Developing global standards for predicting adult overweight and obesity from childhood body mass index – a comparison of estimates obtained from follow up of a pooled international longitudinal cohort to current standards derived from cross-sectional survey data

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ABSTRACT

Background Historically, cut-points for childhood and adolescent overweight and obesity have been based on population-specific percentiles derived from cross-sectional data. To obtain cut-points that might better predict overweight and obesity in adulthood, we examined the association between childhood body mass index (BMI) and adult BMI status in a longitudinal cohort.

Methods Using the International Childhood Cardiovascular Cohort (i3C) Consortium data from the United States and Finland we determined childhood overweight and obesity cut-points that best predict BMI status at the age of 18 in 3,779 children who were followed up from year 1970 onwards and had at least one childhood BMI measurement between ages 6 and 17 and a BMI measurement specifically at age 18. Logistic regression analysis was used to assess the association between BMI in childhood and adult obesity. Area under the Receiver Operating Characteristic curve (AUROC) was used to assess the ability of fitted models to discriminate different BMI status groups in adulthood. The cut-points were then compared to those defined by the International Obesity Task Force (IOTF), which used cross-sectional data, and tested for sensitivity and specificity in a separate, independent longitudinal sample with BMI measurements available from both childhood and adulthood.

Findings The cut-points derived from the longitudinal i3C Consortium data were lower than the IOTF cut-points. Consequently, a larger percentage of the sample was classified as overweight or obese when using the i3C cut-points in the independent sample. Especially for obesity, i3C cut-points were significantly better at identifying those who would later in life become obese. In the independent sample, the AUROC values for overweight ranged from 0.75 to 0.88 for the i3c cut-points; the corresponding values for the IOTF cut-points ranged from 0.69 to 0.87. For obesity, the AUROC values ranged from 0.84 to 0.90 and 0.57 to 0.76 for the i3c and IOTF cut-points, respectively.

Interpretation The childhood BMI cut-points based on the i3C Consortium longitudinal data provide better predictors of future risk of adult overweight and obesity than estimates based on cross-sectional data. The result is more specific identification of the childhood population at risk of adult overweight or obesity than currently used standards.

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INTRODUCTION

The obesity pandemic is currently a major threat to public health.[1] Body mass index (BMI) levels have been shown to track strongly from childhood to adulthood, and childhood BMI levels are important independent predictors of cardiovascular (CV) risk factors and CV morbidity in adulthood.[2-9] For these reasons accuracy in defining levels of BMI in children that predict the risk of obesity in adulthood is important because it defines children that can benefit from direct intervention efforts more accurately.

The BMI cut points most commonly used for defining childhood overweight and obesity, such as those recommended by the Centers for Disease Control (CDC) and Prevention, and the World Health Organization (WHO), were developed using percentiles for BMI within the chosen child population to define the thresholds for obesity.[10,11] However, these defined childhood standards have not been examined in relation to adult obesity outcomes, and they may vary depending on the population selected to define them and the time period in which that population is measured.

The International Obesity Task Force (IOTF) addressed this by relating the distribution of BMI in children to levels known to be associated with risk of obesity in adults in the same population as the children.[12] The data used to determine the childhood cut-points produced by the IOTF in 2000 were obtained from cross-sectional surveys of 192,727 participants aged 0-25 years between 1963 and 1993 from six populations: Brazil, Great Britain, Hong Kong, the Netherlands, Singapore, and the U.S.A. In the IOTF approach, the proportion of the adult population (defined as 18 year olds) that was overweight or obese was first estimated, using standard adult BMI thresholds of 25 kg/m^2 and 30 kg/m^2, respectively. The cut-point for each population was calculated using the LMS method so that each population specific centile curve corresponds to the percentile of adulthood overweight or obesity in that population. To obtain the single cut-points, the population-specific curves

were averaged.[12] A concern about this method of defining childhood BMI risk for adult obesity is that if it is used in a setting where a secular change in obesity prevalence is occurring in the populations from which the sample was chosen, the inferences on cut-points in childhood would not be valid. If the trend in overweight and obesity was upwards the estimates from the cross-sectional approach would underestimate the proportion of children who would become overweight adults. Further, the method used specifies that the same percentage of children will be at risk in all age groups. This is unlikely to be so.

