2) | -16.5(12) | -8.4(11.2) | -8.5(10.9) | -0.1(11.8) | -4(17) | -10.5(11.4) | -4.2(11.8) | 8.7(15.2) | -19.5(14) | -23.2(19.3) |
| Glucose, mg/dL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 30 | 9 / 30 | 14 / 42 | 17 / 52 | 19 / 52 | 15 / 45 | 25 / 69 | 18 / 37 | 17 / 32 | 7 / 33 | 12 / 17 | 5 / 10 |
| Black | -1.4(2.6) | 1.7(2.7) | 4(2.2) | 0.5(2.1) | 2(2) | -1.5(2.2) | 94(2) | 1(2) | -3.3(2.1) | -0.9(2.9) | -5(2.4)* | -0.1(3.4) |
| White | -0.3(1.5) | 0.5(1.5) | -0.5(1.3) | -0.5(1.2) | -0.3(1.2) | 1.1(1.3) | 95(1) | 1.2(1.4) | 1(1.4) | -0.7(1.4) | 1.6(1.9) | -4(2.4) |
| Difference | -1.1(3) | 1.2(3) | 4.4(2.6) | 0.9(2.4) | 2.3(2.3) | -2.7(2.5) | -1(2) | -0.1(2.4) | -4.3(2.5) | -0.2(3.3) | -6.6(3)* | 3.8(4.1) |
| Insulin, mU/mL | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 30 | 8 / 30 | 14 / 41 | 17 / 50 | 19 / 50 | 15 / 41 | 25 / 67 | 18 / 36 | 17 / 27 | 7 / 31 | 12 / 15 | 5 / 10 |
| Black | -5.1(13) | 11.8(14.3) | 3(11.2) | 1.6(10.4) | -5.3(9.9) | -17.4(10.9) | 10(1.1) | -0.6(10.1) | -6.8(10.4) | 7(15) | -1(12) | -2.3(17.6) |
| White | -11.5(7.6) | -13.2(7.6) | 3.6(6.6) | -4.6(6.1) | 0.4(6.1) | 10.6(6.6) | 8.4(0.6) | 2.8(7) | 13.9(7.9) | 9.6(7.4) | 21.6(10.2)* | 8.2(12.2) |
| Difference | 6.4(15) | 25(16.1) | -0.5(13) | 6.2(12) | -5.7(11.7) | -27.9(12.8)* | 1.7(1.2) | -3.5(12.3) | -20.7(13) | -2.6(16.7) | -22.7(15.7) | -10.5(21.4) |
| HOMA-IR | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 30 | 8 / 30 | 14 / 41 | 17 / 50 | 19 / 50 | 15 / 41 | 25 / 67 | 18 / 36 | 17 / 27 | 7 / 31 | 12 / 15 | 5 / 10 |
| Black | -4.9(14) | 15.5(15.3) | 8.5(12.1) | 4.5(11.2) | -3.2(10.7) | -17.8(11.8) | 2.4(0.3) | 2(10.9) | -8.4(11.2) | 6.5(16.1) | -5.1(12.9) | -0.7(18.9) |
| White | -11.2(8.1) | -12(8.1) | 2.5(7.1) | -4.8(6.6) | 0.7(6.6) | 12.1(7.1) | 2(0.2) | 3.7(7.5) | 16(8.5) | 9.1(8) | 24.8(10.9)* | 4.8(13.1) |
| Difference | 6.4(16.2) | 27.5(17.4) | 6(14) | 9.3(13) | -3.9(12.6) | -30(13.8)* | 0.4(0.3) | -1.7(13.3) | -24.4(14) | -2.5(18) | -29.9(16.9) | -5.5(23) |
| QUICKI | | | | | | | | | | | | |
| <i>n</i> (B/W) | 10 / 30 | 8 / 30 | 14 / 41 | 17 / 50 | 19 / 50 | 15 / 41 | 25 / 67 | 18 / 36 | 17 / 27 | 7 / 31 | 12 / 15 | 5 / 10 |
| Black | 2.2(2.1) | -1(2.3) | 0.3(1.8) | 1.6(1.7) | 1.5(1.6) | 4.2(1.8)* | 0.3(0) | 2.1(1.7) | 2.9(1.7) | -0.3(2.4) | 1.7(1.9) | 1.5(2.8) |
| White | 4(1.2)* | 3.6(1.2)* | 2.2(1.1)* | 3.4(1)* | 2.1(1)* | -0.4(1.1) | 0.4(0) | 0.4(1.1) | -0.3(1.3) | 0.1(1.2) | -1.3(1.6) | 0.5(2) |
| Difference | -1.8(2.4) | -4.6(2.6) | -1.9(2.1) | -1.9(2) | -0.6(1.9) | 4.6(2.1)* | 0.0(0) | 1.7(2) | 3.2(2.1) | -0.3(2.7) | 3(2.5) | 0.9(3.4) |

Abbreviations: B, Black; HDL, high-density lipoprotein cholesterol; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein cholesterol; QUICKI, quantitative insulin-sensitivity check index; W, White.

¹Data at menopause onset (Year 0) presented as raw mean (SEM). Significant differences in mean percent change (SEM) from Year 0 ($p < 0.05$) are denoted with an asterisk (*). Negative numbers indicate the percent that the raw value is less than Year 0.

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