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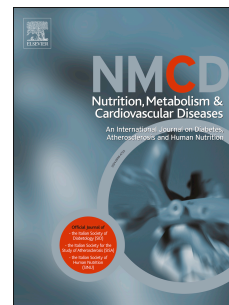
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# Journal Pre-proof

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## 1 Genetic loci implicated in meta-analysis of body shape in Africans

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## 37 **Abstract**

### 38 **Background and aims**

39 Obesity is one of the leading causes of non-communicable diseases (NCD). Thus, NCD risk  
40 varies in obese individuals based on the location of their fat depots; while subcutaneous  
41 adiposity is protective, visceral adiposity increases NCD risk. Although, previously  
42 anthropometric traits have been used to quantify body shape in low-income settings, there is  
43 no consensus on how it should be assessed. Hence, there is a growing interest to evaluate  
44 body shape derived from the principal component analysis (PCA) of anthropometric traits;  
45 however, this is yet to be explored in individuals of African ancestry whose body shape is  
46 different from those of Europeans. We set out to capture body shape in its multidimensional  
47 structure and examine the association between genetic variants and body shape in individuals  
48 of African ancestry.

### 49 **Method and results**

50 We performed a genome-wide association study (GWAS) for body shape derived from PCA  
51 analysis of anthropometric traits in the Ugandan General Population Cohort (GPC,  $n = 6,407$ )  
52 and the South African Zulu Cohort (SZC,  $n = 2,595$ ), followed by a GWAS meta-analysis to  
53 assess the genetic variants associated with body shape. We identified variants in *FGF12*,  
54 *GRM8*, *TLX1NB* and *TRAP1* to be associated with body shape. These genes were different  
55 from the genes been associated with BMI, height, weight, WC and waist-hip ration in  
56 continental Africans. Notably, we also observed that a standard deviation change in body  
57 shape was associated with an increase in blood pressure and blood lipids.

### 58 **Conclusion**

59 Variants associated with body shape, as a composite variable might be different for those of  
60 individual anthropometric traits. Larger studies are required to further explore these  
61 phenomena.

62

63 **Keywords:** Body shape, Principal components, Anthropometric traits, Uganda, Zulu

## 64 Introduction

65 The prevalence of obesity has tripled since 1975, accounting for over 650 million obese  
66 individuals, globally. It is now one of the leading causes of non-communicable diseases, such  
67 as cardiovascular diseases (CVDs), metabolic diseases and cancer [1, 2]. Anthropometric  
68 traits provide information about an individual's obesity through body shape, size and adiposity  
69 [3]. Body shape indicates body fat distribution and different types of adiposity that can reveal  
70 an individual risk of developing certain diseases [4]. The gold standard methods of measuring  
71 adiposity include dual-energy X-ray absorptiometry (DXA) and magnetic resonance imaging  
72 (MRI) [5]. However, these methods are often not available in most low-income clinical settings  
73 and are also expensive to run. Whereas inexpensive methods of measuring body fat include  
74 the use of anthropometric traits such as weight, height, body mass index (BMI), waist  
75 circumference (WC), hip circumference (HC), waist to hip ratio (WHR) and a body shape index  
76 (ABSI), derived from weight, height, and WC.

77 Although inexpensive measures of body fat are readily available in most clinical  
78 settings from lower-to-high income and even rural-to-urban, these measures are often not  
79 robust enough to differentiate between fat and muscle mass, nor visceral adiposity and  
80 peripheral adiposity; therefore, poorly predicting body shape as an index for obesity. Thus,  
81 there is a growing interest to evaluate body shape derived from the principal component  
82 analysis (PCA) of anthropometric traits in large diverse datasets of uncorrelated variables that  
83 are combined to denote body shape. Only a few studies have applied a PCA approach to  
84 investigate genetic loci associated with a complex trait like body shape, predominately in  
85 Europeans [6–8]. However, due to the history of steatopygia and its elevated prevalence in  
86 Africans, a PCA approach assessing body shape as an index of obesity is needed in  
87 continental Africans.

88 To capture body shape in its multidimensional structure and to identify genetic loci  
89 associated with body shape in individuals of African ancestry, we applied PCA to several  
90 anthropometric traits, including weight, height, BMI, WC, HC and WHR. Herein, we performed

91 a GWAS meta-analysis from two African cohorts to identify genetic loci associated with body  
92 shape as an index of obesity in individuals of African ancestry.