An alternative approach to the cross-sectional comparisons used by the IOTF, WHO, and CDC would be to identify cut-points by examining the association between childhood and adult BMI in the same individuals who had been followed in a cohort as they aged. We aimed to obtain cut-points that might better predict overweight and obesity in adulthood by examining the association between childhood and adult BMI status in a longitudinal cohort, the International Childhood Cardiovascular Cohort (i3C) Consortium that includes seven cohorts from three countries, the U.S.A., Finland, and Australia.

METHODS

The i3C Consortium, has been described previously.[13] Briefly, it includes seven large childhood cohorts - five from the United States (Bogalusa Heart Study[BHS, Louisiana]); Minnesota Cohorts[MN, Minnesota]; Muscatine Study[Iowa]; National Growth and Health Study[NGHS, Ohio]; and Princeton Lipid Research Study[PLRS, Ohio]); and one each from Finland ([Cardiovascular Risk in Young Finns Study [YFS]); and Australia (Childhood Determinants of Adult Health Study[CDAH]), which collectively recruited over 40,000 children and adolescents in the 1970s and 1980s for assessment of a variety of cardiometabolic risk factors. The study participants were born between the early 1950s and early 1990s, the median birth year being 1970. A subset of each of these cohorts has been re-

evaluated at least once in adulthood. For each study, ethical approval was obtained by the appropriate institutional review board. Informed consent was obtained from all parents and adult participants; assent was obtained from participants while they were children/adolescents.

There were 41,086 participants who had childhood BMI (age 3-17). For the main analysis, to allow a direct comparison between i3C and IOTF cut-points, the sample size was restricted to 3,779 participants (9.2% of the original population, Table 1) who had at least one childhood BMI measurement between ages 6 and 17 and a BMI measurement specifically at age 18, the age defining adulthood used by IOTF. Measurements in early childhood (age 3-5) were excluded from the analyses due to insufficient sample size. We conducted parallel analyses using the extended 'young adult' age range of 18-20 (n=5,019, 12.2% of the original population) and 'later young adulthood' age range of 21-29 (n=9,039, 22.0% of the original population). Data from all visits for these individuals were used in the analysis, as described below. The outcome was defined as being overweight (BMI≥25kg/m^2) or obese (BMI ≥30kg/m^2) at the age of 18 in the main analyses and correspondingly being overweight or obese between ages 18-20 and 21-29 in the additional analyses. Because the participants in the CDAH cohort had their youngest adult measurement at age 26 and did not have measurements between ages 18 and 20, they were excluded from the main analysis. However, they were included in the analysis for 'later young adulthood' (ages 21-29 years).

We validated the results in an independent sample for which we used data from the STRIP (Special Turku Coronary Risk Factor Intervention Project) study, which is a longitudinal prospective randomized controlled study to prevent atherosclerosis.[14] The participants were enrolled in the study at their 5-month visit at Turku City well-baby clinics. At the age of 6 months, 1,062 infants (56.5% of the eligible age cohort) were randomly assigned to an intervention group (n = 540), which was followed biannually, and a control

group (n =522), which was followed biannually up to the age of 7 years and after that on a yearly basis. The intervention, which included dietary counselling and information on physical activity and smoking prevention, continued until the study participants were 20 years old.[14] For the analyses in this study, we included individuals based on the same criteria as for the i3C Consortium sample: adult BMI at the age of 18 and at least one BMI measurement in childhood between ages 6 and 17 (n=500). The participants in the STRIP study were 18 years old during the years 2007-09.

In a longitudinal study that continues for as long as the STRIP study, loss to follow-up is inevitable. However, the characteristics of the participants who remained in the study and those who discontinued have been compared on several occasions, with no systematic differences found between the groups.[14-16] Additionally, we compared those who were in the study at the age of 18 years to those who were not and found no differences in sex, BMI, height or weight at baseline (age 0.7 months) or 10-year follow-up visit, or parental socioeconomic status (education and occupation) at the age of 13 months. Intervention was, however, modestly associated with loss to follow-up at age 18; as only 44% of those in the sample at age 18 were from the intervention group (Supplementary Table 1). Intervention, though was not associated with BMI[15] and thus the results presented below should not be biased by this difference in proportion of those who remained in the study.

