International waist circumference percentile cut-offs for central obesity in children and adolescents aged 6-18 years

Authors

Bo Xi, PhD [1†*] Xin'nan Zong, MS [2†] Roya Kelishadi, MD[3†] Mieczysław Litwin, MD, PhD [4†] Young Mi Hong, MD [5†] Bee Koon Poh, PhD [6†] Lyn M. Steffen, PhD [7†] Sonya V Galcheva, MD[8†] Isabelle Herter-Aeberli, MD[9†] Tadeusz Nawarycz, PhD[10] Małgorzata Krzywińska-Wiewiorowska, MD, PhD [11] Anuradha Khadilkar, MD [12] Michael D. Schmidt, PhD[13] Hannelore Neuhauser, MD [14] Anja Schienkiewitz, MPH[15] Zbigniew Kułaga, MD [16] Hae Soon Kim, MD[5] Barbara Stawińska-Witoszyńska, *MD, PhD*[11] Mohammad Esmaeil Motlagh, MD[17] Abd Talib Ruzita, PhD [6] Violeta M. Iotova, MD [8] Aneta Grajda, MD [16] Mohd Noor Ismail, PhD [18] Alicja Krzyżaniak, MD, PhD [11] Ramin Heshmat, MD, PhD [19] Velin Stratev, MD [20] Agnieszka Różdżyńska-Świątkowska, MD [21] Gelayol Ardalan, MD [3] Mostafa Qorbani, PhD [22] Anna Świąder-Leśniak, MD [21] Lidia Ostrowska-Nawarycz, MD [10] Yoto Yotov, MD [23] Veena Ekbote, MD [12] Vaman Khadilkar, MRCP [12] Alison J. Venn, PhD [24] Terence Dwyer, MD [24,25] Min Zhao, PhD,[26] Costan G. Magnussen, PhD,[24,27] Pascal Bovet, MD [28†] International Child waist circumference References Establishment Consortium.

Affiliations

1. Department of Epidemiology, School of Public Health, Shandong University, Jinan, China

2. Department of Growth and Development, Capital Institute of Pediatrics, Beijing, China.

3. Department of Pediatrics, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran

4. Department of Nephrology and Arterial Hypertension, The Children's Memorial Health Institute, Warsaw, Poland.

5. Department of Pediatrics, Ewha Womans University School of Medicine, Seoul, Korea

6. Nutritional Sciences Programme and Centre for Community Health, Faculty of Health Sciences, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia

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7. Division of Epidemiology and Community Health, University of Minnesotas School of Public Health, Minneapolis, USA.

8. Department of Pediatrics, Varna Medical University, Varna, Bulgaria

9. Institute of Food, Nutrition and Health, Human Nutrition Laboratory, ETH Zurich, Zürich, Switzerland.

10. Department of Biophysics, Chair of Experimental and Clinical Physiology, Medical University of Lodz, Lodz, Poland

11. Department of Epidemiology and Hygiene, Chair of Social Medicine, Poznan University of Medical Sciences, Poznan, Poland

12. Hirabai Cowasji Jehangir Medical Research Institute, Jehangir Hospital, Pune, India.

13. Department of Kinesiology, University of Georgia, Athens, Georgia, USA

14. Department of Epidemiology and Health Monitoring, Robert Koch Institute, Berlin, Germany and DZHK (German Center for Cardiovascular Research), partner site Berlin, Germany

15. Department of Epidemiology and Health Monitoring, Robert Koch Institute, Berlin, Germany.

16. Department of Public Health, The Children's Memorial Health Institute, Warsaw, Poland

17. Department of Pediatrics, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

18. Faculty of Social Sciences and Leisure Management, Taylor's University, Subang Jaya, Selangor, Malaysia

19. Department of Epidemiology, Chronic Diseases Research Center, Endocrinology and Metabolism Population Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

20. Department of Internal Medicine, Varna Medical University, Varna, Bulgaria

21. Department of Anthropometry, The Children's Memorial Health Institute, Warsaw, Poland.

22. Department of Community Medicine, Alborz University of Medical Sciences, Karaj, Iran

23. Department of cardiology, Medical University Varna, Varna, Bulgaria

24. Menzies Institute for Medical Research, University of Tasmania, Hobart, Tasmania, Australia.

25. George Institute for Global Health, Oxford Martin School and Nuffield Department of Population Health, Oxford University, UK

26. Departments of Nutrition and Food Hygiene, School of Public Health, Shandong University, Jinan, China

27. Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland.

28. Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland

† These authors contributed equally to this work.

*** Corresponding author**

Bo Xi, Department of Epidemiology, School of Public Health, Shandong University, Jinan, China. E-mail: xibo2010@sdu.edu.cn OR xibo2007@126.com.

Contributors

B.X., X.Z., R.K., P.B., M.L., Y.M.H., B.K.P., L.M.S., S.V.G., I.H-A., T.N., M.K-W., and A.K. designed the study. B.X., X.Z. and P.B. led the writing of the manuscript. Z.K., H.S.K., M.E.M., A.T.R., V.M.I., A.G., M.N.I., A.K., R.H., V.S., A.R-Ś., G.A., M.Q., A.Ś-L., L.O-N., V.E., V.K., M.Z., A.J.V., T.D. and M.Z. were involved in data collection. X.Z. analyzed the data. All authors contributed to the interpretation of the results and revision of the manuscript for important intellectual content and approved the final version of the manuscript. B.X. is guarantor.

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Abbreviations:

BMI body mass index

BP blood pressure

CVD cardiovascular disease

HDL-C high density lipoprotein cholesterol

IDF International Diabetes Federation

IOTF International Obesity Task Force

GAMLSS general additive model for location scale and shape

LDL-C low density lipoprotein cholesterol

ROC receiver operator characteristics

TC total cholesterol

TG triglycerides

WC waist circumference

Abstract

Context No universal waist circumference (WC) percentile cut-offs used have been proposed for screening central obesity in children and adolescents.

Objective To develop international WC percentile cut-offs for children and adolescents with normal weight based on data from eight countries in different regions and examine the relation with cardiovascular risk.

Design and Setting We used pooled data on WC in 113,453 children and adolescents (males, 50.2%) aged 4-20 years from eight countries in different regions (Bulgaria, China, Iran, Korea, Malaysia, Poland, Seychelles, and Switzerland). We calculated WC percentile cut-offs in samples including or excluding children with obesity, overweight or underweight. WC percentiles were generated using the general additive model for location scale and shape (GAMLSS). We also estimated the predictive power of the WC 90th percentile cut-offs to predict cardiovascular risk using receiver operator characteristics curve analysis based on data from three countries that had available data (China, Iran and Korea). We also examined which WC percentiles connected with WC cut-offs for central obesity in adults (at age of 18 years).

Main Outcome Measure WC measured based on recommendation by the World Health Organization.

Results We validated the performance of the age- and sex- specific 90th percentile WC cut-offs calculated in children and adolescents (6-18 years of age) with normal weight (excluding youth with obesity, overweight or underweight) by linking it with cardiovascular risk (AUC: 0.69 for boys; 0.63 for girls). In addition, WC percentile among normal weight children linked relatively well with established WC cut-offs for central obesity in adults (e.g., AUC in US adolescents: 0.71 for boys; 0.68 for girls).

Conclusion The international WC cut-offs developed in this study could be useful to screen central obesity in children and adolescents aged 6-18 years and allow direct comparison of WC distributions between populations and over time.