93

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## 94 **Results**

95 Overall, our study had 6,407 Ugandans from the general population cohort (GPC) and  
96 2,598 South African Zulu cohort (SZC). The majority of our study participants were females in  
97 both the GPC (57.1%) and SZC (73.8%) datasets (Table 1). The median age of our study  
98 participants was 29.8 years in the Ugandan GPC and 52.0 years in the SZC, indicating SZC  
99 was predominately made up of older women. Moreover, we observed SZC had a higher  
100 median BMI, height, weight, WHR, HC, and WC compared with the Ugandans (Table 1).

### 101 **PCA and body shape**

102 In the Ugandans, our first PC explained 61.93% of the variation for all anthropometric  
103 traits. We noted that the first PC has high loadings for BMI, weight, HC and WC, thus capturing  
104 body fatness among Ugandans from GPC and we named it “weight driven body shape” (Fig.1).  
105 In the SZC, our first PC explained 56.41% of the variation and had high loadings for BMI,  
106 weight, HC and WC (Fig.2). This PC also driven by weight, BMI , HC and WC, among the SZC  
107 and it was also named “weight driven body shape” to match with the one retained for the  
108 Ugandans. Based on the Kaiser rule, which chooses only PCs with eigenvalues  $>1$  (to retain  
109 only PCs that explain more than one variable)[9], we chose to retain the first and second PCs  
110 after PCA. We used the first PC of both Ugandans and Zulus, because of the similar  
111 anthropometric variables that were driving these principal components, which are the proxy  
112 for body shape in our analysis (Table S1, Fig S1). We then averaged loadings of first PC for  
113 Ugandans and Zulus to generate the PC which is representative of the most common body  
114 shape in Uganda and South African Zulu (Fig.S1). This first PC explained 60% of the variation  
115 for all anthropometric traits and had high loadings for weight, BMI, HC and WC; highlighting  
116 weight, BMI, HC and WC, as the main drivers of body shape in this context. The same  
117 approach was repeated for the sex stratified analysis. The male PC1 bodyshape was similar  
118 that of the combined analysis, while the female pc1 body shape, had increased loadings in  
119 the for waist-hip ration compared to the male and the combined PC1 body shape (Fig. 1) .

120

## 121 **Body shape association with cardiometabolic traits**

122 We performed a linear regression to assess whether any changes in body shape in  
123 both the Ugandans and Zulus were associated with blood pressure (systolic and diastolic) and  
124 blood lipids (low-density lipoprotein cholesterol, triglycerides, total cholesterol, and high-  
125 density lipoprotein cholesterol) traits in individuals of African ancestry. In our analysis, we  
126 observed that body shape changes were positively associated with blood pressure and blood  
127 lipids traits in Ugandans after adjusting for age and sex (Table.S2). Similarly, in the Zulus, the  
128 body shape was also positively associated with blood pressure traits, however, for blood lipid  
129 traits, the body shape was only positively associated with low-density lipoprotein cholesterol  
130 (Table.S2).

## 131 **Discovery of body shape genetic loci**

132 We then performed genome-wide association analyses for body shape in Ugandans  
133 and Zulus and meta-analysed the summary statistics to identify genetic loci associated with  
134 body shape, as an index of obesity in both cohorts (Methods). Furthermore, we performed a  
135 meta-analysis using the summary statistics from the Ugandans and Zulus to identify additional  
136 genetic loci associated with body shape. We identified rs150717769 to be associated with  
137 body shape at genome-wide significance,  $P$ -value =  $4.01e-09$  (Table 2). The Manhattan and  
138 QQ plot for the meta-analysis of body shape in individuals of African ancestry is shown in  
139 Fig.3. Moreover, rs150717769 is mapped onto the intron in the *TRAP1* gene (Table 2). For  
140 the sex stratified meta-analysis we found four variants that were significant associated ( $p <$   
141  $5e-08$ ) with body shape in women and one in men. These were rs111783937 (*TRAP1*),  
142 rs17867127 (*FGF12*), rs17867127 (*GRM8*), rs75156321 (*FGF12*), rs17126580 (*RNU4ATAC*)  
143 in females and rs7089940 (*TLX1NB*) in men. These variants and their related genes were  
144 different from those identified for the individual traits. (Fig. S4). We explored other traits these  
145 SNPs had been associated with in the Europeans using a PHEWAS approach and the TRAP1  
146 variant was associated with anthropometric traits. This variant based on the Diabetes  
147 Epigenome atlas is involved in regulatory activities as an enhancer in the adipose



148 tissues. The other variants were involved in the regulation of the central nervous system as  
149 enhancers and binding sites in the mammary glands. (Table 2).