Table 1: *Details of the total number of participants who have anthropometric data in between age 6 and 17 and at the age of 18 and age-point specific numbers of observations from i3C Consortium cohorts by sex. The total Ns refer to the number of unique individuals in each cohort. The second row of the table presents the range of birth years for the analysed subsets for each of the cohorts.*

	BHS (n=878)		Muscatine (n=536)		NGHS (n=568)	MN (n=769)		PRLS (n=16)		YFS (n=1,012)		*Total* (N=3,779)	
yob	1958-82		1954-74		1976-78	1966-89		1957-59		1965-74		1954 - 89	
age	M	F	M	F	F*	M	F	M	F	M	F	M	F
6	19	21	40	24		38	37			49	48	146	120
7	60	40	3			172	138					235	178
8	34	33	16	9		328	257					378	299
9	106	107	52	53	322	325	250			85	76	568	808
10	116	82	112	74	543	298	221					526	920
11	66	66	38	33	528	294	223					398	850
12	157	168	166	137	530	386	283			266	306	975	1424
13	156	133	17	14	496	396	306					569	949
14	149	146	178	169	453	391	299	4	4			722	1071
15	216	210	14	28	542	361	272	8	4	458	531	1057	1587
16	139	108	181	171	479	332	245	6	7			658	1010
17	146	162		1	477	291	227	30	20			467	887

**The NGHS cohort includes only females*

Abbreviations: yob=year of birth, BHS = Bogalusa Heart Study, NGHS = National Growth and Health Study, MN = Minnesota Cohorts, PRLS = Princeton Lipid Research Study, YFS = Cardiovascular Risk in Young Finns Study, M = Male, F = Female

Statistical methods

All analyses were performed separately by sex and integer age group for ages 6 to 17. The data from different i3C Consortium cohorts were pooled. For those cohort members who had more than one BMI measurement within one age, we used the first measurement.

We used logistic regression to assess the relation between childhood BMI and adult overweight and obesity status for each age-sex defined stratum. The linearity in the logit was assessed using fractional polynomials. If a non-linear transformation of BMI was found to best characterize the association between BMI and the logit, the validity of the original logistic regression model was ensured by using suitable transformations of BMI. The calibration of the models was assessed using the Hosmer-Lemeshow goodness-of-fit test.[17] Receiver Operating Characteristic (ROC) curve analysis was used to estimate preliminary childhood cut-points for overweight and obesity. The optimal cut-points were defined from the ROC curve by calculating sensitivity and specificity and deriving Youden's J (*YJ)* index *=sensitivity + specificity -1*.[18] Sensitivity describes the probability of correctly predicting a participant will be overweight or obese; specificity describes the probability of correctly predicting a participant will be normal weight. YJ index summarizes the performance of a predictor in terms of a single statistic.

The cut-point was then calculated based on the equation:

$$Cut - point = (logit - \alpha)/\beta$$

Where α and β are the intercept and slope from the logistic regression model, respectively, and logit describes log of the odds in favour of overweight or obesity[19].

The final cut-points at different ages in childhood and adolescence that best predicted being overweight or obese at age 18 for males and females were obtained by fitting a smooth loess curve through the series of preliminary cut-points over age. The smoothing parameter on each loess was obtained by corrected Akaike information criteria (AICc). Using the same methods,

we conducted additional analysis by computing cut-points for being overweight or obese in early adulthood during the ages 18-20, and later in adulthood during ages 21-29.

As an additional validation to our cut-points, we investigated how the results would change if we further adjusted the models for 'region', these being: Finland (YFS), the US Midwest (MN, NGHS, PRLS, and Muscatine), and South (BHS) (Supplementary Table 2 and Supplementary Figures 1 and 2). Adjusting for this additional covariate changed the cut-points very little. We also looked into the changes that excluding one of the cohorts would cause by re-analysing the data excluding one cohort at a time. Removing any individual cohort did not seem to cause major changes to the cut-points (Supplementary Figures 3, 4, 5, and 6).

To determine which of the two estimated sets of age- and sex-specific cut-points in childhood, IOTF or i3C, might more validly estimate risk of adult overweight or obesity, we applied the two sets of cut-points to an independent cohort dataset, the STRIP Study. We classified children in the STRIP study as overweight or obese based on the cut-points at each age point. In order to compare their predictive ability, we determined the area under the ROC curve (AUROC) for both sets of cut-points and computed p-values for comparing the AUROCs. Additionally, we compared i3C cut-points to those defined by the CDC and WHO.

