

Obesity, genetic ancestry and socio-economic variables in Latin American mestizos

Anahí Ruderman*¹, Orlando Pérez*¹, Kaustubh Adhikari^{2,3}, Pablo Navarro¹, Virginia Ramallo¹, Carla Gallo⁴, Giovanni Poletti⁴, Gabriel Bedoya⁵, Maria Cátira Bortolini⁶, Victor Acuña-Alonzo⁷, Samuel Canizales-Quinteros⁸, Francisco Rothhammer⁹, Andres Ruiz-Linares^{3,10,11}, Rolando González-José¹.

¹*Instituto Patagónico de Ciencias Sociales y Humanas-CONICET. Bvd. Alte. Brown 2915, Puerto Madryn, Chubut, Argentina.*

²*School of Mathematics and Statistics, Faculty of Science, Technology, Engineering and Mathematics, The Open University, Milton Keynes, UK.*

³*Department of Genetics, Evolution and Environment, and UCL Genetics Institute, University College London, London, United Kingdom.*

⁴*Laboratorios de Investigación y Desarrollo, Facultad de Ciencias y Filosofía, Universidad Peruana Cayetano Heredia, Lima, Perú.*

⁵*Grupo de Genética Molecular (GENMOL), Universidad de Antioquia Medellín Colombia.*

⁶*Departamento de Genética, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brasil.*

⁷*Escuela Nacional de Antropología e Historia, Ciudad de México, Mexico.*

⁸*Unidad de Genómica de Poblaciones Aplicada a la Salud, Facultad de Química, UNAM-Instituto Nacional de Medicina Genómica, Mexico City, 4510, Mexico.*

⁹*Instituto de Alta Investigación Universidad de Tarapacá, Programa de Genética Humana ICBM Facultad de Medicina Universidad de Chile.*

¹⁰*Ministry of Education Key Laboratory of Contemporary Anthropology and Collaborative Innovation Center of Genetics and Development, School of Life Sciences and Human Phenome Institute, Fudan University, Shanghai, China.*

¹¹*Laboratory of Biocultural Anthropology, Law, Ethics, and Health (Centre National de la Recherche Scientifique and Etablissement Français du Sang, UMR-7268), Aix-Marseille University, Marseille, France.*

*These authors contributed equally to this work.

+Correspondant author:

Rolando González-José

Instituto Patagónico de Ciencias Sociales y Humanas-CONICET. Bvd. Alte. Brown 2915, Puerto Madryn, Chubut, Argentina.

rolando@cenpat-conicet.gob.ar

KEYWORDS

Obesity, genomic ancestry, Latin American mestizos, anthropometric indexes, socio-economic status.

ABSTRACT

Objectives: This article aims to assess the contribution of genetic ancestry and socio-economic status to obesity in a sample of admixed Latin Americans.

Methods: The study comprised 6776 adult volunteers from Brazil, Chile, Colombia, Mexico and Peru. Each volunteer completed a questionnaire about socio-economic variables. Anthropometric variables such as weight, height, waist and hip circumference were measured to calculate body indices: body mass index, waist to hip ratio, and waist to height ratio (WHtR). Genetic data were extracted from blood samples, and ancestry was estimated using chip genotypes. Multiple linear regression was used to evaluate the relationship between the indices and ancestry, educational level, and economic well-being. The body indices were dichotomized to obesity indices by using appropriate thresholds. Odds ratios were calculated for each obesity index.

Results: The sample showed high percentages of obesity by all measurements. However, indices did not overlap consistently when classifying obesity. WHtR resulted in the highest prevalence of obesity. Overall, women with low education level and men with high economic wellness were more likely to be obese. American ancestry was statistically associated with obesity indices, although to a lesser extent than socioeconomic variables.

Conclusions: The proportion of obesity was heavily dependent on the index and the population. Genetic ancestry has a significant influence on the anthropometric measurements, especially on central adiposity. As a whole, we detected a large inter-population variation that suggests that better approaches to overweight and obesity phenotypes are needed in order to obtain more precise reference values.

INTRODUCTION

During the past decades, most of the world's population has experienced a progressive change in dietary habits and lifestyles that has had a great impact on the overall health condition. Overweight and obesity have become an increasingly widespread issue, to the point of being considered one of the main health challenges of the twenty-first century (OMS, 2017). This disease is characterized by an unwanted accumulation of fat, often accompanied by numerous outcomes that can be categorized into physical, psychological, and social complications. The most serious concerns are associated with a higher risk for diabetes, cardiovascular (CV) problems, metabolic syndrome, and acceleration of the aging process of many organs (Apovian & Gocke, 2012; Legler et al., 2015; Nakamura et al., 2014).

Latin America has been no exception to the demographic and life-style changes that led to increased overweight and obesity throughout the world in recent years. Specifically, rapid urbanization was accompanied by a great demand for industrialization of food supplies, which resulted in increasing availability at the expense of quality. In Latin America, this worldwide process occurred in synchronicity with inherent regional characteristics, such as social inequality and genetic and non-genetic admixture, with varying patterns depending on country and locality.

It has been reported by several studies that obesity and overweight are influenced by socioeconomic variables, such as family economic income, place of residence (urban versus rural), education level (Acosta, 2013; Azar et al., 2015; Kurspahić-Mujčić & Zećo, 2017; Shang et al., 2013), and the interaction of these factors with gender. Some previous studies indicated that people in developing societies achieving high socioeconomic status (SES) were the most affected by overweight and obesity (Sobal & Stunkard, 1989). However, recent studies have shown that such gap has been closing, and reinforce the idea that overweight is no longer a disease typical of higher incomes. In this sense, Acosta (2013) noted that among men in Colombia overweight is concentrated within the population at the upper part of the income scale, whereas in women it is concentrated in the poorest population. In the United States, obesity has been found to be mainly concentrated in minority groups and among those with low socioeconomic levels (Zhang & Wang, 2007). Other variables such as eating and daily habits related to physical activity have been shown to be strongly related to obesity (Acosta, 2013; Azar et al., 2015; Cárdenas et al., 2013; García-Continente et al., 2014;

Kurspahić-Mujčić & Zećo, 2017). For example, Pérez (2011) suggested a link between the consumption of industrialized foods in rural communities of Yucatan, Mexico, and an increase in the additional energy stored in fats and sugars and the consequent negative impact on health due to its association with the development of obesity.

Furthermore, previous evidence indicates some effect of population and ancestry on obesity incidence (Nettleton et al., 2015; Roy et al., 2015). It has been found that at a given level of body mass index (BMI), some Asian populations have a higher level of body fat and central fat, compared to populations of European origin (WHO, 2011). Some researchers have suggested that the greater susceptibility to obesity among some populations has a significant genetic basis that may be triggered when confronted with an obesogenic environment, like a westernized lifestyle. This hypothesis is known as the “thrifty genotype” (Neel, 1962). Evidence supporting this hypothesis is the higher rates of obesity and type 2 diabetes that have been observed among Native Americans and Polynesians, among others (Aguilar-Salinas et al., 2009; Lara Riegos et al., 2015).

Regarding genetic risk factors, Latin American cosmopolitan populations are characterized by substantial genetic admixture, with predominant contributions from the Native American populations, Europe, and Africa (Morner, 1967). However, only a few studies (e.g., Florez et al., 2009) have explored Latin American populations through an approach that includes the study of genetic ancestry, phenotypic variables, and the socio-economic context.

The robustness and precision of anthropometric measurements used to quantify overweight and obesity is central to assessments of individual and population-level nutrition status. For decades, epidemiologists and clinicians have identified persons with excess weight based on a widely used and easy-to-calculate index: BMI. However, although BMI is commonly used in public health, an obvious limitation is its inability to distinguish between fat and fat-free mass. In this sense, recent epidemiological studies have shown that abdominal obesity is increasing in western populations, irrespective of BMI categories, highlighting the importance of the distribution of body fat (Kabat et al., 2008; Koster et al., 2008; Ladabaum et al., 2014; Masala et al., 2008; Wang et al., 2008). An increasing number of studies have shown that other indexes, such as waist-to-hip ratio (WHR) and waist-to-height ratio (WHtR), are better predictors of cardiovascular risk than BMI (Ge et al., 2014; Hsieh & Muto 2005, Motamed et al., 2015; Selvaraj et al., 2017; Yan et al., 2009).

In 1998, the WHO provided international BMI standards for classifying overweight and obesity in adults, based on the risk of obesity-related disease for Europeans at each BMI category. In recent years, the importance of selecting an adequate index and the need for specific cut-off points for each population, country, or geographical region has been emphasized. This information is beginning to be registered in regions such as Asia, Africa and the Pacific Islands (WHO, 2011); however, there is less information regarding Latin American populations.