Keywords Waist circumference; Central obesity; Cut-off points; Children and adolescents

Introduction

Obesity in children and adolescents has become a major global health challenge because the prevalence is increasing (1,2) and excess weight is associated with increased risk of morbidity and mortality, including hypertension, dislipidemia, type 2 diabetes, cardiovascular disease (CVD) and overall mortality (3). Body mass index (BMI), calculated as weight divided by height squared (kg/m^2), is frequently used to classify overweight and obesity in epidemiological studies and in clinical practice. International age- and sex-specific BMI percentile cut-offs to define child overweight and obesity have been developed by Cole et al on behalf of the International Obesity Task Force (IOTF)(4) and are intended to correspond, at the age of 18 years, to the criteria in adults for overweight (BMI ≥25 kg/m^2) and obesity (BMI ≥30 kg/m^2). However, BMI cannot distinguish accurately between fat and fat-free mass (5). Waist circumference (WC), another adiposity measure indicating abdominal fat accumulation, may better predict risk of CVD and mortality (6,7). Also, WC is the essential component of metabolic syndrome definition endorsed by the International Diabetes Federation (IDF) (8,9), the National Heart, Lung, and Blood Institute (10,11) and other medical organizations (12).

Cut-offs of WC to define central obesity in adults have been proposed by the IDF in different populations (≥94/80 cm in males/females for Europeans, Africans and Middle East; ≥90/80 cm in males/females for Asians) (13,14). However, WC cut-offs to define central obesity in children and adolescents based on multiple populations in different regions have not yet been proposed (15), although several country-specific pediatric WC percentile cut-offs have been developed (16-25). Thus, it is important to develop international WC cut-offs that could be used as a common yardstick to enable direct comparison between populations and for monitoring central adiposity over time.

This study aims to develop international WC cut-offs for defining central obesity in children and adolescents aged 6-18 years based on pooled data from eight countries from several regions, i.e. Bulgaria (16), China (26), Iran (27), Korea (28), Malaysia (17), Poland (29,30), Seychelles

(31), and Switzerland (18).

Methods

Subjects

Data on WC for children and adolescents aged 4-20 years were available from eight large population-based cross-sectional surveys from Bulgaria, China, Iran, Korea, Malaysia, Poland, Seychelles, and Switzerland (**Table 1**). While all surveys were representative of their underlying populations, the choice of the countries included in this study was based on the availability of adequate data and country selection can therefore be considered as convenient. In addition, although we aimed to develop international WC references for youth aged 6-18 years, we also included data on individuals aged 4 and 5 years, and 19 and 20 years in order to avoid left-edge and right-edge effects when modeling WC curves according to age(32). Details on sampling and methods of these studies have been described elsewhere (16-18,26-31). Data from China, Korea and Seychelles included pooled samples collected over several years; data from Malaysia were pooled from two national surveys conducted in 2008 and 2009; and other data (from Iran, Poland and Switzerland) were based on single cross-sectional surveys. A total of 113,453 subjects aged 4-20 years from eight countries were included in this study. Obesity, overweight and underweight status were defined based on age- and sex-specific BMI percentile values of the IOTF (4). The prevalence of obesity, overweight and underweight in the whole sample of each survey is shown in **Table 2**. Written informed consent was obtained from parents and children and adolescents. Each survey was approved by the respective Institutional Ethics Review Board in each country.

WC measurement

In all countries, WC was measured midway between the lowest rib and the superior border of the iliac crest at the end of a normal expiration with a flexible non-elastic anthropometric tape, to the nearest 0.1 cm, as recommended by the World Health Organization (33). The mean value of two measurements was used for data analysis. Quality control was performed in all the

surveys including adequate training for the survey officers.

Design outline of this study

We pooled WC data from the eight countries, consistent with the recommendation to include 5 to 10 sites when attempting to develop an international standard (34). Because different prevalence of obesity, overweight or underweight in different populations may shift upward or downward the values of the country specific WC cut-offs (35) at the population level, we calculated age- and sex-specific 90th percentiles of WC in four different samples including or excluding children with obesity, overweight or underweight (4,36) (**Figure 1**). Sample 1 (N=113,453) included the whole sample; Sample 2 (N=108,031) excluded obese individuals based on the IOTF BMI cut-offs; Sample 3 (N=93,295) excluded obese and overweight individuals; and Sample 4 (N=72,841) excluded obese, overweight and underweight individuals. We then compared the performance of the age- and sex-specific 90th percentile values of WC (i.e., a sex- and age-specific binary WC variable defined as "high WC or non-high WC") to predict cardiovascular (CV) risk in the four samples using receiver operator characteristics (ROC) curve analysis. This analysis was done in pooled data from the three populations (China, Iran, and Korea) in which data on CV risk factors were available. Based on the strength of the association between WC and CV risk, we determined which sample (i.e. including or excluding children with obesity, overweight or underweight) was the best base population to calculate WC 90th percentile cut-offs.

Finally, we generated age- and sex-specific trajectories of percentile values throughout childhood to the age of 18 years and examined how well these calculated trajectories linked, at the age of 18 years, with established adult WC cut-offs for central obesity as recommended by the IDF (i.e. ≥94/80 cm in males/females for Europeans, Africans and Middle East population; ≥90/80 cm in males/females for Asians). Previous studies had suggested differences in WC levels across different racial/ethnic populations in adults (13,14).

Statistical analysis

Percentile curves

The data were pooled using weights according to the population size of each survey from the eight countries (37). The generalized additive model for location, scale and shape (GAMLSS) model for Box-Cox power exponential distribution with cubic spline smoothing (38) was used to construct smoothed age- and sex- specific 90th percentile curves of WC for each of the four samples (i.e. including or excluding children with obesity, overweight or underweight). In addition, we also calculated the age- and sex- specific WC percentile values in children and adolescents that linked, at the age of 18 years, with accepted adult WC cut-offs similarly to the method used by Cole *et al*. to establish age- and sex- specific BMI percentile values for children and adolescents (4). The Box-Cox power exponential distribution has four parameters including μ, σ, ν, and τ which represent location (median), scale (approximate coefficient of variation), skewness (power transformation to symmetry) and kurtosis (degrees of freedom or power exponential parameter), respectively. The GAMLSS models were adjusted for skewness and kurtosis of WC from mixed data sources. Calculation of sex- and age-specific WC curves were based on data in children and adolescents aged 4-20 years to avoid an edge effect at low and high age values, but data in this paper are presented only for age of 6-18 years(32). Analyses were performed using the GAMLSS 4.3-1 library running under R 3.1.2 (39). Goodness of fit of the models was assessed by the Bayesian Information Criterion and by Q-Q plots (40).

WC and CV risk

Three populations (China: 750 children aged 7-17, 2009; Iran: 8393 children aged 6-17, 2003 and 2009; and Korea: 8688 children aged 10-17, 1998-2013) had data on CV risk and they were used to assess the performance of age- and sex- specific 90th percentile cut-offs of WC (i.e., a sex- and age-specific binary WC variable) for predicting CV risk, and analysis was done in the four samples (i.e., samples including or excluding obesity, overweight or underweight).

In these three countries, measurements were available for systolic blood pressure (SBP),

diastolic blood pressure (DBP), total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and fasting glucose, as described elsewhere (41-44). High BP was defined as SBP and/or DBP equal to or above age-, sex-, and height-specific 90th percentile of an international child BP reference (45). High TG (≥150mg/dl), low HDL-C (<40mg/dl), and high fasting glucose (≥100mg/dl) were defined using cut-offs recommended by the IDF (46) and high TC (≥200mg/dl) and high LDL-C (≥130mg/dl) were defined based on the ATP III (11). The prevalence of these 6 CV risk factors in the three populations is presented in **Table 3**.