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RESULTS

Table 2 displays the cut-points at different ages in childhood and adolescence that best predict being overweight or obese at age 18 in the pooled i3C Consortium data.

For the early adulthood responses (age 18-20), the cut-points were similar to those that were derived based on the data at age 18. If BMI during ages 21-29 was used, the cut-points were even lower than when the BMI at age 18 or 18-20. The cut-points from these responses are presented in supplementary Tables 3, 4, 5 and 6 and supplementary Figures 7 and 8.

Table 2 Cut-points for overweight (BMI>25kg/m^2 at the age of 18) and obesity (BMI>30kg/m^2 at the age of 18) for males and females.

	Age 18 Overweight		**Age 18 Obesity**	
Age	**Males**	**Females**	**Males**	**Females**
6	16·13	15·68	16·81	16·78
7	16·66	16·43	17·55	17·52
8	17·22	17·20	18·29	18·29
9	17·79	18·01	19·03	19·08
10	18·36	18·79	19·78	19·86
11	19·08	19·76	20·58	20·99
12	19·84	20·76	21·38	22·25
13	20·60	21·59	22·28	23·53
14	21·43	22·12	23·48	24·60
15	22·27	22·61	24·73	25·64
16	23·10	23·08	26·00	26·65
17	23·94	23·53	27·31	27·63

Figures 1 and 2 illustrate comparison of the cut-points estimated from the i3C data to the IOTF standards. The i3C estimates are lower than those produced by the IOTF.

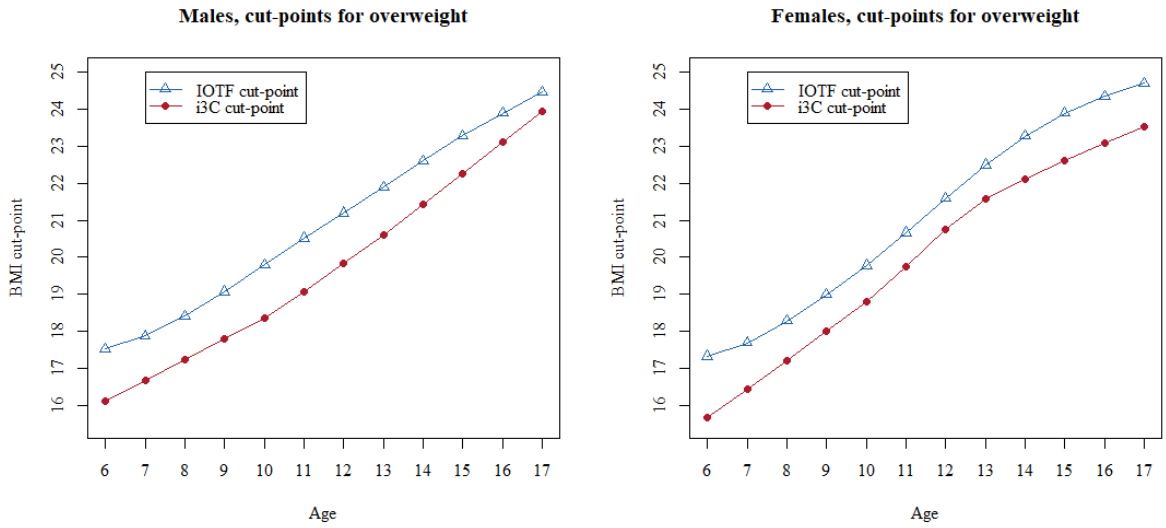

Figure 1 *Cut-points for overweight for males and females. The blue line with triangular symbols represents the values of International Obesity Task Force (IOTF) cut-points, whereas the red line with circular symbols represents cut-points derived from i3C Consortium pooled longitudinal data based on ROC analysis.*