150

## 151 **Discussion**

152 In this study, we performed a GWAS of PC derived body shape in two different African  
153 populations, as well as a meta-analysis of the most similar PCs, which presented several novel  
154 genetic loci associated with body shape in individuals of African ancestry. BMI, weight, WC  
155 and HC contributed the most in driving body shape patterns and they explained most of the  
156 variances for all the six anthropometric traits measured. We identified *HNRNPC* and *GBE1*  
157 genetic loci to be associated with body shape in Ugandans and Zulus, respectively. Overall,  
158 our meta-analysis of the Ugandan and Zulu GWASs identified *TRAP1* as a mutual, additional  
159 genetic locus associated with body shape, using the average loadings of the first PC for our  
160 six anthropometric traits.

161 Using average PC from 20 studies, Reid *et al.* (2016) reported body shape  
162 characterised by high loadings for all traits (weight, BMI, WC, WHR, and HC), except height  
163 in individuals of European ancestry [6]. Subsequently, in our analysis of continental Africans,  
164 we observed that the PC1 had high loadings for weight, BMI, WC and HC, and not in height  
165 nor WHR, thus, overall adiposity/body fatness in body shape in Africans is mostly driven by  
166 the former four traits. The loadings are in the same direction; meaning that the average PC1  
167 captures inter-individual variation in either increased or decreased BMI, weight, WHR, HC and  
168 WC. Interestingly, we observed that the first PC loadings in both Ugandans and Zulus were  
169 consistent in weight, BMI, WC and HC, even though the exact variances were different. This  
170 observation suggests that the body shape as an index of adiposity has predominantly common  
171 measures and features with variability in individuals of African ancestry residing in southern  
172 and eastern parts of Africa, as well as Europeans.

173 On the other hand, the notable differences between Reid *et al.* (2016), and our meta-  
174 analysis in the average PC1 are the low loadings of WHR in individuals of African ancestry.

175 Since the majority of our study participants were women, hence, the observed differences that  
176 are probably true for women of African ancestry, as they often tend to have wider hips, a lower  
177 WHR, and a higher prevalence of steatopygia, than women of European ancestry [10, 11].  
178 Furthermore, we also observed that both the WHR and height in both Ugandans and South  
179 African Zulus had low loadings in opposite directions, suggesting the average PC1 does not  
180 capture inter-individual variation in either increased or decreased WHR/height. However, the  
181 cause is not clear. For example, our second PCs in Ugandans and South African Zulus were  
182 driven more by WHR (and then height) and height (and then WHR, both in the opposite  
183 direction), respectively, compared to other anthropometric traits. Thus, our individual cohort  
184 loadings for our second to sixth PCs were not consistent between Ugandans and South  
185 African Zulus to use for meta-analyses.

186 After linear regression, with blood pressure and blood lipids traits in individuals of  
187 African ancestry in Uganda, our first PC was positively associated with adiposity derived body  
188 shape. However, in the Zulus, our PC1 was positively associated with blood pressure traits  
189 and only LDL; whereas, HDL exerted a protective effect. The observed differences in  
190 cardiometabolic trait prediction using PC1 between Ugandans and Zulus may be due to  
191 genetic and some environmental exposure differences between these cohorts [12–14] and  
192 future studies are needed to examine this association further.

193 .Using PC GWAS meta-analysis we identified rs150717769 ( $p = 4.01e-09$ ) to be  
194 associated with body shape in individuals of African ancestry. This variant is mapped in the  
195 intergenic region between *TRAP1* (Table 2). *TRAP1* acts as a key regulator of mitochondrial  
196 homeostasis, bioenergetics and metabolism, thus contributing to the regulation of the body  
197 shape. Moreover, *TRAP1* have been previously identified to be associated with BMI in  
198 individuals of diverse ancestry population [17]; and *TRAP1* was also associated with height in  
199 individuals of European ancestry [18]. Using the GTEx Portal, we observed that *TRAP1* is  
200 strongly expressed in visceral and subcutaneous adipose tissue, supporting our findings that  
201 the average PC1 captures largely adiposity in both Ugandans and South African Zulu. The  
202 other variants associated with sex stratified body shape located in *GRM8*, *TLX1NB*, *FGF12*

203 were noted to be involved in the regulatory activities in the central nervous system as  
204 enhancers. This is similar to what has been reported in related anthropometric GWAS where  
205 variants with function in the central nervous system have been implicated with obesity.