Considering the above, this paper aims to test the agreement between several indexes developed to quantify overweight and obesity. Furthermore, and due to the complex and non-linear nature of risk factors underlying the expression of overweight and obesity, including genetic and non-genetic effects and potential interaction effects, we aim here to estimate the contribution of both genetic ancestry and SES to weight gain, as estimated by BMI, WHR, and WHtR.

The detection of such effects requires using composite samples including, for each specimen, several indices aimed to measure overweight and obesity, estimations of socioeconomic (and other environmental) factors, and genetic ancestry data on populations of varying admixture composition. The CANDELA (Consortium for the Analysis of the Diversity and Evolution of Latin America) initiative has been successful in compiling such a metadata biobank (Ruiz-Linares et al., 2014), and these data are used here.

MATERIALS AND METHODS

Sample. The CANDELA (Consortium for the Analysis of the Diversity and Evolution of Latin America) initiative collected data from more than seven thousand people from five countries in Latin America. A sample of 6776 adult volunteers from Brazil, Chile, Colombia, Mexico, and Peru was included in this study. Recruitment took place mainly in five locations: México City (México), Medellín (Colombia), Lima (Perú), Arica (Chile) and Porto Alegre (Brazil). All participants provided written informed consent, and ethics committee's approval was obtained from: Universidad Nacional Autónoma de México (Mexico), Universidad de Antioquia (Colombia), Universidad Peruana Cayetano Heredia (Peru), Universidad de Tarapaca (Chile), Universidade Federal do Rio Grande do Sul (Brazil) and University College London (UK). For further sample details, see Ruiz-Linares et al. (2014).

A structured questionnaire was given to each volunteer. This included questions about education level, lifestyle variables, dietary patterns and information regarding salary, home appliances, domestic services, transportation and infrastructure, among others. From these variables, two indices of socioeconomic position were used: education, and an SES score, which is a wealth index constructed using the lifestyle and ownership questions. For further sample details, see Ruiz-Linares et al. (2014). Briefly, education level was assessed as a categorical variable containing three levels: (1) none/primary/technical, (2) secondary and (3) university and post-graduate. Given the multifactorial and complex nature of economic wellness, the SES index was estimated from the information available in the CANDELA database on different lifestyle and ownership questions. A multivariate composite measure of SES was constructed using a Principal Component Analysis approach, aggregating the scores from all such questions. This analysis is a validated method to describe SES differentiation within a population (Cahill, & Sánchez, 2001; Vyas, & Kumaranayake, 2006).

An anthropometric survey of each volunteer was carried out by the local research team using a standardized protocol and instruments, including height, weight, and hip and waist circumference (WC). All measurements were obtained twice, and the mean of the two measurements was retained for further analyses.

The following body indices were calculated: BMI, WHR and WHtR. The body indices were dichotomized to obesity indices by using appropriate thresholds. Cut-off values of obesity for BMI and WHR were taken from the World Health Organization recommendations (WHO 1998 and 2011, respectively). Normal BMI values were established as 18.5-24.9 kg/m², and "obesity" after a BMI greater or equal to 30 kg/m². For WHR, values above 0.85 and 0.9 were considered not healthy for women and men, respectively. Regarding WHtR, "obesity" was taken to be values greater than 0.5, as suggested by Browning et al. (2010).

A certified phlebotomist collected blood samples and the DNA was extracted following standardized protocols (Ruiz-Linares et al., 2014). Samples were genotyped using the Illumina OmniExpress array (~730K SNPs), and combined with a global panel of reference samples. Supervised ancestry estimation using ADMIXTURE was performed, estimating three ancestry components: Native American, European, and African (Chacón-Duque et al., 2018).

Statistical methods

The effect of genetic ancestry, age, education and SES on the three body index phenotypes was evaluated by multiple linear regression. Each of the body indices (BMI, WHR, and WHtR) were regressed as the dependent variable onto five independent variables: age, Native ancestry, African ancestry, education, and SES. The analyses were performed separately for each combination of country and sex. With five independent variables being used, the significance threshold was adjusted using Bonferroni correction to allow for multiple testing. The significance threshold used was, therefore, $0.05/5 = 0.01$.

We divided the sample by countries since there are variables that depend on public policies implemented by each state and only affect the population that receives such policies (Mussini & Temporelli, 2013). In this sense, and considering that income is an important factor to avoid deterioration of the nutritional status, Latin American countries have developed a series of state regulations and social policies aiming to eradicating hunger and poverty in the most vulnerable populations (Cash Transfer Programs), with different targets and goals depending on the region. The outcome of these programs has been positive in the reduction of hunger and poverty until recently, when some countries showed a turndown in the 2011-2013 period, after which an alarming increase in obesity has been observed (FAO, 2017).

It is relevant to note that the samples collected were convenience samples within each country and, therefore, do not represent the entire population of these countries. The recruitment was also biased to certain demographics, most commonly university students and staff. This presents another reason to perform the analysis separately within countries, and the results have to be interpreted cautiously with reference to these facts.

To estimate the relative risk of obesity associated with a high proportion of genetic ancestry, we used a multivariate logistic regression model. The body indices were transformed to binary variables (obese or non-obese), and these obesity indices were used as the outcome variable. The same set of independent variables were used as before. However, only the effects of Native ancestry on these obesity indices were investigated. Therefore, there was no need for Bonferroni correction for the P-value threshold. The analyses were performed separately for each combination of country and sex. Note that for WHR, the cut-off values were different for the two sexes. All analyses were performed using the software Statistical Package for Social Sciences (SPSS) 20.2 and R 3.4.

As the distribution of the dependent and independent variables were non-normal, to better account for skewed distributions and possibility of outliers, robust versions of linear and logistic regressions were used, via the R package 'robust'.

RESULTS

General Description

Table 1 shows the mean and standard deviation of genetic ancestry according to country, along with the sample size and proportion of female participants. A more detailed description of the geographical variation of genetic estimates and an interpolated map based on coordinates for the participants' birthplaces can be found in Ruiz-Linares et al. (2014) and Chacón-Duque et al. (2018). The country with the highest Amerindian ancestry was Peru, followed by Mexico. The country with the lowest contribution to Amerindian ancestry was Brazil. Informative markers for African ancestry were higher in Brazil and Colombia (6.3% and 8.7% respectively) than the rest of the countries, which stayed well below 3.1%. The Brazilian sample had the highest proportion of European ancestry (84.5%), followed by Colombia (62.2%) and Chile (49.5%).

A description of the obesity indexes (BMI, WHR, and WHtR) computed on a slightly larger sample (7236 individuals) with missing genomic data, using the recommended cut-off values, is shown in Table 2. The prevalence of obesity according to the BMI ranged from 16.8% in Mexican males to 2.9% in Peruvian females. BMI average (both sexes) values ranged from 4.6% in Colombia to 14.2% in Mexico. Peru, Brazil and Chile were intermediate with 5.9%, 10.9 %, and 13.8%, respectively. Taking all individuals together, the overall prevalence of obesity (>30 kg/m²) was 9.9% for BMI, 31.9% for WHR and 48.3% for WHtR. In this sense, the incidence of obesity measured by indexes that included WC was higher than the incidence measured by BMI. Indexes showed a different distribution depending on the subsample, although in general WHtR resulted in the highest proportions. As expected, obesity increased with age. Therefore, cross-country differences were greater among young people and tended to homogenize in later stages of life. Indexes were moderate-to-highly correlated with each other. WHtR was highly correlated with BMI ($r_p = 0.87$) and with WHR ($r_p = 0.728$), whereas the least correlated variables were BMI and WHR ($r_p = 0.480$). Figure 1 shows a Venn diagram comparing the number of people classified as obese according to the different indices. In accordance to correlation, indices did not fully agree on assigning obesity. Individuals

who were simultaneously classified as obese or not healthy by the three indices comprised just 6.8% (493/7236) of the sample. Only one individual was classified as obese according to both BMI and WHR. Chilean women, for instance, displayed the highest proportion of obesity among people below the age of 30 years for BMI, but at the same time, they had the lowest percentage of obesity among women for WHR (Table 2). On average, Chilean women had a tendency for a peripheral distribution of fat, which is characterized by accumulation of weight in the lower half, near the hips and gluteus, while women in Mexico and Peru had a tendency for a central distribution of fat, characterized by excess weight around the midsection. In this sense, women from Peru and Mexico showed the highest percentage of obesity as measured by WHR. These results indicate a disparity regarding the ability of several indexes to classify persons as obese versus non-obese.

Linear regression

The results of the multiple linear regression models (coefficients and P-values) are depicted in table 3. Each model had a relatively low percentage of explained variance and the number of significant predictors varied with regard to each population. European ancestry was excluded from the models because it could be linearly predicted from the American and African ancestries (i.e., multicollinearity).