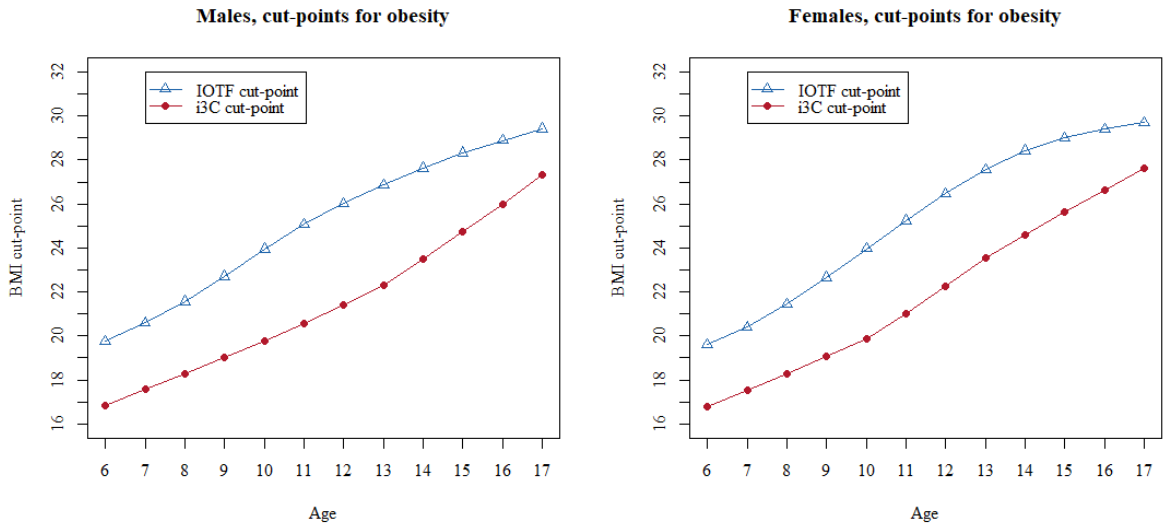

Figure 2 *Cut-points for obesity for males and females. The blue line with triangular symbols represents the values of IOTF cut-points, whereas the red line with circular symbols represents cut-points derived from i3C data using the ROC analysis.*

Figure 3 presents the percentages of the STRIP Study participants classified as overweight or obese based on both sets of cut-points. Since the cut-points derived based on the longitudinal i3C data are lower than the IOTF cut-points, a larger percentage of the participants are classified as overweight or obese based on i3C cut-points.

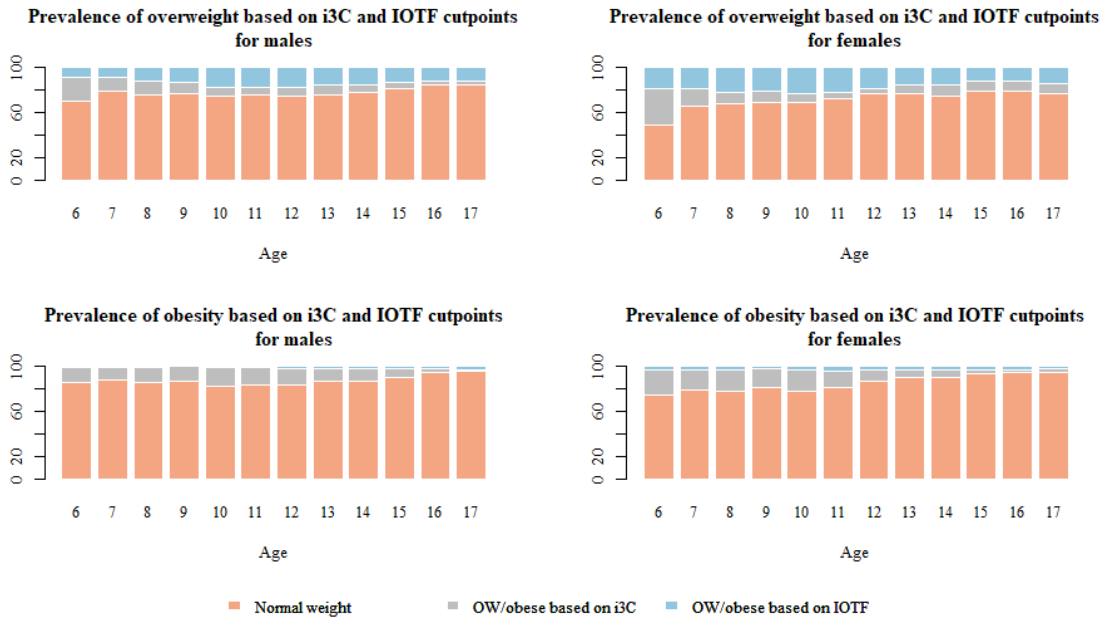

Figure 3 *The percentages of STRIP Study population classified as overweight (OW) or obese based on i3C and IOTF cut-points*