In this study, we defined elevated CVD risk as having ≥3 out of 6 CV risk factors (i.e., high BP, high TG, low HDL, high TC, high LDL, and high glucose) when testing sensitivity, specificity and area under the curve (AUC) of the age- and sex- specific WC 90th percentile cut-offs to predict CV risk, consistent with previous studies (20,47). Analysis was done in the four samples (i.e. including or excluding children with obesity, overweight or underweight).

In addition, the performance of several WC percentiles linking with adult WC cut-offs for specific racial/ethnic populations were also assessed for predicting CV risk (i.e., presence of ≥3 risk factors) in the pooled data (age 6-17 years) in the three populations (China, Iran and Korea) and in one separate US adolescent population (age 12-17 years) with different racial/ethnic groups (data from the National Health and Nutrition Examination Survey 1999-2014) (48). ROC curve analysis was performed using SAS v9.4 (SAS Institute, Cary, North Carolina).

Comparison of our international WC percentiles with European WC percentiles

Finally, the age- and sex-specific 75th and 90th percentiles of WC from the sample of children and adolescents with normal weight (i.e. after exclusion of children with obesity, overweight or underweight) were compared with the corresponding percentiles in the IDEFICS study (35), which presented the first WC percentiles based on normal-weight children aged 2-10 years from a large sample size of 12,381 from eight European countries.

Results

Figure 2 displays the age- and sex-specific 90th percentile values of WC from the four samples of children and adolescents aged 6-18 years based on pooled data from the eight countries. In both males and females, the 90th percentile values of WC in Sample 1 (the whole sample) were, as expected, higher than those in Sample 2 (excluding individuals with obesity), and substantially higher than those in Sample 3 (excluding individuals with obesity or overweight) and Sample 4 (excluding individuals with obesity, overweight or underweight). However, the 90th percentile values in Sample 3 and Sample 4 were similar.

Tables 4-7 present the smoothed 50th, 75th, 80th, 85th, 90th, 95th, 97th, and 99th percentiles of WC by age and sex for children and adolescents aged 6-18 years from the four samples (including or excluding individuals with obesity, overweight or underweight) based on pooled data from the eight countries.

Table 8 shows the performance of the age- and sex-specific 90th percentile WC cut-offs, from each of the four samples, for predicting CV risk in three countries (China, Iran and Korea) with data on CV risk factors. The 90th percentile cut-offs for Sample 3 (excluding children with obesity or overweight) or Sample 4 (excluding children with obesity, overweight, or underweight) had higher AUC values for predicting CV risk (i.e., presence of ≥3 CV risk factors) than Sample 1 (the whole sample) or Sample 2 (excluding children with obesity). There was no marked difference in predictive values between estimates from Sample 3 and Sample 4. Of note, findings were similar according to age categories (age 6-12 vs. 13-17 yrs) (**Table 8**) and when stratified by country (**Table 9**). Based on these results, we chose to derive our final 90th WC percentile from Sample 4 (including children with normal weight and excluding those with obesity, overweight or underweight).

Table 10 presents the age- and sex- specific WC 90th percentile and other percentiles at the age

of 18 years which linked with adult WC cut-offs for central obesity (85 cm, 90 cm and 94 cm in males and 80 cm in females) based on the sample of individuals with normal weight (Sample 4).

In the 3 countries with data on CV risk factors, the WC percentile in childhood linking, at the age of 18 years, with the WC cut-off of 85 cm for adult men recommended by the Obesity in Asia Collaboration (49,50) predicted CV risk better than the WC percentile in childhood linking with the WC cut-off of 90 cm for adult men recommended by the IDF (AUC of 0.68 vs. 0.64) (**Table 11**). In addition, the WC percentiles in adolescents linking, at the age of 18 years, with the adult WC cut-offs of 94 cm for men and 80 cm for women (i.e., the WC cut-offs recommended by the IDF for European and African adults) performed relatively well in predicting CV risk (AUC of 0.71 for males and 0.68 for females) (**Table 12**).

Figure 3 displays the comparisons of our age- and sex-specific 75th and 90th WC percentiles in normal weight children and adolescents (Sample 4) with the corresponding WC percentiles among normal weight European children in the IDEFICS study. Our WC percentile values were similar to those from the IDEFICS study (in males aged 6-8 years and in females aged 6-10 years), but slightly higher for males aged 9 and 10 years (e.g., our 90th WC percentile is +1.1 cm at age 9 years and +1.6 cm at age 10 years).

Discussion

To our knowledge, this is the first study presenting age- and sex-specific WC cut-offs to define elevated central obesity in children and adolescents aged 6-18 years based on data from several countries in different regions. These international WC percentile cut-offs can be useful for identifying central obesity in different countries and for allowing direct comparison of the prevalence of central obesity between populations and trends over time.

Given the adverse effects of central obesity on several health outcomes observed among

children and adolescents, it is important to establish standard WC percentile cut-offs to define elevated WC in children and adolescents, which could be used in different countries. However, it is challenging to choose a reference population for the establishment of universally valid WC cut-offs because overweight and obesity (defined by BMI criteria) largely differ between countries. In this study, we adopted several reasonable assumptions to develop pediatric percentile-based WC cut-offs that can be validly used in different countries. First, our data came from eight countries from several regions. It is recommended by some expert that the number of countries needed to establish an international standard should range between 5 and 10 (34). Second, we used a weighted sampling design for pooling data from studies from different countries, to account for differences sample sizes (4,51). Third, since different prevalence of unhealthy weight (i.e., overweight/obesity or underweight) may shift upwards or downwards the distribution of weight-influenced parameters such as WC (52,53), we developed 90th percentile WC cut-offs in terms of best CV risk prediction, which was found to occur in the population sample (Sample 4) in which individuals with obesity, overweight or underweight were excluded. We believe that these different assumptions and steps we used to establish our reference WC percentiles allow to generalize their validity and use to identify abdominal adiposity in different countries.

We chose the 90th WC percentile as the cut-off to identify central obesity in children and adolescents for two main reasons. First, the 90th percentile WC cut-off is also used by the IDF(46) and the modified ATP III (10). Second, the 90th percentile WC cut-off linked best, at age of 18 years, with several criteria for adult central obesity in the present study. We assessed CV risk, based on CV risk factors (presence of ≥3 from 6 CV risk factors) consistent with an absolute CVD risk score approach. A similar approach was also used for validating country-specific WC percentile cut-offs in children and adolescents (20,54). We found that the 90th WC percentile in children with normal weight performed well to predict CV risk. With regards to how WC percentiles in children and adolescents linked with adult criteria for abdominal obesity (13,14), we used a method similar to that used to establish international BMI criteria to define

child overweight and obesity (4); we found good linkage of the 90th WC percentile with several criteria of adult central adiposity (i.e., 85 cm and 80 cm for Asian males and females, respectively).

The National Institute of Health / National Heart, Lung, and Blood Institute, NCEP ATPIII (11) and the American Heart Association (AHA) (55) have recommended WC cut-offs >102 cm for men and >88 cm for women to prevent CVD risk in the US adult population. However, several studies have shown that these high WC cut-offs performed poorly to predict CV risk in the US adults (47). Thus, when linking childhood WC percentiles to adult WC cut-offs, we preferred to use the adult WC values recommended by the IDF (94 cm for men and 80 cm for women), which have been shown to have fairly high sensitivity and specificity to identify CV risk (47).