As seen in the table, the influence of genetic ancestry showed some trends in the regression models derived from all the indexes. Although the contribution to total variance was relatively low in these models, Amerindian ancestry was positively correlated with obesity, irrespective of the index used as a dependent variable. In addition, Amerindian ancestry showed significant relationships to WHR and WHtR in more subsamples than BMI, suggesting that indexes that included waist and/or hip circumference are more influenced by genetic ancestry than BMI. In the case of African ancestry, only one subsample was associated with obesity: in Colombian males, high prevalence of African markers was associated with low values of WHR ($\beta = -0.005$, p-value < 0.004).

SES and educational level showed an interesting pattern with regard to their association with the indexes. Even when Bonferroni corrected p-values resulted in mostly non-significant associations, there is a clear trend, and significant associations using $p < 0.05$, indicating that increasing obesity is associated with low levels of education among women, and with high levels of SES among men (Table 3).

Obesity indices were used via a logistic regression model to assess the effect of Native ancestry on obesity status. Odds ratio, confidence intervals, and P-values are presented

in Table 4. When we ran the models without adjusting for SES and education, the OR values did not vary significantly with respect to the model adjusted for education and economic well-being. As seen in the linear regression, European and Amerindian ancestry variables were highly collinear; therefore, the first parental population was excluded from the analysis for simplicity. In general, higher proportions of Amerindian ancestry were associated with higher ORs, independently of the obesity index used, and in several of the subsamples the association was statistically significant. Mexico, a sample with a high proportion of Amerindian ancestry, had elevated and significant ORs for almost every sex/obesity index comparison (OR = 7.49 and 12.76 for WHR in males and females, respectively, OR= 7.87 for BMI in males, and OR= 5.15 and 11.15 for WHtR in males and females, respectively). The Brazilian sample results should be taken with caution due to its low percentage of Native American ancestry (see Table 1). When the remaining countries were explored, the subsample of Peruvian females (WHtR) exhibited the highest OR, whereas the lowest value was observed in Colombian males (BMI). As a whole, these results suggest that individuals with Amerindian ancestry are at higher risk of obesity, when adjusting for age, sex, country, and socioeconomic level.

DISCUSSION

The cultural, genetic and phenotypic characteristics of Latin American populations are a result of an ongoing admixture process that began with the arrival of the European conquerors to the American continent in the 15th century and continues to this day. Although the health problems associated to overweight and obesity are a serious concern affecting human populations worldwide, these diseases affect Latin America populations in a particular way due to their distinctive genetic, social, economic, and historic-cultural background (FAO, 2007).

Our sample presented a high percentage of obesity, independent of the index used to quantify it. However, obesity prevalence and its distribution differed across subsamples and according to the observed index. For instance, Chilean women had the largest percentage of obesity according to BMI, an observation that was accentuated in the youngest age groups. In contrast, they had the lowest percentage of central obesity according to WHR. Mexican and Peruvian women showed the highest levels of central obesity measured by both WHR and WHtR, but not by BMI. Using WHR usually results in a higher estimate of obesity compared to BMI, as previously reported in a study focused on obesity in developing countries (Dinsa et al., 2017).

These results show that a single index is not enough for a reasonable description of a complex phenotype such as body fat distribution. Even when using two different indices to measure obesity, one person can be normal weight according to an index and obese according to the other. Unfortunately, research studies have to be confined to a few standardized markers, but advances in new technology like 3D scanning may lead to better measurements and improvements in the screening of large populations. This will likely allow a rapid and precise quantification of the human body (Daniell et al., 2014; Jaeschke et al., 2015), with non-invasiveness and high accuracy (Medina-Inojosa et al., 2016). Various types of handheld scanning systems are available in the market, which have progressively reduced the costs and installation complications, making it an accessible technology (Knoops et al, 2017; Soileau et al, 2016). However, improvements in cameras and computer processing power allow the development of scanning software systems on smartphone technologies (Navarro et al, 2018)

As described above, the studied indexes show different aspects of obesity across subsamples and seem to be sensitive to several biological and non-biological factors. A simple explanation could be found in the design of each index. The WHR and WHtR quantify abdominal obesity, while the BMI does not address the accumulation of central fat, which is a problem when trying to distinguish how adiposity is distributed. In addition, the differential coverage may be exacerbated by the underlying differences in the body shape of each population. This contrast can be clearly observed in our sample. Most women from Mexico and Peru exhibited an android body shape, a pattern characterized by central obesity, while women from Chile tended more to a gynoid body shape. Participants from Brazil and Colombia showed a mixed or intermediate pattern. It is necessary to mention that the current WHtR and WHR cut-offs have been defined after studies based on predominantly European-derived populations. Several authors have stated that these cut-offs may not be appropriate for other ethnic groups. For example, some studies have found that Asian samples tend to have a higher percentage of adipose tissue than their European counterparts when low BMI values are considered, (Deurenberg et al., 1998); and a similar trend is observed for higher WHRs in Native Australians when compared to European Australians (Piers et al., 2003). In South America, reported cut-offs for WHR ranged wildly across studies, with no determined reference standards (Lear et al., 2010, Berber et al., 2001).

Currently there is no consensus about the best adiposity measure. Some studies tend to find WHtR a better predictor for health risk (Janssen et al., 2004; Browning et al., 2010). Others show better correlations for WHR criteria when assessing cardio-vascular disease risk (Browning et al., 2010; Feldstein et al, 2005). Conversely, two large studies

support WC as a strong predictor of high blood glucose and related conditions (Mamtani et al., 2013; Huerta et al., 2013; Schneider et al., 2007). However, WC does not consider height, potentially under or overestimating risk in short or tall people. Despite all controversies, a prospective report on 4000 adults in the US (Reis et al., 2015), two studies of 46,024 and 244,266 Chinese adults (Hou et al., 2013; Zeng et al., 2014), and a study of 1,891 Singapore subjects (Lam et al., 2015) concluded that a combination of BMI and abdominal obesity (WC/WHR) are better predictors of cardio-vascular disease than BMI or WC/WHR alone.

The role of SES in relation to diet underlies a complex interplay woven between the macroeconomic and micro-social spheres. In the first scale, trade policies have a direct role in the food chain by controlling food availability through imports and production. Policies influence competition, price changes, income, occupation, services, and to some extent the characteristics of dietary patterns by promoting the presence of certain foods over others and increasing the convergence of food habits (social facilitation) (Aguirre, 2004; FAO, 2017). In the microsocial sphere, the factors that determine the access to food in the household setting change across the regions. Families need accessibility to supplies and the ability to obtain food to fulfill their overall needs (FAO, 2017).

In a systematic review of SES and obesity, Dinsa et al. (2012) observed that in middle-income countries, such as those in our study, the association becomes largely mixed for men and mainly negative for women. Even though Bonferroni correction indicates non-significance for many of the regression tests we performed, least conservative p-values (p-value=0.05) indicate a positive relationship between some obesity indexes and SES in men (e.g., Brazil, Chile, Mexico), but largely undetermined relationships when exploring the female subsample. Conversely, and using the same criteria, our results suggest an inverse relationship between education level and obesity in women. Previous work has shown that education is the variable more strongly associated with body dissatisfaction and may have implications in the perception of society standards of attractiveness or health. This observation indicates that it is plausible that women with high education value a thinner body, which is a feature seen in studies performed in developed countries (McLaren, 2007). Another putative reason for the negative association between education and obesity may be part of a residual feature of the traditional role that women have in selecting and buying the food for all the family, despite the changes in gender roles of the last decade (McLaren, 2007; Dinsa et al., 2012).

Regarding genomic ancestry, Native American and European markers were inversely correlated in the CANDELA sample. People carrying a high Native American signature were associated with more abdominal fat than people with low Native American ancestry. When quantifying this influence, BMI was the least influenced index. Since our multiple regression models included education and economic wellness as covariates, our results suggest that genetic ancestry would have a significant effect on obesity, independent of economic status or education. We did not find interaction effects among variables, with the sole exception of an attenuated influence of Amerindian ancestry on education in Mexican Women. However, there are other factors that can influence such relationships. For instance, recent studies on the UK Biobank sample found that the effect of genetic variants on BMI is modified by several lifestyle risk factors such as alcohol consumption, sleep patterns, diet and physical activity (Rask-Andersen et al., 2017).

Another potentially confounding variable is access to health care. Perreira et al. (2014) observed that individuals who self-reported as indigenous people have lower self-rated health than non-indigenous people in Latin America. Several studies confirm these observations and suggest that access to obesity treatments is not equally available to some specific social sub-groups such as Native American descendants living in isolated or marginal conditions (Montegro & Stephens, 2006), or people of low-incomes (Bastos et al., 2004; Ortiz-Hernandez, et al. 2015).