206

207         The main strength of this study is that our PC1 which explains much of anthropometric  
208 traits variation was associated with cardiometabolic traits including blood pressure and blood  
209 lipids traits in individuals of African ancestry. However, our study was limited by a few SNPs  
210 reaching genome-wide significance in both cohorts and our analyses were limited to PC1.  
211 Nevertheless, the other PCs have loadings similar to the single-trait GWASs and they do not  
212 explain much of the variation for anthropometric traits.

213         In summary, we identified five genomic loci to be associated with body shape in  
214 individuals of African ancestry that are different from those identified for individual traits in this  
215 population group. Our findings suggest that the body shape assessed by PCs provide more  
216 detailed information about an individual's body shape, size and adiposity that is not fully  
217 captured by individual anthropometric traits. If applied to other highly correlated phenotypes,  
218 PCA might reveal novel genetic loci and pathways that have not been identified in single-trait  
219 GWAS.

220

## 221 **Methods**

### 222 **Study Population**

223 The Medical Research Council (MRC) United Kingdom, together with the Uganda Virus  
224 Research Institute (UVRI) launched the General Population Cohort in the 1980s with the  
225 primary aim of investigating the epidemiology of Human Immunodeficiency Virus (HIV)  
226 infection in Uganda's. In 2011, the University of Cambridge, Wellcome Sanger Institute (WSI),  
227 in collaboration with the MRC/UVRI began the GPC round 22 study to investigate the genetics  
228 and epidemiology of communicable and non-communicable diseases in Uganda's, using both  
229 populations genetic and epidemiological approaches. A total of 4,778 Uganda's from the GPC  
230 round 22 study and 1,629 individuals from the Uganda 2,000 Genomes project (UG2G) [19,  
231 20], making up a total of 6,407 individuals were used as the discovery cohort.

232 The South African Zulu study, is a combination of the Durban Diabetes Study (DDS)  
233 and the Durban Case-Control Study (DCC) in KwaZulu-Natal, South Africa. DDS is a  
234 population-based cross-sectional study of individuals aged >18 years residing in the urban  
235 black communities in Durban, KwaZulu-Natal, South Africa. DCC is a case-control study of  
236 individuals aged >40 years with diabetes recruited from tertiary hospitals in Durban. Data  
237 collection was conducted from 2009 to 2013 for the DCC and from 2013 to 2014 for the DDS.  
238 The survey questionnaire included socioeconomic factors, health information, lifestyle factors,  
239 anthropometric measurements (including height, weight, systolic blood pressure, diastolic  
240 blood pressure, and hip and waist circumferences), biomarkers for communicable and non-  
241 communicable diseases, and genetic data. Of the 2,804 individuals surveyed, 1,204 were  
242 from the DDS and 1,600 were from the DCC; more detailed information on the study design  
243 and quality controls has been published previously [22]. The DDS was approved by the  
244 University of KwaZulu-Natal Biomedical Research Ethics Committee (UKZN BREC)  
245 (BF030/12) and the UK National Research Ethics Service (14/WM/); the DCC was approved  
246 by UKZN BREC (BF078/08) and the UK National Research Ethics Service (11/H0305/6). All

247 study participants in the GPC Ugandan and Zulu cohorts had anthropometric measurements  
248 and provided written informed consent to participate in the studies.

#### 249 **Anthropometric traits measurements**

250 At recruitment anthropometric traits including height, weight, WC and HC were  
251 measured from all the study participants. Height and weight were measured using the  
252 Leicester stadiometer and the Seca 761 class III mechanical flat scales, respectively [21]. WC  
253 and HCs were measured using the non-stretch Seca 201 ergonomic circumference measuring  
254 tape. WC was measured at the mid-point between the lower costal margin and the level of the  
255 anterior superior iliac crests. HC was measured at the greater trochanter of the femur as  
256 previously described [21]. BMI values were derived from weight over height whilst WHR was  
257 derived from WC values over HC values.