Furthermore, two large prospective studies conducted by the Obesity in Asia Collaboration suggested that a WC cut-off of 85 cm, rather than 90 cm, is more suitable to predict hypertension and diabetes in Asian adult males, while the WC cut-off of 80 cm for adult females was shown to be equally valid in Asians vs. other populations (49,50). Hence, we also calculated the corresponding WC percentile values for Asian boys that link with a WC of 85 cm in male adults. Among males, our results show that the percentile WC values linking, at the age of 18 years, with an adult WC cut-off of 85 cm (Obesity in Asia Collaboration) performed better than the percentile WC values in boys linking with an adult WC of 90 cm (IDF). It should be noted that our 90th percentile WC cut-offs at age of 18 years, based on normal-weight individuals, are close to the adult WC percentile recommended by the Obesity in Asia Collaboration (i.e., 85 cm for men and 80 cm for women). In addition, the IDF recommended the 90th percentile WC cut-offs for defining central obesity for youth aged 6-15 years, but the adult WC cut-offs for adolescents aged 16-17 years (46). However, the modified ATP III recommend 90th percentile WC cut-offs for youth until 17 years of age (10). Thus, we also calculated the 90th percentile WC cut-offs for adolescents aged 16-17 years (Table 3), so that researchers or clinicians can use either the 90th percentile WC cut-offs or the adult WC cut-offs

for adolescents aged 16-17 years.

Cole et al. used a reference sample that largely preceded the obesity epidemic to derive the IOTF BMI cut-offs (4), i.e., data which included only few children with overweight or obesity. Unfortunately, it is not possible to derive WC cut-offs from these historical survey data because WC was not routinely collected in children until recently. To avoid the distorting effect of largely different prevalence of obesity in different populations in recent decades, it is reasonable to determine WC cut-offs for central obesity in virtually comparable populations, i.e., in sub-samples of current surveys that only include individuals with normal weight. This approach is further supported by our finding that the 90th WC percentile predicted CV risk better in sample of children and adolescents with normal weight rather than in samples including varying proportions of overweight or obese children. It should be further emphasized that WC reference cut-off values to identify elevated WC should, as much as possible, reflect the normal biological variation in a healthy population (35). While it is not useful to exclude individuals with abnormal weight when establishing normative data unrelated to adiposity (e.g., height) (56), excluding individuals with extreme values is useful when developing normative data related to body weight status, which can be used universally (56).

Strengths and Limitations

Our study has two main strengths. First, we used data from eight population-based samples involving over 110,000 children and adolescents in several regions, which strengthens the generalizability of our findings to other populations. Second, we used a combination of several CV risk factors to assess the association of CV risk with the 90th percentile WC cut-offs. However, several limitations should also be noted. First, although the number of countries in our study is not large and data lack populations from some parts of the world, such as North and South America, the number of countries included in our study is still significant (n=8) and rise from different regions (4 global regions). This is consistent with recommendations for establishing international standards (where a minimal number of 5-10 countries is advised),

hence our WC norms have a good, albeit not perfect, potential for generalizability to other countries (34). Second, our analysis linking WC cut-offs with CV risk relied on data from only 3 countries. Future studies should further evaluate the performance of our proposed WC percentile cut-offs in other populations. Third, the predictive ability of WC to predict CV risk was limited, with AUC values of 0.69 for boys and 0.63 for girls. In addition, WC percentile (about 10 cm higher than the 90th percentile) linked relatively well with established WC cut-offs for central obesity in adults (e.g., AUC in US adolescents: 0.71 for boys; 0.68 for girls), although lower than the more complex Framingham risk score (AUC of 0.75 for predicting 10-year CVD risk) (57). This is however still impressive given that CV risk is predicted on the basis of WC as a sole risk factor which is, furthermore, dichotomized (i.e. elevated WC vs. non elevated WC). Fourth, we developed our final WC cut-off values after excluding children with obesity or overweight based on BMI. Sensitivity and AUC of WC to predict CV risk were lower in the total population (i.e. also including individuals with overweight/obesity or underweight) than found after excluding children with obesity, overweight or underweight. However, our use of assessing overweight, obesity and underweight based on selected BMI cut-offs is somehow arbitrary. Fifth, although WC measurements in each country followed the recommendations by the World Health Organization, differences in accuracy and precision of WC measurements may have occurred between countries. In addition, the instruments used for analyses of blood samples in China, Iran and Korea were different, which might have influenced the comparability of blood variables.

Conclusions

This study provides, for the first time, cut-offs for increased WC, based on data in several countries in different regions, which are demonstrably associated with an increased CV risk and closely correspond to adult criteria for abdominal adiposity at the age of 18 years. These WC cut-offs may be useful to assess abdominal adiposity in children and adolescents aged 6-18 years in different countries. While recognizing that country-specific norms for elevated WC may also be useful, our international WC cut-offs have the advantage of providing a standard

metric, particularly for countries that have not developed their own national WC references, and allow direct comparison of the prevalence of central obesity in children and adolescents between countries and over time.

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Table 1. Description of surveys assessing waist circumference in children and adolescents aged 4-20 years from eight countries

Country	Surveyed year	Description	Total	No. of males	No. of females	Age range (y)	Ethnicity	Reference
Bulgaria	2006-2007	Varna representative growth and obesity survey	3786	2040	1746	6-18	European	(16)
China	2000-2011	Data pooled from five cycles of the China Health and Nutrition Survey	8811	4693	4118	4-20	Asian	(26)
Iran	2011-2012	National survey "Childhood and Adolescence Surveillance and Prevention of Adult Non-communicable Diseases"	18557	9373	9184	6-18	Middle East	(27)
Korea	2001-2013	Data pooled from 5 cycles of the Korea National Health and Nutrition Examination Survey	16547	8573	7974	4-20	Asian	(28)
Malaysia	2008-2009	National surveys of the Nutritional Status of Primary and Secondary School Children in Malaysia	16026	7972	8054	6-16	Asian	(17)
Poland	2007-2010	National survey "Elaboration of reference blood pressure ranges for children and adolescents in Poland"	20495	9822	10673	4-18	European	(29,30)
Seychelles	2000-2014	School-based National Surveillance Programs	26940	13340	13600	4-18	Black	
Switzerland	2007	National survey "Prevalence of overweight and obesity in 6-13 year old children"	2291	1123	1168	6-13	European	(18)
Total			113453	56936	56517	4-20		

Table 2. Prevalence of obesity, overweight and underweight based on the IOTF BMI criteria in children and adolescents from eight countries

Country	Survey year	Age range	N	Obesity, n (%)	Overweight, n (%)	Underweight, n (%)
Bulgaria	2006-2007	6-18	3786	306 (8.1)	753 (19.9)	172 (4.5)
China	2000-2011	4-20	8811	156 (1.8)	643 (7.3)	1905 (21.6)
Iran	2011-2012	6-18	18557	739 (4.0)	2520 (13.6)	4060 (21.9)
Korea	2001-2013	4-20	16547	664 (4.0)	2808 (17.0)	1600 (9.7)
Malaysia	2008-2009	6-16	16026	1227 (7.7)	2163 (13.5)	3985 (24.9)
Poland	2007-2010	4-18	20495	643 (3.1)	2570 (12.5)	2556 (12.5)
Seychelles	2000-2014	4-18	26940	1646 (6.1)	3021 (11.2)	5989 (22.2)
Switzerland	2007	6-13	2291	41 (1.8)	258 (11.3)	187 (8.2)
Total	–	4-20	113453	5422 (4.8)	14736 (13.0)	20454 (18.0)

Table 3. Prevalence of cardiovascular risk factors and their clustering in children and adolescents aged 6-17 years in China, Iran and Korea