Excess body fat in Latin America could be generally explained by shifts in lifestyle and diet patterns, but also by a susceptibility component with a genetic basis. The “thrifty genotype” hypothesis tries to explain why Native American groups exhibit alarming rates of obesity and diabetes. This postulates that populations exposed to inadequate or fluctuating food consumption generate adaptive methods to achieve a high level of efficiency in the use of energy and deposition of fats. If these mechanisms are conserved after the group succeeds in obtaining food regularly, there may be an increase in the prevalence of overweight and type II diabetes. This hypothesis could be applied to Native American populations that made recent contact with the western way of life (Williams et al 2000, Burrows et al 2000, Chakraborty et al 1986). For instance, there is a significant effect of Native American ancestry on the effect of B-cell function in the Colombian population, one of the leading drivers of type II diabetes (Caro-Gómez et al., 2018). In this sense, genetic association studies have identified a set of genes (over 30) linked to obesity, such as FTO (fat mass and obesity-associated protein), the first gene discovered by GWAS, MC4R (melanocortin 4 receptor), LEPR (leptin receptor) and NEGR1 (Neuronal Growth Regulator I) (Speakman, Loos, O'Rahilly, Hirschhorn & Allison, 2018). However, it has been observed that the loci that promote obese phenotypes vary from

population to population, depending on their genetic architectures. According to these results, each gene has a low effect of penetrance and the socio-cultural variables take a preponderant role as predictive factors for obesity risk, e.g., mainly daily caloric intake and the level of physical activity. In addition, the effect of other factors on the nutritional status, such as the action of the intestinal microbiota (Baothman, Zamzami, Taher, Abubaker and Abu-Farha, 2016) and epigenetic information (Rosen et al., 2018; Van Dijk, Tellam, Morrison, Muhlhausler & Molloy, 2015), has been proposed by growing lines of research.

Due to this complexity, monitoring overweight and obesity is the foundation strategy for confronting the increased rate of chronic diseases associated with the current epidemiological transition. However, the classical anthropometric approach is not free of problems, since each index emphasizes a certain aspect of body shape but disregards others. Furthermore, inter-population variation indicates that reference values of obesity should be revised and adapted to the admixed Latin American populations. Further studies using more flexible methods instead of the predefined categories are necessary for a better understanding of the nutritional status across several contexts and populations. This is more valuable in the surveillance field, where efficient, massive and safe methods are being developed. Methods such as 3D scanning based on smartphone technologies can help to implement fast, accurate and cheap surface data (Medina-Inojosa et al., 2016; Navarro et al., 2018). Due to the nature of raw data (e.g., meshes that can be stored in digital platforms), such solutions not only solve the problem of reducing a complex three-dimensional shape phenotype to simplistic indexes, but facilitate the development of massive, population-specific databases that can be used to provide better reference values.

Conclusions

Genomic ancestry is positively associated with obesity in most studied Latin American subsamples and is a reliable predictor of body shape. Furthermore, we suggest that education and economic wellness have significant but different roles with regard to gender. Women with a high educational level tend to display lower levels of obesity, while overweight in men is related to higher economic status. These results indicate that the pattern and magnitude of obesity among several countries of Latin America reflect the complex interrelation between cultures, social factors acting at large-scales, and genetics. Unless a successful program is developed and sustained to stimulate people to remain physically active throughout their lives, it is expected that the proportion of sedentary people will continue to increase, and concomitantly, the prevalence of obesity

and associated conditions. Under this scenario, novel methodological and technical devices need to be developed in order to achieve a better capture of body shape, larger databases, and population-based reference values.

Acknowledgements

We are grateful to the volunteers of the CANDELA sampling for their enthusiastic support for this research. We thank Alvaro Alvarado, Mónica Ballesteros Romero, Ricardo Cebrecos, Miguel Ángel Contreras Sieck, Joyce De la Piedra, María Teresa Del Solar, William Flores, Martha Granados Riveros, Ilich Jafet Moreno, Jodie Lampert, Paola León-Mimila, Francisco Quispealaya, Diana Rogel Diaz, Ruth Rojas, Norman Russell, Vanessa Sarabia, Rosilene Paim, Ricardo Gunski, Sergeant João Felisberto Menezes Cavalheiro and Major Eugenio Correa de Souza Junior for assistance with volunteer recruitment, sample processing and data entry. We also want to thank Maria Dolores Marrodan Serrano for her contributions to this work. The following institutions kindly provided facilities for the assessment of volunteers: Escuela Nacional de Antropología e Historia and Universidad Nacional Autónoma de México (México); Pontificia Universidad Católica del Perú, Universidad de Lima and Universidad Nacional Mayor de San Marcos (Perú); Universidade Federal do Rio Grande do Sul (Brazil). This work was funded by grants from: the Leverhulme Trust (F/07 134/DF to ARL), BBSRC (BB/I021213/1 to ARL).

Author Contributions

A.R., O.P., V.R. and R.G.J. designed the study, V.R., C.G., G.B., M.C.B., S.C.Q, F.R. and A.R.L. managed data acquisition and curation, A.R., O.P., P.N., V.R. and R.G.J performed the analyses, A.R.L., acquired funding, A.R., O.P. and R.G.J. wrote the original draft with assistance of all authors.

References

- Acosta, K. (2014). La obesidad y su concentración según nivel socioeconómico en Colombia. *Revista de Economía del Rosario*, 16, 171-200.
- Aguilar-Salinas, C. A., Canizales-Quinteros, S., Rojas-Martinez, R., Mehta, R., Villarreal-Molina, M. T., Arellano-Campos, O., ... Tusie-Luna, M. T. (2009). Hypoalphalipoproteinemia in populations of Native American ancestry: an opportunity to assess the interaction of genes and the environment. *Curr. Opin. Lipidol*, 20 (2) 92-97.
- Aguirre, P. (2004). SEGURIDAD ALIMENTARIA. Una visión desde la antropología alimentaria. Desarrollo Integral en la Infancia: El Futuro Comprometido. Fundación CLACYD- Córdoba.

- Apovian, C. M., Gokce, N. (2012). Obesity and Cardiovascular Disease. *Circulation*, 125, 1178-1182.
- Azar, A., Franetovic, G., Martínez, M. and Santos, H. (2015). Individual, social and environmental determinants of overweight and obesity among Chilean adolescents. *Revista médica de Chile*, 143, 598-605. <https://dx.doi.org/10.4067/S0034-98872015000500007>
- Bastos, J. L., Barros, A. J., Celeste, R. K., Paradies, Y. and Faerstein, E. (2014) Age, class and race discrimination: their interactions and associations with mental health among Brazilian university students. *Cad Saude Publica*, 30(1),175-86.
- Berber, A., Gómez-Santos, R., Fanghänel, G., & Sánchez-Reyes, L. (2001). Anthropometric indexes in the prediction of type 2 diabetes mellitus, hypertension and dyslipidaemia in a Mexican population. *International Journal of Obesity*, 25(12), 1794–1799. doi:10.1038/sj.ijo.0801827.
- Browning, L. M., Hsieh, S. D. and Ashwell, M. (2010) A systematic review of waist-to-height ratio as a screening tool for the prediction of cardiovascular disease and diabetes: 0.5 could be a suitable global boundary value. *Nutr Res Rev* , 23, 247–269
- Burrows, N. R., Geiss, L. S., Engelgau, M. M. and Acton, K. J. (2000) Prevalence of diabetes among Native Americans and Alaska Natives, 1990–1997: an increasing burden. *Diabetes Care*, 23, 1786–1790.
- Cahill, M. B., & Sánchez, N. (2001). Using principal components to produce an economic and social development index: An application to Latin America and the U.S. *Atlantic Economic Journal*, 29(3), 311–329. doi:10.1007/bf02300552.
- Caro-Gomez, M. A., Naranjo-González, C. A., Gallego-Lopera, N., Parra-Marín, M. V., Valencia, D. M., Arcos, E. G., Villegas-Perrasse, A., Bedoya-Berrio, G. (2018) Association of Native American ancestry and common variants in ACE, ADIPOR2, MTNR1B, GCK, TCF7L2 and FTO genes with glycemic traits in Colombian population. *Gene*. 677:198-210. doi: 10.1016/j.gene.2018.07.0
- Cerqueira, C. C. S., Hünemeier, T., Gomez-Valdés, J., Ramallo, V., Volasko-Krause, C. D.,Barbosa, A. A. L. (2014). Implications of the Admixture Process in Skin Color Molecular Assessment. *PLoS ONE*, 9(5), e96886. doi:10.1371/journal.pone.0096886.
- Chacón-Duque, J.C., Adhikari, K., Fuentes-Guajardo, M., Mendoza-Revilla, J., Acuña-Alonzo, V., Barquera, R., Quinto-Sánchez, M., Gómez-Valdés, J., Everardo Martínez, P., Villamil-Ramírez, H., Hünemeier, T., Ramallo, V., Silva de Cerqueira, C.C., Hurtado, M., Villegas, V., Granja, V., Villena, M., Vásquez, R., Llop, E., Sandoval, J.R., Salazar-Granara, A.A., Parolin, M.L., Sandoval, K., Peñaloza-Espinosa, R.I., Rangel-Villalobos, H., Winkler, C.A., Klitz, W., Bravi, C., Molina, J., Corach, D., Barrantes, R., Gomes, V., Resende, C., Gusmão, L., Amorim, A., Xue, Y., Dugoujon, J.M., Moral, P., González-José, R., Schuler-Faccini, L., Salzano, F.M., Bortolini, M.C., Canizales-Quinteros, S., Poletti, G., Gallo, C., Bedoya, G., Rothhammer, F., Balding, D., Hellenthal, G., Ruiz-Linares A. (2018) Latin Americans show wide-spread Converso ancestry and imprint of local Native ancestry on physical appearance. *Nat Commun*. 9(1):5388.
- Chakraborty, R., Ferrell, R. E., Stern, M. P., Haffner, S. M., Hazuda, H. P., Rosenthal, M., & Rao, D. C. (1986). Relationship of prevalence of non-insulin-dependent