#### 258 **Genotype Data**

259 Information on sample collection, genotyping, imputation and quality control procedures were  
260 described in detail by previous studies [8, 21] Participant samples from the Uganda GPC were  
261 genotyped on the Illumina Human Omni 2.5M Bead Chip array at the Wellcome Trust Sanger  
262 Institute (WTSI). The samples were chosen as a subset of the survey population with the most  
263 complete phenotype data on the traits measured. Samples from the South African Zulu study  
264 were genotyped on the consortium-driven Illumina HumanOmni Multi-Ethnic GWAS/Exome  
265 Array (MEGA pre-commercial v1) using the Infinium Assay. Quality control was carried out  
266 collectively, with sample QC including filtering for called proportion ( $< 97\%$ ), heterozygosity ( $>$   
267  $4SD$  from mean), sex check fails (F statistic  $< 0.8$  for men, and  $> 0.2$  for women). Sample QC  
268 was followed by SNP QC, including filtering for called proportion ( $< 97\%$ ), Hardy Weinberg  
269 disequilibrium ( $p < 1e-06$ ), and relatedness (IBD  $> 0.90$ ). Samples and variants that did not  
270 pass the quality thresholds for the SNP and samples quality control were excluded. Principal  
271 Component Analysis (PCA) was carried out to correct for population/ancestry outliers.  
272 Following quality control, phasing and imputation for both cohorts were carried out with  
273 SHAPEIT2 using default parameters and IMPUTE2 respectively. Transformation of traits was

274 carried out uniformly for each cohort to make effect sizes comparable across cohorts, allowing  
275 meta-analyses of summary results.

276

### 277 **Estimation of PCs loadings and association testing**

278 To capture body shape in its multidimensional structure, we carried out PCA on six  
279 anthropometric traits. For each study, we performed a PCA on the standardized residuals of  
280 the anthropometric traits and adjusted for age and sex for the Uganda study. Diabetes status  
281 in addition to age and sex were corrected for in the South African Zulu study in the combined  
282 analysis. In the sex stratified analysis age and diabetes status were corrected for. The  
283 standardized residuals were decomposed into six principal components (PCs) according to  
284 eigenvectors, and principal loadings. The six resulting PCs is an aggregate and an orthogonal  
285 linear representation of individual PCs of the six anthropometric traits. In our analysis loadings  
286 is used to describe the weight of each PCs. The loadings and explained variances were  
287 comparable between Uganda's and Zulu from South Africa. The association between genetic  
288 variants and body shape was tested using the linear mixed model implemented in genome-  
289 wide efficient mixed-model analysis (GEMMA) [23]. In our analysis, we used PC1 as the  
290 phenotype of interest in both Uganda's and Zulu. Furthermore, we adjusted for cryptic  
291 relatedness by including a kinship matrix in the model. The kinship matrix was estimated using  
292 genetic variants with MAF >1% and pruned to an  $r^2$  threshold of 0.5

### 293 **Meta-Analysis and annotation of genetic variants**

294 Meta-analyses of 8769 participants was performed on the summary statistics of the  
295 PC1 of the Ugandan GPC (N = 6178) and South African Zulu cohort (N = 2591), , using the  
296 inverse variance weighted fixed-effects model as implemented in Metal. We also later  
297 conducted meta-analysis in men and women for the PC1 bodyshape. This is a free, efficient,  
298 and open-source meta-analysis software tool for GWASs analysis [24]. We used FUMA [25],  
299 to annotate, prioritize, visualize, and interpret GWASs results for body shape. Genetic variants  
300 with  $p < 5 \times 10^{-8}$  were selected as signals with genome-wide significance.  
301 The SNP2GENE function within FUMA takes GWAS summary statistics as an input and

302 provides extensive functional annotation in genomic areas identified by lead SNPs, while the  
303 GENE2FUNC annotates genes in a biological context [25].

#### 304 **Body shape and cardiometabolic traits**

305           Based on the Kaiser rule, we chose to retain the first and second PCs after PCA.  
306 However, in our analysis, we focused on the first PC in Ugandans as it was similar to the first  
307 PC in the South African Zulu dataset. We further evaluated whether our PC1 in both cohorts  
308 are associated with cardiometabolic traits, we then performed a linear regression analysis in  
309 both Ugandans and South African Zulu. In both cohorts, we adjusted for age and sex. We  
310 further adjusted for T2D in the South African Zulu dataset. In this analysis, our cardiometabolic  
311 traits were blood pressure (systolic and diastolic) and blood lipids (low-density lipoprotein  
312 cholesterol, triglycerides, total cholesterol, and high-density lipoprotein cholesterol) traits. The  
313 linear regression analysis was performed using the generalised linear model (GLM) and all  
314 statistical analyses were performed using the R language [26].

315

316

**317 Contribution statement**

318  
319 SF and TC conceptualized the study. MN, OS, TM, TC and SF performed the data analyses.  
320 ABK validated the analyses. MN and OS wrote the first draft. ABK, TM, TC, SF reviewed the  
321 first draft. SF and TC supervised the project. All the authors read and provided critical  
322 feedback on the paper.