Country	N	Age range, years	High BP	High Glucose	High TC	High TG	Low HDL	High LDL	≥3 risk factors
China									
Males	411	7-17	79 (19.2)	41 (10.0)	13 (3.2)	45 (10.9)	40 (9.7)	15 (3.6)	11 (2.7)
Females	339	7-17	61 (18.0)	20 (5.9)	14 (4.1)	30 (8.8)	27 (8.0)	17 (5.0)	6 (1.8)
Total	750	7-17	140 (18.7)	61 (8.1)	27 (3.6)	75 (10.0)	67 (8.9)	32 (4.3)	17 (2.3)
Iran									
Males	4151	6-17	957 (23.3)	328 (8.1)	237 (5.7)	370 (9.0)	1399 (36.3)	225 (6.3)	193 (4.6)
Females	4242	6-17	836 (20.0)	408 (9.9)	257 (6.1)	400 (9.5)	1456 (36.6)	272 (7.5)	210 (5.0)
Total	8393	6-17	1793 (21.6)	736 (9.0)	494 (5.9)	770 (9.3)	2855 (36.5)	497 (6.9)	403 (4.8)
Korea									
Males	4589	10-17	1057 (23.0)	637 (14.0)	269 (5.9)	443 (9.7)	899 (19.6)	194 (4.5)	253 (5.5)
Females	4099	10-17	618 (15.1)	497 (12.2)	357 (8.7)	413 (10.1)	539 (13.2)	250 (6.5)	185 (4.5)
Total	8688	10-17	1675 (19.3)	1134 (13.1)	626 (7.2)	856 (9.9)	1438 (16.6)	444 (5.4)	438 (5.0)

Data are presented as n (%).

Table 4. Smoothed percentile values of WC (cm) by age and sex from the Sample 1 (based on the whole population)

Age	Males												Females											
(years)	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99
6	54.048	0.094	-1.549	1.523	54.0	57.4	58.4	59.7	61.5	64.5	66.9	72.2	53.058	0.099	-1.057	1.521	53.1	56.5	57.5	58.7	60.5	63.5	65.7	70.5
7	55.748	0.104	-1.652	1.637	55.7	59.8	61.0	62.5	64.6	68.3	71.1	77.7	54.578	0.109	-1.123	1.666	54.6	58.6	59.8	61.3	63.3	66.7	69.2	74.7
8	57.669	0.115	-1.723	1.768	57.7	62.4	63.9	65.7	68.2	72.5	75.9	83.8	56.423	0.118	-1.204	1.800	56.4	61.2	62.5	64.2	66.5	70.4	73.3	79.6
9	59.753	0.125	-1.685	1.888	59.8	65.3	66.9	69.0	71.9	76.9	80.8	89.7	58.476	0.126	-1.240	1.911	58.5	63.9	65.4	67.3	69.9	74.3	77.5	84.5
10	61.890	0.134	-1.534	1.962	61.9	68.1	70.0	72.3	75.4	80.9	85.1	94.6	60.588	0.130	-1.265	2.001	60.6	66.5	68.2	70.3	73.1	77.8	81.2	88.8
11	64.045	0.139	-1.388	1.950	64.0	70.7	72.7	75.1	78.5	84.3	88.6	98.5	62.718	0.131	-1.374	2.047	62.7	69.0	70.7	72.9	75.9	80.9	84.6	92.8
12	66.159	0.139	-1.310	1.861	66.2	72.9	74.9	77.4	80.9	86.8	91.3	101.7	64.706	0.128	-1.528	2.042	64.7	71.0	72.9	75.1	78.2	83.4	87.3	96.1
13	68.170	0.135	-1.271	1.729	68.2	74.7	76.7	79.2	82.6	88.7	93.2	103.9	66.370	0.124	-1.645	2.000	66.4	72.6	74.4	76.6	79.7	85.0	88.9	97.9
14	70.040	0.130	-1.259	1.611	70.0	76.3	78.2	80.6	84.0	90.0	94.6	105.3	67.695	0.119	-1.748	1.941	67.7	73.7	75.5	77.7	80.7	85.9	89.9	99.0
15	71.682	0.125	-1.166	1.513	71.7	77.6	79.4	81.7	85.0	90.8	95.2	105.5	68.641	0.114	-1.814	1.879	68.6	74.4	76.1	78.2	81.2	86.3	90.2	99.2

16	73.051	0.121	-0.975	1.462	73.1	78.8	80.5	82.7	85.9	91.3	95.4	104.9	69.238	0.109	-1.823	1.824	69.2	74.8	76.4	78.4	81.2	86.1	89.9	98.5
17	74.193	0.119	-0.802	1.482	74.2	79.9	81.6	83.7	86.7	91.9	95.7	104.3	69.638	0.106	-1.793	1.800	69.6	75.0	76.5	78.5	81.2	85.9	89.4	97.5
18	75.176	0.118	-0.725	1.568	75.2	81.0	82.7	84.9	87.8	92.7	96.4	104.2	69.925	0.104	-1.715	1.812	69.9	75.2	76.7	78.6	81.2	85.7	89.0	96.5

Table 5. Smoothed percentile values of WC (cm) by age and sex from the Sample 2 (based on the population excluding obese children)

Age	Males												Females											
(years)	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99
6	53.745	0.084	-0.719	1.654	53.7	56.7	57.6	58.6	60.0	62.2	63.8	67.1	52.773	0.089	-0.373	1.666	52.8	55.9	56.7	57.8	59.2	61.4	63.0	66.2
7	55.322	0.093	-0.970	1.747	55.3	58.8	59.8	61.0	62.7	65.3	67.2	71.1	54.218	0.098	-0.498	1.764	54.2	57.8	58.8	60.0	61.7	64.2	66.0	69.7
8	57.109	0.102	-1.152	1.845	57.1	61.2	62.4	63.8	65.7	68.8	71.0	75.7	55.984	0.107	-0.647	1.861	56.0	60.2	61.3	62.7	64.6	67.5	69.6	73.9
9	59.073	0.110	-1.220	1.949	59.1	63.8	65.1	66.8	69.0	72.5	75.1	80.5	57.982	0.115	-0.768	1.953	58.0	62.8	64.1	65.6	67.7	71.1	73.4	78.3
10	61.132	0.118	-1.181	2.043	61.1	66.5	68.0	69.8	72.2	76.2	79.0	85.0	60.064	0.119	-0.876	2.037	60.1	65.3	66.8	68.5	70.8	74.5	77.1	82.4
11	63.261	0.123	-1.107	2.066	63.3	69.1	70.7	72.6	75.2	79.5	82.5	88.9	62.174	0.120	-1.033	2.081	62.2	67.7	69.3	71.1	73.6	77.6	80.4	86.2
12	65.402	0.123	-0.994	1.983	65.4	71.3	73.0	75.0	77.7	82.0	85.2	91.8	64.157	0.118	-1.187	2.072	64.2	69.8	71.4	73.3	75.8	80.0	82.9	89.1
13	67.483	0.121	-0.885	1.848	67.5	73.3	74.9	76.9	79.6	84.0	87.2	93.9	65.844	0.114	-1.286	2.027	65.8	71.4	73.0	74.9	77.4	81.6	84.6	90.9
14	69.444	0.117	-0.782	1.719	69.4	75.0	76.6	78.5	81.2	85.6	88.7	95.5	67.210	0.110	-1.363	1.970	67.2	72.6	74.2	76.0	78.5	82.7	85.7	92.1
15	71.188	0.113	-0.610	1.614	71.2	76.5	78.0	79.9	82.5	86.8	89.9	96.4	68.220	0.106	-1.405	1.916	68.2	73.5	74.9	76.8	79.2	83.3	86.2	92.6