- diabetes mellitus to Amerindian admixture in the Mexican Americans of San Antonio, Texas. *Genetic Epidemiology*, 3(6), 435–454. doi:10.1002/gepi.1370030608.
- Cossrow, N., & Falkner, B. (2004). Race/Ethnic Issues in Obesity and Obesity-Related Comorbidities. *The Journal of Clinical Endocrinology & Metabolism*, 89(6), 2590–2594. doi:10.1210/jc.2004-0339.
- Daniell N, Olds T, Tomkinson G. (2014) Volumetric differences in body shape among adults with differing body mass index values: An analysis using three-dimensional body scans. *Am J Hum Biol.* 26(2):156-63.
- Deurenberg, P., Yap, M. and van Staveren, W. A. (1998). Body mass index and percent body fat: a meta analysis among different ethnic groups. *Int J Obes Relat Metab Disord*,22 (12):1164-1171.
- Deurenberg-Yap, M., Schmidt, G., van Staveren, W. A. and Deurenberg, P. (2000) The paradox of low body mass index and high body fat percentage among Chinese, Malays and Indians in Singapore. *Int J Obes Relat Metab Disord*, 24(8):1011-7.
- Dinsa, G. D., Goryakin, Y., Fumagalli, E. and Suhrcke, M. (2012). Obesity and socioeconomic status in developing countries: a systematic review. *obesity reviews*, 13, 1067–1079.
- FAO and PAO. (2017). Panorama of food and nutrition in Latin America and the Caribbean. Food and agriculture organization of the United Nations and the pan American health organization. Santiago de Chile.
- Feldstein, C. A., Akopian, M., Olivieri, A. O., Kramer, A. P., Nasi, M., & Garrido, D. (2005). A comparison of body mass index and waist-to-hip ratio as indicators of hypertension risk in an urban Argentine population: A hospital-based study. *Nutrition, Metabolism and Cardiovascular Diseases*, 15(4), 310–315. doi:10.1016/j.numecd.2005.03.001.
- Florez, J. C., Price, A. L., Campbell, D., Riba, L., Parra, M. V., Yu, F., ... Reich, D. (2009). Strong association of socioeconomic status with genetic ancestry in Latinos: implications for admixture studies of type 2 diabetes. *Diabetologia*, 52(8), 1528–1536. doi:10.1007/s00125-009-1412-x.
- Fuentes, M., Pulgar, I., Gallo, C., Bortolini, M.-C., Canizales-Quinteros, S., Bedoya, G., ... Rothhammer, F. (2014). Geografía génica de Chile: Distribución regional de los aportes genéticos americanos, europeos y africanos. *Revista Médica de Chile*, 142(3), 281–289. doi:10.4067/s0034-98872014000300001.
- Galanter, J. M., Fernandez-Lopez, J. C., Gignoux, C. R., Barnholtz-Sloan, J., Fernandez-Rozadilla, C., ... Via, M. (2012). Development of a Panel of Genome-Wide Ancestry Informative Markers to Study Admixture Throughout the Americas. *PLoS Genetics*, 8(3), e1002554. doi:10.1371/journal.pgen.1002554
- Garcia-Contiente, X., Allué, N., Pérez-Giménez, A., Ariza, C., Sánchez-Martínez, F., López, M. J. and Nebot, M. (2015). Hábitos alimentarios, conductas sedentarias y sobrepeso y obesidad en adolescentes de Barcelona. *An Pediatr (Barc)*, 83:3-10.
- Ge, W., Parvez, F., Wu, F., Islam, T., Ahmed, A., Shaheen, I., ... Chen, Y. (2014). Association between anthropometric measures of obesity and subclinical atherosclerosis in Bangladesh. *Atherosclerosis*, 232(1), 234-41. doi: 10.1016/j.atherosclerosis.2013.11.035.

- Hsieh, S. H. and Muto, T. (2005). The superiority of waist-to-height ratio as an anthropometric index to evaluate clustering of coronary risk factors among non-obese men and women. *Preventive Medicine*, 40 (2): 216-220.
- Hou, X., Lu, J., Weng, J., Ji, L., Shan, Z., ... Liu, J. (2013). Impact of Waist Circumference and Body Mass Index on Risk of Cardiometabolic Disorder and Cardiovascular Disease in Chinese Adults: A National Diabetes and Metabolic Disorders Survey. *PLoS ONE*, 8(3), e57319. doi:10.1371/journal.pone.0057319.
- Huerta, J. M., Tormo, M. J., Chirlaque, M. D., Gavrila, D., Amiano, P., Arriola, L., ... Navarro, C. (2013). Risk of type 2 diabetes according to traditional and emerging anthropometric indices in Spain, a Mediterranean country with high prevalence of obesity: results from a large-scale prospective cohort study. *BMC Endocr Disord*, 6, 13-7.
- Jaeschke, L., Steinbrecher, A., and Pischon, T. (2015). Measurement of waist and hip circumference with a body surface scanner: Feasibility, validity, reliability, and correlations with markers of the metabolic syndrome. *PLoS ONE*, 10(3).
- Janssen, I., Katzmarzyk, P. T. and Ross, R. (2004). Waist circumference and not body mass index explains obesity-related health risk. *Am J Clin Nutr* 79: 379–384.
- Kabat, G. C., Kim, M., Hunt, J. R., Chlebowski, R. T. and Rohan, T. E. (2008). Body mass index and waist circumference in relation to lung cancer risk in the Women's Health Initiative. *Am J Epidemiol*, 168, 158–169.
- Knoops Paul G.M. , Beaumont Caroline A.A., Borghi Alessandro, Rodriguez-Florez Naiara, Breakey Richard W.F., Rodgers William, Angullia Freida, Jeelani N.U. Owase, Schievano Silvia, Dunaway David J. (2017) Comparison of three-dimensional scanner systems for craniomaxillofacial imaging. *Journal of Plastic, Reconstructive & Aesthetic Surgery*, 70(4), pages: 441 – 449, ISSN 1748-6815.
- Kosoy, R., Nassir, R., Tian, C., White, P. A., Butler, L. M., Silva, G., ... Seldin, M. F. (2009). Ancestry informative marker sets for determining continental origin and admixture proportions in common populations in America. *Human Mutation*, 30(1), 69–78. doi:10.1002/humu.20822.
- Koster, A., Leitzmann, M. F., Schatzkin, A., Mouw, T., Adams, K. F. van Eijk, J. T., ... Harris, T. B. (2008). Waist circumference and mortality. *Am J Epidemiol*, 167, 1465–1475.
- Kurspahić-Mujčić, A. and Zećo, E. (2017). Socioeconomic and demographic factors associated with abdominal obesity in women of childbearing age. *Med Glas (Zenica)*, 14, 218-223.
- Ladabaum, U., Mannalithara, A., Myer P. A., and Singh, G. (2014). Obesity, Abdominal Obesity, Physical Activity, and Caloric Intake in US Adults: 1988 to 2010. *The American Journal of Medicine*. 127(8): 717-727.e12.
- Lam, B. C., Koh, G. C., Chen, C., Wong, M. T. and Fallows, S. J. (2015). Comparison of Body Mass Index (BMI), Body Adiposity Index (BAI), Waist Circumference (WC), Waist-To-Hip Ratio (WHR) and Waist-To-Height Ratio (WHtR) as predictors of cardiovascular disease risk factors in an adult population in Singapore. *PLoS One* 10, e0122985.
- Lara-Riegos, J.C., Ortiz-López, M.G., Peña-Espinoza, B.I., Montúfar-Robles, I., Peña-Rico, M.A., Sánchez-Pozos, K., Granados-Silvestre, M.A., Menjivar, M. (2015) Diabetes susceptibility in Mayas: Evidence for the involvement of polymorphisms in

HHEX, HNF4 α , KCNJ11, PPAR γ , CDKN2A/2B, SLC30A8, CDC123/CAMK1D, TCF7L2, ABCA1 and SLC16A11 genes. *Gene*. 565(1):68-75.