323

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341

342

343

**344 Conflicts of interest**

345 None



346 **References**

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**Table 1.** Participant characteristics

Variables	Ugandan study ( <i>n</i> = 6,407) median (IQR)	South African Zulu ( <i>n</i> = 2,595) median (IQR)
Female, <i>n</i> (%)	3,660 (57.1)	1,919 (73.8)
Age, years	29.8 (17.8-46.1)	52.0 (39.0-60.0)
BMI, kg/m <sup>2</sup>	20.7 (18.8-23.0)	31.4 (26.1-36.9)
Height, m <sup>2</sup>	1.57 (1.51-1.63)	1.60 (1.55-1.65)
Weight, kg	52.0 (45.0-60.0)	80.0 (67.5-93.6)
WHR	0.84 (0.80-0.88)	0.92 (0.85-1.00)
HC, cm	89.0 (83.5-94.5)	109 (100-120)
WC, cm	74.0 (69.1-79.5)	103 (91.0-113)

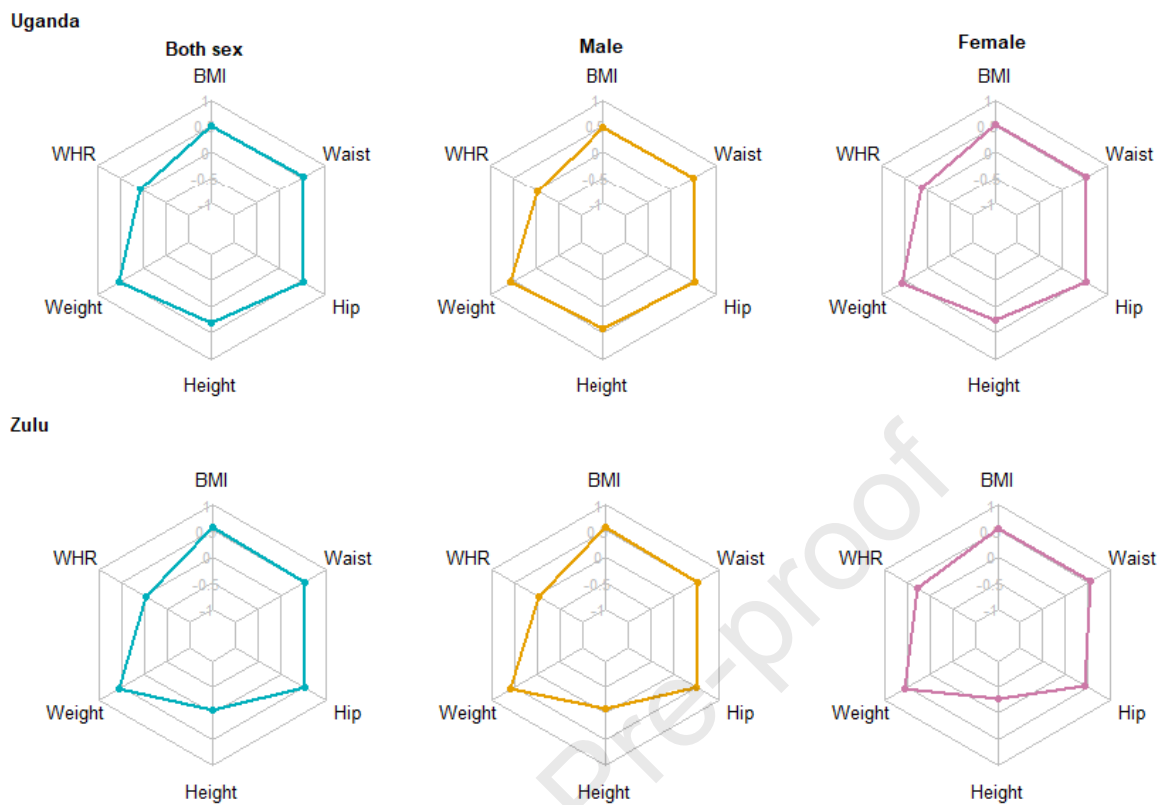
IQR; interquartile range, BMI; body mass index, WHR; waist-hip-ratio, HC; hip circumference, WC; weight circumference

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**Table 2.** Genetic loci associated with body shape composite phenotype in individuals of African ancestry