16	72.666	0.111	-0.367	1.566	72.7	77.9	79.4	81.2	83.7	87.8	90.7	96.9	68.903	0.102	-1.411	1.871	68.9	74.0	75.4	77.2	79.6	83.5	86.4	92.6
17	73.919	0.109	-0.168	1.597	73.9	79.2	80.6	82.4	84.9	88.8	91.6	97.3	69.395	0.100	-1.401	1.857	69.4	74.4	75.8	77.5	79.8	83.7	86.5	92.6
18	75.013	0.109	-0.069	1.702	75.0	80.4	81.9	83.7	86.1	89.9	92.5	97.9	69.773	0.099	-1.356	1.876	69.8	74.7	76.1	77.8	80.1	83.9	86.7	92.5

Table 6. Smoothed percentile values of WC (cm) by age and sex from the Sample 3 (based on the population excluding obese and overweight children)

Age	Males												Females											
(years)	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99
6	53.138	0.074	0.018	1.639	53.1	55.7	56.3	57.2	58.3	60.0	61.2	63.6	52.098	0.079	0.177	1.644	52.1	54.7	55.4	56.3	57.4	59.2	60.5	62.9
7	54.486	0.079	-0.203	1.699	54.5	57.3	58.1	59.0	60.2	62.2	63.5	66.2	53.365	0.085	0.089	1.720	53.4	56.3	57.1	58.1	59.4	61.3	62.7	65.4
8	55.999	0.084	-0.375	1.759	56.0	59.1	60.0	61.0	62.4	64.5	66.0	69.0	54.908	0.091	-0.052	1.774	54.9	58.2	59.1	60.2	61.6	63.8	65.3	68.3
9	57.666	0.089	-0.460	1.809	57.7	61.1	62.1	63.2	64.7	67.1	68.7	72.0	56.685	0.096	-0.212	1.808	56.7	60.4	61.3	62.5	64.1	66.5	68.2	71.6
10	59.462	0.093	-0.448	1.834	59.5	63.3	64.3	65.5	67.2	69.8	71.5	75.1	58.604	0.099	-0.370	1.827	58.6	62.6	63.7	64.9	66.7	69.4	71.2	75.0
11	61.436	0.097	-0.408	1.823	61.4	65.5	66.6	67.9	69.7	72.5	74.4	78.3	60.623	0.100	-0.565	1.833	60.6	64.8	66.0	67.3	69.2	72.1	74.1	78.3
12	63.554	0.098	-0.330	1.773	63.6	67.8	68.9	70.3	72.1	75.1	77.1	81.2	62.592	0.099	-0.764	1.823	62.6	66.9	68.1	69.5	71.4	74.5	76.6	81.1
13	65.711	0.097	-0.230	1.705	65.7	69.9	71.1	72.5	74.4	77.4	79.4	83.7	64.338	0.096	-0.900	1.805	64.3	68.6	69.8	71.3	73.2	76.4	78.6	83.2
14	67.811	0.095	-0.122	1.636	67.8	72.0	73.2	74.6	76.5	79.5	81.6	85.9	65.814	0.094	-0.993	1.786	65.8	70.1	71.3	72.7	74.7	77.8	80.1	84.8
15	69.703	0.093	0.032	1.579	69.7	73.9	75.0	76.4	78.3	81.3	83.4	87.7	66.974	0.091	-1.009	1.768	67.0	71.2	72.3	73.8	75.7	78.8	81.1	85.7

16	71.290	0.093	0.245	1.566	71.3	75.5	76.6	78.0	79.9	82.8	84.9	89.1	67.830	0.089	-0.950	1.762	67.8	72.0	73.1	74.5	76.4	79.5	81.6	86.2
17	72.613	0.093	0.426	1.614	72.6	76.9	78.1	79.5	81.3	84.2	86.2	90.2	68.492	0.088	-0.866	1.782	68.5	72.6	73.8	75.2	77.0	80.0	82.1	86.5
18	73.753	0.094	0.491	1.715	73.8	78.2	79.4	80.9	82.7	85.6	87.5	91.4	69.032	0.088	-0.752	1.828	69.0	73.2	74.4	75.8	77.6	80.6	82.6	86.8

Table 7. Smoothed percentile values of WC (cm) by age and sex from the Sample 4 (based on the population excluding obese, overweight and underweight children)

Age	Males												Females											
(years)	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99	mu	sigma	nu	tau	P50	P75	P80	P85	P90	P95	P97	P99
6	53.875	0.069	0.106	1.561	53.9	56.2	56.9	57.7	58.7	60.4	61.5	63.8	52.921	0.073	0.182	1.565	52.9	55.4	56.0	56.9	57.9	59.7	60.9	63.3
7	55.349	0.073	-0.155	1.613	55.3	58.0	58.7	59.6	60.7	62.6	63.8	66.5	54.419	0.078	0.096	1.648	54.4	57.2	57.9	58.8	60.0	61.9	63.2	65.8
8	56.992	0.078	-0.376	1.684	57.0	59.9	60.7	61.7	62.9	65.0	66.4	69.3	56.162	0.083	-0.085	1.709	56.2	59.2	60.0	61.0	62.3	64.4	65.8	68.7
9	58.797	0.081	-0.499	1.743	58.8	62.0	62.9	63.9	65.3	67.6	69.1	72.3	58.102	0.086	-0.321	1.735	58.1	61.4	62.3	63.4	64.9	67.2	68.8	72.0
10	60.730	0.085	-0.526	1.769	60.7	64.2	65.2	66.3	67.8	70.3	71.9	75.3	60.131	0.088	-0.573	1.727	60.1	63.7	64.7	65.9	67.5	70.0	71.8	75.5
11	62.787	0.087	-0.530	1.755	62.8	66.5	67.5	68.7	70.4	73.0	74.8	78.4	62.176	0.089	-0.883	1.718	62.2	65.9	67.0	68.3	70.0	72.8	74.8	78.9
12	64.909	0.088	-0.520	1.707	64.9	68.7	69.8	71.1	72.8	75.5	77.5	81.4	64.098	0.088	-1.174	1.712	64.1	68.0	69.1	70.4	72.2	75.2	77.4	82.0
13	67.005	0.088	-0.495	1.643	67.0	70.9	71.9	73.3	75.0	77.9	79.9	84.0	65.762	0.087	-1.378	1.719	65.8	69.7	70.8	72.2	74.1	77.2	79.4	84.2
14	69.013	0.086	-0.429	1.574	69.0	72.8	73.9	75.3	77.0	79.9	82.0	86.3	67.150	0.085	-1.533	1.745	67.1	71.1	72.2	73.6	75.5	78.6	80.9	85.8
15	70.836	0.085	-0.251	1.507	70.8	74.6	75.7	77.0	78.8	81.7	83.8	88.1	68.237	0.083	-1.568	1.761	68.2	72.2	73.3	74.7	76.5	79.6	81.9	86.7

16	72.415	0.084	0.019	1.481	72.4	76.2	77.2	78.6	80.3	83.2	85.2	89.4	69.052	0.081	-1.465	1.759	69.1	72.9	74.0	75.4	77.2	80.2	82.4	86.9
17	73.795	0.084	0.239	1.521	73.8	77.6	78.7	80.0	81.8	84.6	86.5	90.5	69.708	0.081	-1.309	1.760	69.7	73.6	74.7	76.0	77.8	80.7	82.8	87.2
18	75.038	0.084	0.343	1.625	75.0	79.1	80.2	81.5	83.2	86.0	87.8	91.6	70.281	0.081	-1.147	1.778	70.3	74.2	75.3	76.6	78.4	81.2	83.2	87.4

Table 8. Performance of the 90th percentile cut-off of waist circumference (WC) based on four separate participant samples in eight countries (including or excluding children with obesity, overweight or underweight) for predicting cardiovascular risk (≥3 risk factors) in pooled data from three populations aged 6-17 years (China, Iran and Korea)