- Lear, S. A., James, P. T., Ko, G. T., & Kumanyika, S. (2009). Appropriateness of waist circumference and waist-to-hip ratio cutoffs for different ethnic groups. *European Journal of Clinical Nutrition*, 64(1), 42–61. doi:10.1038/ejcn.2009.70.
- Legler, J., Fletcher, T., Govarts, E., Porta, M., Blumberg, B., Heindel, J. J. and Trasande, L. (2015). Obesity, Diabetes, and Associated Costs of Exposure to Endocrine-Disrupting Chemicals in the European Union. *The Journal of Clinical Endocrinology & Metabolism*, 100, 1278–1288. <https://doi.org/10.1210/jc.2014-4326>
- Mamtani, M., Kulkarni, H., Dyer, T. D., Almasy, L., Mahaney, M. C., Duggirala, R., ... Curran, J. E. (2013). Waist Circumference Independently Associates with the Risk of Insulin Resistance and Type 2 Diabetes in Mexican American Families. *PLoS ONE*, 8(3), e59153. doi:10.1371/journal.pone.0059153.
- Marín Cárdenas, A. D., Sánchez Ramírez, G. and Maza Rodríguez, L. (2013). Prevalencia de obesidad y hábitos alimentarios desde el enfoque de género: el caso de Dzutóh, Yucatán, México. *Revista de Alimentación Contemporánea y Desarrollo Regional*. Vol. 22, Núm. 44.
- Masala, G., Bendinelli, B., Versari, D., Saieva, C., Ceroti, M., Santagiuliana, F., ... Palli, D. (2008). Anthropometric and dietary determinants of blood pressure in over 7000 Mediterranean women: the European Prospective Investigation into Cancer and Nutrition-Florence cohort. *Journal of Hypertension*, 26(11), 2112–2120. doi:10.1097/hjh.0b013e32830ef75c.
- McLaren, L. (2007). Socioeconomic status and obesity. *Epidemiol Rev*, 29,29-48.
- Medina-Inojosa, J., Somers, V. K., Ngwa, T., Hinshaw, L. and Lopez-Jimenez, F. (2016). Reliability of a 3D Body Scanner for Anthropometric Measurements of Central Obesity. *Obesity, open access*, 2(3):10.16966/2380-5528.122.
- Monteiro, C., Moura, E., Conde, W. and Popkin, B. (2005). Socioeconomic Status and Obesity in Adult Populations of Developing Countries: A Review. *Bulletin of the World Health Organization*. 82. 940-6.
- Montenegro, R. A., & Stephens, C. (2006). Indigenous health in Latin America and the Caribbean. *The Lancet*, 367(9525), 1859–1869. doi:10.1016/s0140-6736(06)68808-9.
- Morner, M. (1967) *Race Mixture in the History of Latin America*. Little Brown & Company. 178 p.
- Motamed, N., Perumal, D., Zamani, F., Ashrafi, H., Haghjoo, M., Saeedian, F. S., ... Asouri, M. (2015). Conicity Index and Waist-to-Hip Ratio Are Superior Obesity Indices in Predicting 10-Year Cardiovascular Risk Among Men and Women. *Clinical Cardiology*, 38(9), 527–534. doi:10.1002/clc.22437
- Mussini, M. and Temporelli, K. L. (2013). Obesidad: un desafío para las políticas públicas. *Estudios sociales (Hermosillo, Son.)*, 21(41), 165-184.
- Navarro, J. P., Cintas, C., Ramallo, V., de Azevedo, S., Morales, A. L., Trujillo, A, Pazos, C.B., González-José, R & Delrieux, C. (2018). Escaneo corporal 3D de bajo costo para monitoreo y seguimiento remotos de sobrepeso. In IX Congreso Argentino de Informática y Salud (CAIS)-JAIIO 47, pages 10-13, ISSN 2451-7607

- Nakamura, K., Fuster, J. J. and Walsh, K. (2014). Adipokines: A link between obesity and cardiovascular disease. *Journal of Cardiology*, 63, 250–259.
- Neel, J. V. (1962). Diabetes mellitus: a 'thrifty' genotype rendered detrimental by 'progress'?. *Am J Hum Genet*, 14:353–362
- Nettleton, J. A., Follis, J. L, Ngwa, J. S., Smith, C. E., Ahmad, S., Tanaka, T., ... Franks, P. W. (2015). Gene x dietary pattern interactions in obesity: analysis of up to 68 317 adults of European ancestry. *Human Molecular Genetics*, Volume 24, 4728–4738, <https://doi.org/10.1093/hmg/ddv186>
- Ortiz-Hernández, L., Pérez-Salgado, D. and Tamez-González, S. (2015). Socioeconomic inequality and health in Mexico. *Rev Med Inst Mex Seguro Soc*, 53(3), 336-47.
- Pérez, O. (2011). Cambios en la alimentación de dos comunidades mayas del estado de Yucatán. Elementos para una política integral de educación nutricional. Tesis de doctorado, El Colegio de la Frontera Sur.
- Perreira, K. M. and Telles, E. E. (2014). The color of health: skin color, ethnoracial classification, and discrimination in the health of Latin Americans. *Soc Sci Med*, 116, 241-50.
- Piers, L. S., Rowley, K. G., Soares, M. J., & O'Dea, K. (2003). Relation of adiposity and body fat distribution to body mass index in Australians of Aboriginal and European ancestry. *European Journal of Clinical Nutrition*, 57(8), 956–963. doi:10.1038/sj.ejcn.1601630
- Rask-Andersen, M., Karlsson, T., Ek, W. E. and Johansson, Å. (2017) Gene-environment interaction study for BMI reveals interactions between genetic factors and physical activity, alcohol consumption and socioeconomic status. *PLoS Genet* 13(9): e1006977. <https://doi.org/10.1371/journal.pgen.1006977>.
- Reis, J. P., Allen, N., Gunderson, E. P., Lee, J. M., Lewis, C. E., Loria, C. M., ... Liu, K. (2015). Excess body mass index- and waist circumference-years and incident cardiovascular disease: The CARDIA study. *Obesity*, 23, 879–885.
- Rosen, E. D., Kaestner, K. H., Natarajan, R., Patti, M.-E., Sallari, R., Sander, M., & Susztak, K. (2018). Epigenetics and Epigenomics: Implications for Diabetes and Obesity. *Diabetes*, 67(10), 1923–1931. doi:10.2337/db18-0537.
- Roy, S. M., Chesi, A., Mentch, F., Xiao, R, Chiavacci, R., Mitchell, J. A., ... McCormack, S. E. (2015). Body Mass Index (BMI) Trajectories in Infancy Differ by Population Ancestry and May Presage Disparities in Early Childhood Obesity. *The Journal of Clinical Endocrinology & Metabolism*, Volume 100, 1551–1560, <https://doi.org/10.1210/clinem.2014-4028>
- Ruiz-Linares, A. (2014). How Genes Have Illuminated the History of Early Americans and Latino Americans. *Cold Spring Harbor Perspectives in Biology*, 7(6), a008557. doi:10.1101/cshperspect.a008557
- Ruiz-Linares, A., Adhikari, K., Acuña-Alonzo, V., Quinto-Sanchez, M., Jaramillo, C., Arias, W., ... Gonzalez-José, R. (2014). Admixture in Latin America: Geographic Structure, Phenotypic Diversity and Self-Perception of Ancestry Based on 7,342 Individuals. *PLoS Genetics*, 10(9), e1004572. doi:10.1371/journal.pgen.1004572