SNP	Annotation/tissue	Effect Allele	Non-Effect Allele	EAF	Nearest Gene	Zulu		UGR		Meta-analysis		
						Beta	P	Beta	P	Beta	P	Direction
<b>Combined</b>												
rs150717769	Intron/Enhancer/Adipose Tissue	A	G	0.73	<i>TRAP1</i>	-0.58	2.50e-03	-0.58	4.96e-07	0.58	4.01e-09	++
<b>Females</b>												
rs111783937	Intron/Enhancer/Central Nervous Tissue	A	G	0.73	<i>FGF12</i>	-0.43	1.17e-02	-0.12	7.41e-07	-0.21	4.32e-08	--
rs17867127	Intron/Enhancer/Stem Cell	A	G	0.14	<i>GRM8</i>	0.21	3.14e-03	0.14	1.12e-07	0.12	1.74e-09	++
rs75156321	Intron	A	G	0.73	<i>FGF12</i>	-0.32	1.42e-02	-0.31	4.32e-07	-0.25	3.43e-08	--
rs17126580	Intron/Enhancer/central nervous system	T	C	0.02	<i>RNU4ATAC</i>	0.24	7.33e-04	0.18	1.40e-05	0.25	3.79e-08	++
<b>Males</b>												
rs7089940	Intron/Binding site/Mammary gland	A	G	0.12	<i>TLX1NB</i>	0.18	1.34e-02	0.09	8.03e-07	0.29	3.43e-08	++

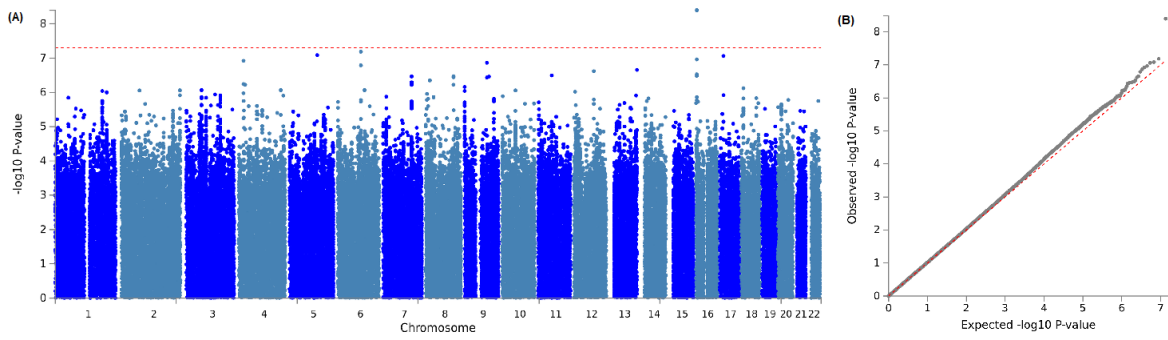
CHR; chromosome, SNP; single nucleotide polymorphisms, BP; base pair position, MAF; minor allele frequency, SE; standard error, P; p-value, UGR; Uganda Cohort,Zulu;South African Zulu Study. Annotation based in the Diabetes Epigenome Atlas