Reference population	Males			Females		
	Sensitivity (%)	Specificity (%)	AUC (95% CI)	Sensitivity (%)	Specificity (%)	AUC (95% CI)
All (n=17831)						
Sample 1	36.3	91.1	0.64 (0.61, 0.67)	28.4	91.9	0.60 (0.57, 0.63)
Sample 2	45.1	87.4	0.66 (0.63, 0.69)	34.2	88.9	0.61 (0.58, 0.65)
Sample 3	60.0	78.6	0.69 (0.67, 0.72)	45.1	81.7	0.63 (0.60, 0.66)
Sample 4	58.6	79.6	0.69 (0.66, 0.72)	43.1	83.6	0.63 (0.60, 0.66)
6-12 years (n=7479)						
Sample 1	37.0	91.0	0.64 (0.59, 0.69)	27.0	93.0	0.60 (0.55, 0.65)
Sample 2	48.1	86.6	0.67 (0.63, 0.72)	36.2	89.9	0.63 (0.58, 0.68)
Sample 3	64.1	76.7	0.70 (0.66, 0.75)	48.6	81.9	0.65 (0.61, 0.70)
Sample 4	61.9	78.2	0.70 (0.66, 0.74)	46.5	83.7	0.65 (0.61, 0.70)
13-17 years (n=10352)						
Sample 1	35.9	91.2	0.64 (0.60, 0.67)	29.6	91.0	0.60 (0.56, 0.65)
Sample 2	43.1	88.0	0.66 (0.62, 0.69)	32.4	88.2	0.60 (0.56, 0.65)
Sample 3	57.2	79.9	0.69 (0.65, 0.72)	42.1	81.6	0.62 (0.58, 0.66)
Sample 4	56.5	80.6	0.69 (0.65, 0.72)	40.3	83.6	0.62 (0.58, 0.66)

Sample 1: whole sample.
Sample 2: sample excluding obese children.
Sample 3: sample excluding obese and overweight children.
Sample 4: sample excluding obese, overweight and underweight children.
Notes: Cardiovascular risk factors include high blood pressure, high total cholesterol, high triglycerides, low high-density lipoprotein (HDL) cholesterol, high low-density lipoprotein (LDL) cholesterol, and high fasting glucose.AUC: Area under the curve of ROC analysis.

Table 9. Performance of the 90th percentile cut-offs of waist circumference (WC) based on four separate samples from eight countries (including or excluding children with obesity, overweight or underweight) for predicting cardiovascular risk (≥3 risk factors) in three separate populations aged 6-17 years (China, Iran and Korea)

Reference population	Males			Females		
	Sensitivity (%)	Specificity (%)	AUC (95% CI)	Sensitivity (%)	Specificity (%)	AUC (95% CI)
China (7-17 years, n=750)						
Sample 1	18.2	93.5	0.56 (0.37, 0.74)	0	92.8	0.46 (0.25, 0.68)
Sample 2	27.3	89.8	0.58 (0.40, 0.77)	16.7	91.0	0.54 (0.29, 0.78)
Sample 3	36.4	82.5	0.59 (0.41, 0.78)	33.3	84.4	0.59 (0.34, 0.84)
Sample 4	36.4	83.8	0.60 (0.42, 0.78)	33.3	85.6	0.60 (0.34, 0.85)
Iran (6-17 years, n=8393)						
Sample 1	21.8	93.7	0.58 (0.53, 0.62)	31.9	90.4	0.61 (0.57, 0.65)
Sample 2	28.5	90.8	0.60 (0.55, 0.64)	36.7	87.3	0.62 (0.58, 0.66)
Sample 3	43.0	83.7	0.63 (0.59, 0.68)	46.7	81.2	0.64 (0.60, 0.68)
Sample 4	43.0	84.1	0.63 (0.59, 0.68)	45.2	82.7	0.64 (0.60, 0.68)
Korea (10-17 years, n=8688)						
Sample 1	48.2	88.5	0.68 (0.65, 0.72)	25.4	93.3	0.59 (0.55, 0.64)
Sample 2	58.5	84.1	0.71 (0.68, 0.75)	31.9	90.4	0.61 (0.56, 0.66)
Sample 3	73.9	73.5	0.73 (0.70, 0.77)	43.8	82.1	0.63 (0.58, 0.67)
Sample 4	71.5	75.1	0.73 (0.70, 0.77)	41.1	84.4	0.63 (0.58, 0.67)

Sample 1: whole sample
Sample 2: sample excluding obese children
Sample 3: sample excluding obese and overweight children
Sample 4: sample excluding obese, overweight and underweight children
Notes: Cardiovascular risk factors include high blood pressure, high total cholesterol, high triglycerides, low high-density lipoprotein (HDL) cholesterol, high low-density lipoprotein (LDL) cholesterol, and high fasting glucose; AUC: Area under the curve of ROC analysis

Table 10. Age- and sex-specific waist circumference (WC) for the 90th percentile, and virtual trajectories of WC during childhood estimated with GAMLSS, which link with WC cut-offs for central obesity in adults from the IDF or the Obesity in Asia Collaboration

Age (years)	Males				Females	
	P_{90}, cm	WC cut-offs for adult central obesity			P_{90}, cm	WC cut-off for adult central obesity
		85 cm †	90 cm ‡	94 cm §		80 cm †‡§
6	58.7	59.8	62.9	65.4	57.9	58.9
7	60.7	61.9	65.4	68.2	60.0	61.1
8	62.9	64.3	68.1	71.2	62.3	63.6
9	65.3	66.8	70.9	74.3	64.9	66.2
10	67.8	69.4	73.9	77.6	67.5	69.0
11	70.4	72.0	76.9	80.9	70.0	71.6
12	72.8	74.6	79.7	84.1	72.2	74.0
13	75.0	76.9	82.3	86.8	74.1	75.8
14	77.0	78.9	84.5	89.2	75.5	77.3
15	78.8	80.7	86.3	91.0	76.5	78.3
16	80.3	82.2	87.6	92.2	77.2	78.9
17	81.8	83.6	88.8	93.1	77.8	79.5
18	83.2	85.0	90.0	94.0	78.4	80.0

† WC ≥85 cm for men and ≥80 cm for women for Asian adults recommended by the Obesity in Asia Collaboration.
‡ WC ≥90 cm for men and ≥80 for women for South Asian, Chinese, and Japanese adults recommended by the IDF.
§ WC ≥94 cm for men and ≥80 for women for European, African and Eastern Mediterranean and Middle East adults recommended by the IDF.
Notes: For males, WC=85 cm at the age of 18 years (i.e., adult) corresponds to P93.6 of WC for children and adolescents aged 6-17 years; WC=90 cm at the age of 18 years corresponds to P98.4 of WC; WC=94 cm to P99.5 of WC. For females, WC= 80 cm at age of 18 corresponds to P93.3 of WC.
GAMLSS: generalized additive model for location, scale and shape, which uses Box-Cox power exponential distribution with cubic spline smoothing.
IDF: International Diabetes Federation.
All estimates are calculated based on data excluding children with obesity, overweight or underweight based on the IOTF BMI pediatric criteria.

Table 11. Performance of those percentiles of WC linking with adult WC cut-offs for predicting cardiovascular risk (≥3 risk factors) in the pooled data from three test populations aged 6-17 years from China, Iran and Korea

WC cut-offs	Sensitivity (%)	Specificity (%)	AUC (95% CI)
Males (n=9151)			
85 cm (at age 18 years) †	47.7	83.3	0.68 (0.65, 0.71)
90 cm (at age 18 years) ‡	37.2	91.2	0.64 (0.61, 0.67)
Females (n=8680)			
80 cm (at age 18 years) †‡	37.9	86.8	0.62 (0.59, 0.65)

Notes: Cardiovascular risk factors include high BP, high TC, high TG, low HDL, high LDL, and high glucose

† WC ≥85 cm for men and ≥80 cm for women for Asian adults recommended by the Obesity in Asia Collaboration.