- Schneider, H. J., Glaesmer, H., Klotsche, J., Bohler, S., Lehnert, H., Zeiher, A. M., ... Wittchen, H. (2007) Accuracy of anthropometric indicators of obesity to predict cardiovascular risk. *J Clin Endocrinol Met*, 92, 589–594.
- Selvaraj, S., Martinez, E. E., Aguilar, F. G., Kim, K.-Y. A., Peng, J., Sha, J., ... Shah, S. J. (2016). Association of Central Adiposity With Adverse Cardiac Mechanics: Findings from the HyperGEN Study. *Circulation. Cardiovascular Imaging*, 9(6), 10.1161/CIRCIMAGING.115.004396 e004396.
<http://doi.org/10.1161/CIRCIMAGING.115.004396>
- Sobal, J., Stunkard A. J. (1989). Socioeconomic status and obesity: a review of the literature, *Psychol Bull*, 105(2):260-75.
- Soileau L, Bautista 2, Johnson C, Gao C, Zhang K, Li X, Heymsfield SB, Thomas D, Zheng J. (2016) Automated anthropometric phenotyping with novel Kinect-based three-dimensional imaging method: comparison with a reference laser imaging system. *Eur J Clin Nutr*. 70(4):475-81.
- Van Dijk, S. J., Tellam, R. L., Morrison, J. L., Muhlhausler, B. S., & Molloy, P. L. (2015). Recent developments on the role of epigenetics in obesity and metabolic disease. *Clinical Epigenetics*, 7(1). doi:10.1186/s13148-015-0101-5.
- Viego, V. and Temporelli, K. (2011). Sobrepeso y obesidad en Argentina. Un análisis basado en técnicas de econometría espacial/Overweigh and Obesity in Argentina. A Spatial Approach. *Estudios de Economía Aplicada* 29(3), 1-26.
- Vyas, S. and Kumaranayake, L. (2006). Constructing socio-economic status indices: how to use principal components analysis. *Health Policy and Planning*, 21, 459–468.
- Wang, Y. and Beydoun, M. A. (2007) The Obesity Epidemic in the United States—Gender, Age, Socioeconomic, Racial/Ethnic, and Geographic Characteristics: A Systematic Review and Meta-Regression Analysis. *Epidemiologic Reviews*, Volume 29, 6–28, <https://doi.org/10.1093/epirev/mxm007>
- Wang, Y., Jacobs, E. J., Patel, A. V., Rodriguez, C., McCullough, M. L., Thun, M. J. and Calle, E. E. (2008). A prospective study of waist circumference and body mass index in relation to colorectal cancer incidence. *Cancer Causes Control*, 19, 783–792.
- Williams, R. C., Long, J. C., Hanson, R. L., Sievers, M. L. and Knowler, W. C. (2000) Individual estimates of European genetic admixture associated with lower body mass index, plasma glucose, and prevalence of type 2 diabetes in Pima Indians 1. *AmJHumGenet*, 66, 527–538.
- World Health Organisation. (2017). 10 facts about obesity. Ginebra, Suiza: World Health Organisation. Recovered from: <http://www.who.int/features/factfiles/obesity/es/>
- World Health Organization. (1998). Obesity: preventing and managing the global epidemic. World Health Organization: Geneva 1998; 276.
- World Health Organization. (2011). Waist Circumference and Waist–Hip Ratio: Report of a WHO Expert Consultation Geneva, 8–11.
- Yan, R. T., Yan, A. T., Anderson, T. J., Buithieu, J., Charbonneau, F., Title, L., ... Lonn, E. M. (2009). The differential association between various anthropometric indices of obesity and subclinical atherosclerosis. *Atherosclerosis*, 207(1), 232–238. doi:10.1016/j.atherosclerosis.2009.03.05

Zeng, Q., He, Y., Dong, S., Zhao, X., Chen, Z., Song, Z., ... Wang, Y. (2014). Optimal cut-off values of BMI, waist circumference and waist:height ratio for defining obesity in Chinese adults. *British Journal of Nutrition*, 112(10), 1735–1744. doi:10.1017/s0007114514002657.

Figure 1: Prevalence of obesity according to each index.



Table 1. Mean and standard deviations (SD) of genetic ancestry by country.

| Country | N | % Female | European | | African | | Native American | |
|----------|------|----------|----------|------|---------|-----|-----------------|------|
| | | | Mean | SD | Mean | SD | Mean | SD |
| Brazil | 682 | 68.3 | 84.5 | 15.8 | 6.3 | 8.9 | 9.3 | 11.6 |
| Chile | 1858 | 39.7 | 49.5 | 15.8 | 2.2 | 2.3 | 48.3 | 16.1 |
| Colombia | 1745 | 55.6 | 62.2 | 12.7 | 8.7 | 8.7 | 29.0 | 10.5 |
| Mexico | 1233 | 61.2 | 39.6 | 18.8 | 3.0 | 2.7 | 57.5 | 19.4 |
| Peru | 1258 | 58.7 | 30.8 | 17.5 | 3.1 | 4.6 | 66.1 | 18.6 |

These ancestry estimates are obtained from the subset of individuals who were chip genotyped. Sample sizes, and proportion of female volunteers, among the total sample of chip genotyped individuals, is also provided.

Table 2. Percentage of men and women classified as obese according to WHR, WHtR, and BMI, by country and age class.

| Country | Age | Women | | | Men | | |
|-----------------|-------|-------------------|-------------------|------------------|------------------|------------------|------------------|
| | | WHR>0.85 | WHtR>0.5 | BMI>30 | WHR>0.9 | WHtR>0.5 | BMI>30 |
| Colombia | 18-30 | (n=538) 21.93 | (n=536) 28.80 | (n=812) 2.58 | (n=364) 12.08 | (n=366) 27.05 | (n=591) 4.56 |
| | 31-40 | (n=48) 39.58 | (n=47) 46.66 | (n=112) 10.71 | (n=56) 33.92 | (n=56) 50.00 | (121) 10.74 |
| | 41-50 | § | § | § | § | § | § |
| | 51-60 | § | § | § | § | § | § |
| | Total | (n=588) 23.46 | (n=585) 34.52 | (n=926) 3.56 | (n=425) 14.82 | (n=427) 29.74 | (n=721) 5.54 |
| Brazil | 18-30 | (n=722) 11.10 | (n=721) 16.88 | (n=723) 4.70 | (n=339) 13.86 | (n=339) 33.92 | (n=339) 8.55 |
| | 31-40 | (n=151) 28.47 | (n=150) 37.59 | (n=151) 14.56 | (n=64) 40.62 | (n=64) 62.50 | (n=65) 13.84 |
| | 41-50 | (n=88) 43.18 | (n=88) 65.06 | (n=88) 19.31 | (n=44) 68.18 | (n=44) 79.54 | (n=44) 15.90 |
| | 51-60 | (n=47) 53.19 | (n=47) 71.11 | (n=47) 23.40 | (n=37) 89.19 | (n=37) 91.89 | (n=37) 35.13 |
| | Total | (n=1044) 18.48 | (n=1042) 30.51 | (n=1045) 8.70 | (n=498) 29.11 | (n=498) 46.98 | (n=499) 13.02 |
| Chile | 18-30 | (n=372) 7.28 | (n=369) 28.32 | (n=372) 9.67 | (n=769) 26.00 | (n=767) 60.76 | (n=775) 11.48 |
| | 31-40 | (n=78) 20.51 | (n=78) 51.35 | (n=78) 23.07 | (n=135) 54.81 | (n=136) 85.29 | (n=137) 15.32 |
| | 41-50 | (n=44) 45.45 | (n=44) 69.05 | (n=44) 20.45 | (n=70) 80.00 | (n=70) 94.28 | (n=70) 31.42 |
| | 51-60 | (n=24) 41.66 | (n=24) 70.83 | (n=24) 25.00 | (n=53) 86.79 | (n=53) 94.33 | (n=53) 28.30 |

| | | | | | | | |
|---------------|-------|---------|---------|---------|----------|----------|----------|
| | Total | (n=518) | (n=515) | (n=518) | (n=1027) | (n=1026) | (n=1035) |
| | | 14.09 | 40.97 | 13.32 | 36.61 | 68.03 | 14.20 |
| México | 18-30 | (n=686) | (n=686) | (n=687) | (n=442) | (n=442) | (n=448) |
| | | 43.29 | 43.41 | 6.25 | 38.00 | 46.60 | 12.50 |
| | 31-40 | (n=115) | (n=115) | (n=115) | (n=88) | (n=89) | (n=90) |
| | | 58.26 | 67.57 | 20.00 | 64.77 | 75.28 | 25.55 |
| | 41-50 | (n=70) | (n=70) | (n=70) | (n=44) | (n=44) | (n=44) |
| | | 68.57 | 85.30 | 32.85 | 81.81 | 77.27 | 29.54 |
| | 51-60 | (n=82) | (n=82) | (n=82) | (n=50) | (n=50) | (n=50) |
| | | 79.27 | 93.75 | 26.83 | 92.00 | 88.00 | 28.00 |
| | Total | (n=953) | (n=953) | (n=954) | (n=624) | (n=625) | (n=632) |
| | | 50.05 | 56.34 | 11.63 | 49.19 | 56.16 | 16.77 |
| Perú | 18-30 | (n=259) | (n=258) | (n=514) | (n=153) | (n=152) | (n=326) |
| | | 44.78 | 52.52 | 2.91 | 37.25 | 59.21 | 6.70 |
| | 31-40 | (n=16) | (n=16) | (n=29) | (n=19) | (n=19) | (n=29) |
| | | 25.00 | 80.00 | 3.44 | 52.53 | 71.42 | 31.03 |
| | 41-50 | § | § | § | § | § | § |
| | 51-60 | § | § | § | § | § | § |
| | Total | (n=276) | (n=275) | (n=545) | (n=176) | (n=175) | (n=360) |
| | | 43.84 | 57.81 | 2.93 | 39.77 | 61.71 | 8.88 |