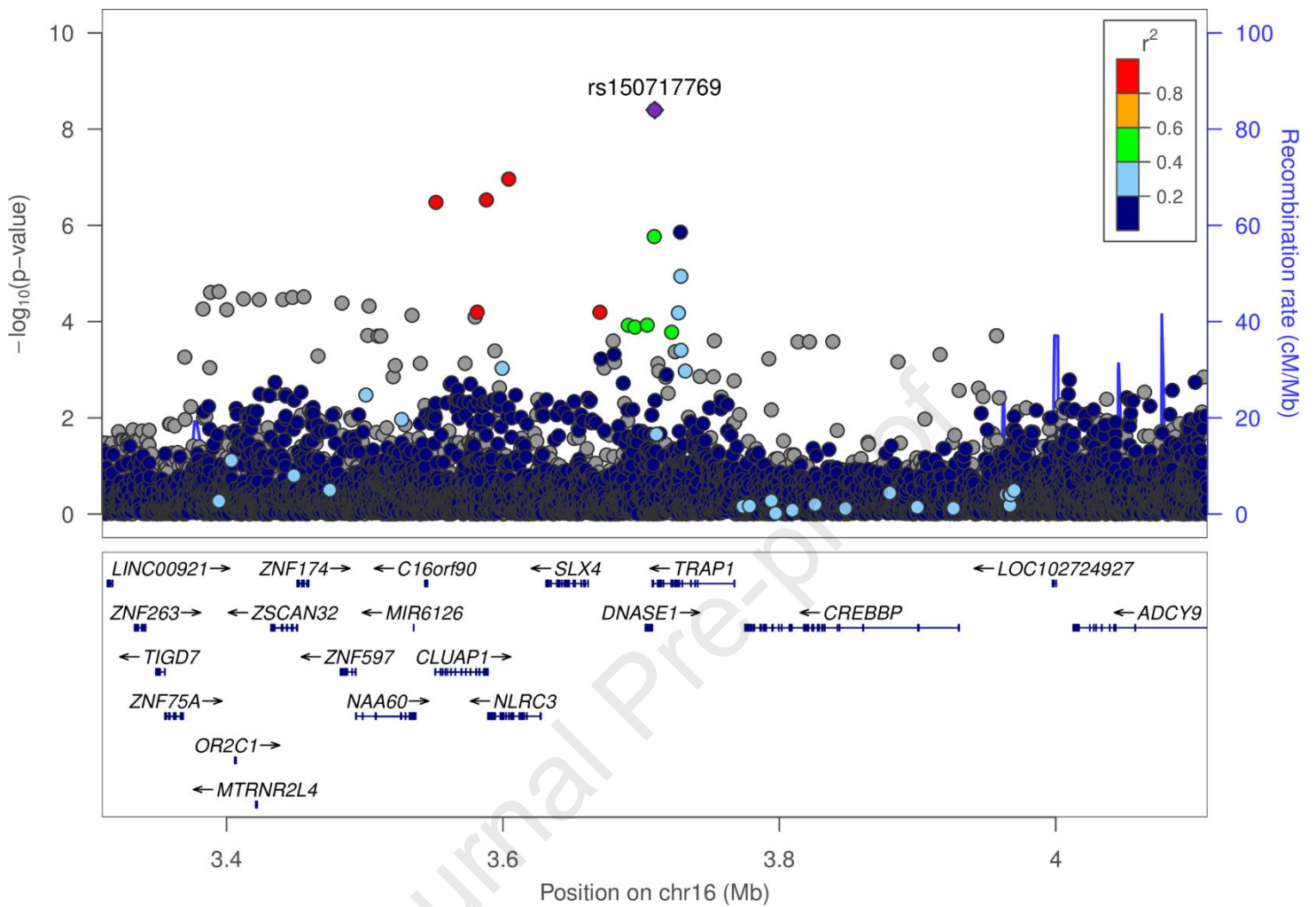
**Fig 1.** First PC was used to capture body shape in its multidimensional structure showing loadings for Ugandan and Zulu cohorts. (a) Loading for all participants in the Ugandan cohort, (b) loadings for male-Ugandan cohort (c) loading for female Ugandans. (d) Loading for all participants in the South African Zulu cohort, (e) loadings for male Zulus (f) loadings for female Zulus



**Fig 2.** PC loadings for Zulu in South Africa using six anthropometric traits to capture body shape in its multidimensional structure. **(A)** The first PC shows high loading for weight, BMI, WC and HC, **(B)** The second PC shows high loading for height, **(C)** The third PC shows high loading for WHR and height, **(D)** The fourth PC shows high loading WC, but opposite loading for HC, **(E)** The fifth PC shows high loading for BMI and opposite loadings for WC and HC **(F)** The sixth PC shows high loading for weight but opposite loading for BMI.



**Fig 3.** Meta-analysis association between genetic variants and body shape in individuals of African ancestry. **(A)** Manhattan plot, **(B)** QQ plot.



**Fig.4** Locus zoom plot for meta-analysis association between genetic variants and body shape showing rs150717769 mapped within the intergenic region between *TRAP1* and *DNASE1*





**Fig 2.** PC loadings for Zulu in South Africa using six anthropometric traits to capture body shape in its multidimensional structure. **(A)** The first PC shows high loading for weight, BMI, WC and HC, **(B)** The second PC shows high loading for height, **(C)** The third PC shows high loading for WHR and height, **(D)** The fourth PC shows high loading WC, but opposite loading for HC, **(E)** The fifth PC shows high loading for BMI and opposite loadings for WC and HC **(F)** The sixth PC shows high loading for weight but opposite loading for BMI.

## Highlights

- First genome-wide association study (GWAS) for body shape in Africans
- Genetic variants in *GBE1*, *HNRNPC* and *TRAP1* are associated with body shape in Africans.
- Those genetic loci are also known to be associated with Body Mass Index (BMI), height and Waist Circumference.
- Our study shows that a standard deviation change in body shape was associated with an increase in blood pressure and blood lipids.