‡ WC ≥90 cm for men and ≥80 for women for South Asian, Chinese, and Japanese adults recommended by the IDF.

Table 12. Performance of those percentiles of WC linking with adult WC cut-offs for predicting cardiovascular risk (≥3 risk factors) in US adolescents aged 12-17 years based on data form the NHANES 1999-2014

WC cut-offs	Sensitivity (%)	Specificity (%)	AUC (95% CI)
Males (n=1927) 94 cm (at age 18 years) [§]	60.5	81.2	0.71 (0.66, 0.76)
Females (n=1837) 80 cm (at age 18 years) [§]	83.1	52.1	0.68 (0.61, 0.74)

Notes: Cardiovascular risk factors include high BP, high TC, high TG, low HDL, high LDL, and high glucose

[§] WC ≥94 cm for men and ≥80 for women for European, African and Eastern Mediterranean and Middle East adults recommended by the IDF.

Figure legends

Figure 1. Flow chart of the study design and analysis

Figure 2. Comparisons of the 90th percentile curves of waist circumference (WC) by age and sex among samples excluding children and adolescents with obesity, overweight or underweight, based on pooled data from eight countries. *Notes:* Sample 1 indicates the P90 of WC based on the whole population; Sample 2 indicates the P90 of WC based on the population excluding obese children; Sample 3 indicates the P90 of WC based on the population excluding obese and overweight children; Sample 4 indicates the P90 of WC based on the population excluding obese, overweight and underweight children

Figure 3. Comparisons of the 75th and 90th percentile values of waist circumference (WC) after exclusion of children and adolescents with underweight, overweight or obesity compared to corresponding percentiles of normal-weight European children in the IDEFICS study

Figure 1

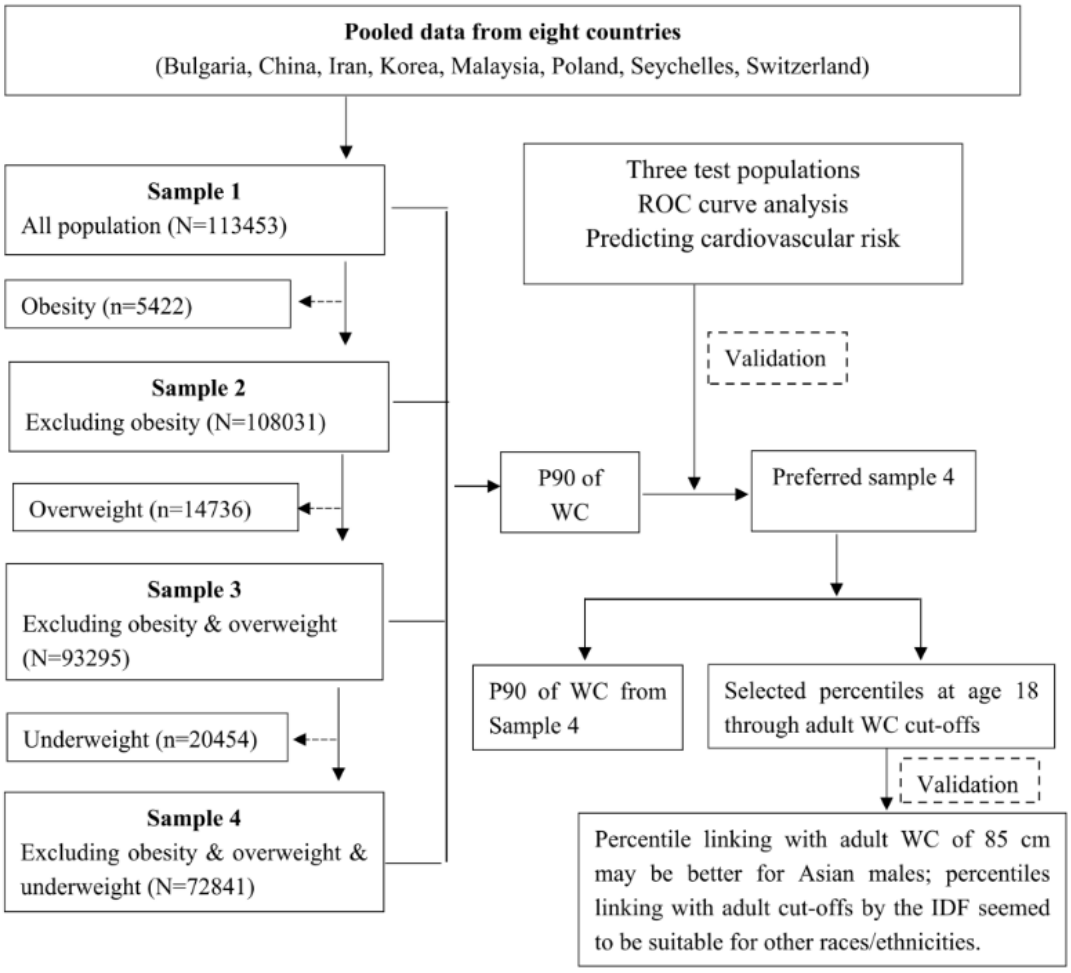

Figure 2

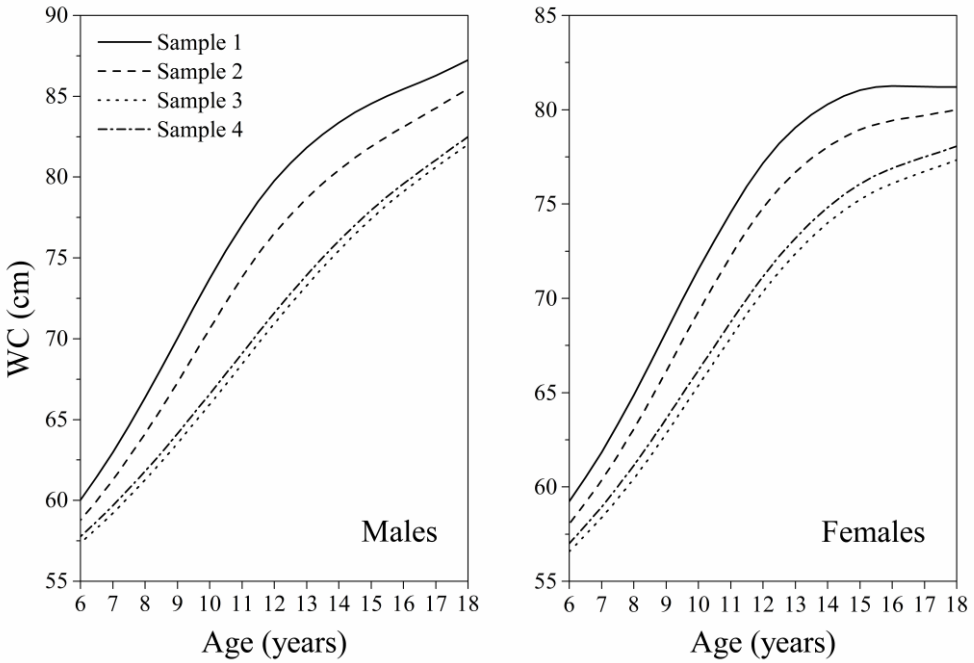

Figure 3