§It indicates the category where the sample size was less than 20. Note. WHR= Waist-to-Hip Ratio, WHtR= Waist-to-Height Ratio, BMI= Body Mass Index

Table 3: Multivariate linear regression results for each index.

| Country | Sex | BMI | | | | | WHR | | | | | WHtR | | | | |
|----------|-----|-------------------------------|-------------------------------|-------------------|-------------------|-------------------|-------------------------------|-------------------------------|-------------------|-------------------------------|--------------------------------|-------------------------------|-------------------------------|-------------------|-------------------------------|--------------------------------|
| | | Age | Native a. | African a. | SES | Education | Age | Native a. | African a. | SES | Education | Age | Native a. | African a. | SES | Education |
| Brazil | M | 0.918 (0.005) | 0.464 (0.187) | 0.383 (0.248) | 0.817 (0.013) | 0.072 (0.823) | 0.027 (<0.001) | 0.003 (0.452) | 0.002 (0.686) | 0.005 (0.311) | 0.000 (0.995) | 0.026 (<0.001) | 0.007 (0.17) | 0.007 (0.153) | 0.01 (0.05) | -0.003 (0.601) |
| | F | 1.174 (<0.001) | 0.349 (0.038) | 0.452 (0.014) | 0.229 (0.172) | -0.437 (0.011) | 0.024 (<0.001) | 0.012 (0.001) | 0.000 (0.965) | -0.003 (0.437) | -0.017 (<0.001) | 0.025 (<0.001) | 0.009 (0.001) | 0.007 (0.02) | 0.000 (0.934) | -0.011 (<0.001) |
| Chile | M | 1.082 (<0.001) | 0.113 (0.307) | 0.071 (0.519) | 0.155 (0.172) | -0.171 (0.133) | 0.022 (<0.001) | 0.003 (0.031) | 0.002 (0.264) | 0.004 (0.012) | 0.002 (0.142) | 0.019 (<0.001) | 0.005 (0.003) | 0.001 (0.356) | 0.004 (0.027) | -0.001 (0.69) |
| | F | 0.781 (<0.001) | 0.158 (0.34) | 0.09 (0.593) | -0.05 (0.755) | -0.254 (0.12) | 0.025 (<0.001) | 0.008 (0.001) | -0.004 (0.17) | -0.005 (0.066) | -0.005 (0.033) | 0.022 (<0.001) | 0.008 (0.001) | -0.001 (0.772) | -0.002 (0.336) | -0.006 (0.01) |
| Colombia | M | 0.753 (<0.001) | 0.248 (0.053) | 0.03 (0.822) | 0.462 (0.001) | 0.207 (0.143) | 0.014 (<0.001) | 0.004 (0.018) | -0.005 (0.004) | 0.006 (<0.001) | 0.000 (0.939) | 0.011 (<0.001) | 0.005 (0.013) | -0.001 (0.679) | 0.008 (<0.001) | 0.003 (0.217) |
| | F | 0.29 (0.009) | 0.144 (0.142) | -0.038 (0.691) | 0.175 (0.076) | 0.043 (0.698) | 0.004 (0.035) | 0.005 (0.003) | -0.003 (0.065) | -0.002 (0.32) | -0.002 (0.354) | 0.006 (<0.001) | 0.006 (<0.001) | -0.003 (0.047) | 0.002 (0.203) | -0.001 (0.443) |
| Mexico | M | 1.277 (<0.001) | 0.749 (<0.001) | 0.326 (0.102) | 0.222 (0.253) | 0.097 (0.632) | 0.021 (<0.001) | 0.013 (<0.001) | 0.000 (0.97) | 0.001 (0.856) | 0.000 (0.898) | 0.022 (<0.001) | 0.014 (<0.001) | 0.004 (0.202) | 0.001 (0.648) | 0.001 (0.804) |
| | F | 0.735 (<0.001) | 0.369 (0.017) | -0.06 (0.674) | -0.081 (0.564) | -0.209 (0.157) | 0.022 (<0.001) | 0.018 (<0.001) | -0.002 (0.458) | -0.005 (0.035) | -0.005 (0.051) | 0.023 (<0.001) | 0.015 (<0.001) | -0.001 (0.776) | -0.003 (0.265) | -0.006 (0.029) |
| Peru | M | 0.724 (<0.001) | 0.421 (0.026) | -0.1 (0.58) | 0.27 (0.12) | 0.082 (0.657) | 0.019 (<0.001) | 0.009 (0.001) | -0.002 (0.503) | 0.002 (0.515) | 0.001 (0.827) | 0.015 (<0.001) | 0.009 (0.001) | -0.003 (0.221) | 0.004 (0.113) | 0.001 (0.688) |
| | F | 0.285 (0.051) | 0.586 (<0.001) | 0.128 (0.321) | -0.046 (0.717) | 0.078 (0.59) | 0.003 (0.247) | 0.014 (<0.001) | -0.001 (0.746) | -0.005 (0.019) | 0.003 (0.266) | 0.006 (0.016) | 0.014 (<0.001) | 0.000 (0.922) | -0.004 (0.095) | 0.003 (0.229) |

Each index variable is regressed via a multivariate linear regression model on age, Native and African ancestries, socioeconomic status (SES), and education. Regression coefficients and P-values (in brackets) are presented. The regressions were done separately for each country and each gender. Significant associations (at 0.01 level, Bonferroni adjusted) is shown in black while non-significant results are shown in grey.

Table 4: Multivariate logistic regression results for each obesity index against Native ancestry.

| Country | Sex | BMI | | | WHR | | | WHtR | | |
|----------|-----|-------|---------------|--------|-------|---------------|--------|-------|----------------|--------|
| | | OR | CI | Pvalue | OR | CI | Pvalue | OR | CI | Pvalue |
| Brazil | M | 3.83 | (0.13-113.86) | 0.438 | 5.09 | (0.29-89.47) | 0.266 | 87.70 | (2.75-2792.97) | 0.011 |
| | F | 19.42 | (1.20-315.61) | 0.037 | 16.67 | (1.58-176.04) | 0.019 | 46.38 | (4.95-434.35) | 0.001 |
| Chile | M | 2.12 | (0.61-7.33) | 0.236 | 2.15 | (0.81-5.68) | 0.123 | 2.71 | (0.94-7.78) | 0.064 |
| | F | 1.03 | (0.30-3.56) | 0.968 | 3.10 | (1.03-9.33) | 0.044 | 5.82 | (2.38-14.24) | <0.001 |
| Colombia | M | 0.99 | (0.04-22.59) | 0.995 | 2.84 | (0.47-17.13) | 0.254 | 3.60 | (0.84-15.43) | 0.084 |
| | F | 14.26 | (0.44-457.62) | 0.133 | 8.84 | (1.89-41.32) | 0.006 | 10.54 | (2.57-43.20) | 0.001 |
| Mexico | M | 7.87 | (1.73-35.79) | 0.008 | 7.49 | (2.51-22.38) | <0.001 | 5.15 | (1.76-15.02) | 0.003 |
| | F | 1.30 | (0.30-5.68) | 0.724 | 12.76 | (5.30-30.75) | <0.001 | 11.15 | (4.68-26.57) | <0.001 |
| Peru | M | 2.90 | (0.41-20.37) | 0.285 | 6.53 | (2.01-21.15) | 0.002 | 9.12 | (2.91-28.53) | <0.001 |
| | F | 1.55 | (0.14-17.21) | 0.722 | 8.30 | (3.32-20.74) | <0.001 | 17.43 | (6.96-43.65) | <0.001 |

Each index variable is converted into a dichotomous obesity index by the following threshold: BMI > 30, WHtR > 0.5, and WHR > 0.85 for women but WHR > 0.9 for men.

The multivariate regression model is same as Table 3 – the obesity index is regressed via a multivariate logistic regression model on age, Native and African ancestries, socioeconomic status (SES), and education. Regression results are shown only for Native ancestry. Odds ratios (OR), 95% confidence intervals (CI), and P-values are presented. The regressions were done separately for each country and each gender. Significant associations (at 0.05 level) is shown in black while non-significant results are shown in grey.