The AUROCs for both classifiers, i3C and IOTF, and the p-value for their comparison are reported in Tables 3 and 4. Based on the AUROCs and p-values, the lower i3C set of childhood cut-points have better overall ability to discriminate those who will be overweight or obese in adulthood than the IOTF cut-points. For all age points for obesity, and for some age points for overweight, i3C cut-points are statistically significantly superior at predicting the adulthood status than the IOTF cut-points. The i3C cut-points were also lower and had better predictive ability than the CDC cut-points (Supplementary Tables 7, 8 and 9 and Supplementary Figures 9 and 10) and WHO cut-points (Supplementary Tables 10 and 11 and figures 11 and 12). The AUROC for the i3C cut-points ranged from 0.75 to 0.88 for overweight and 0.84 to 0.90 for obesity whereas the corresponding values were 0.69 to 0.83 and 0.66 to 0.88 for the CDC cut-points and 0.72 to 0.88 and 0.67 to 0.88 for the WHO cut-points.

Table 3 The performance of i3C and IOTF BMI cut-points for prediction of overweight in adulthood in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC IOTF [95% Wald CI]	p
6	0·75 [0·70 ; 0·80]	0·69 [0·62 ; 0·75]	0·05
7	0·73 [0·67 ; 0·79]	0·70 [0·64 ; 0·76]	0·22
8	0·78 [0·72 ; 0·84]	0·73 [0·67 ; 0·79]	0·07
9	0·78 [0·72 ; 0·84]	0·70 [0·64 ; 0·76]	0·01
10	0·79 [0·73 ; 0·84]	0·76 [0·70 ; 0·82]	0·26
11	0·80 [0·75 ; 0·86]	0·76 [0·70 ; 0·82]	0·04
12	0·78 [0·73 ; 0·84]	0·76 [0·70 ; 0·82]	0·24
13	0·81 [0·75 ; 0·86]	0·75 [0·69 ; 0·81]	0·02
14	0·81 [0·75 ; 0·86]	0·79 [0·73 ; 0·85]	0·41
15	0·84 [0·79 ; 0·90]	0·80 [0·74 ; 0·86]	0·05
16	0·87 [0·83 ; 0·92]	0·83 [0·77 ; 0·88]	0·03
17	0·88 [0·84 ; 0·93]	0·87 [0·82 ; 0·92]	0·41

Table 4 The performance of i3C and IOTF BMI cut-points for prediction of obesity in adulthood in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC IOTF [95% Wald CI]	p
6	0·88 [0·83 ; 0·94]	0·60 [0·51 ; 0·70]	<·001
7	0·87 [0·80 ; 0·95]	0·57 [0·49 ; 0·66]	<·001
8	0·84 [0·75 ; 0·93]	0·57 [0·49 ; 0·66]	<·001
9	0·85 [0·76 ; 0·94]	0·61 [0·51 ; 0·70]	<·001
10	0·86 [0·78 ; 0·93]	0·63 [0·53 ; 0·74]	0·0002
11	0·85 [0·77 ; 0·94]	0·65 [0·55 ; 0·76]	0·001
12	0·86 [0·78 ; 0·95]	0·71 [0·59 ; 0·82]	0·01
13	0·85 [0·76 ; 0·95]	0·71 [0·59 ; 0·82]	0·01
14	0·90 [0·82 ; 0·98]	0·74 [0·63 ; 0·86]	0·01
15	0·89 [0·80 ; 0·98]	0·75 [0·63 ; 0·87]	0·01
16	0·88 [0·79 ; 0·98]	0·76 [0·65 ; 0·88]	0·02
17	0·86 [0·76 ; 0·96]	0·73 [0·62 ; 0·85]	0·02

DISCUSSION

We observed that the overweight/obesity cut-points derived using pooled longitudinal data from the i3C Consortium cohorts are lower than those estimated by the IOTF and identify a larger proportion of the childhood population at risk for adult overweight or obesity. Based on the AUROC, the set of childhood age- and sex-specific cut-points derived in the present analyses are able to better predict the risk of adult overweight or obesity than the commonly used IOTF standards, especially for predicting obesity.

The reason for the i3C cut-points being lower than those estimated from the cross-sectional survey approach used to derive the IOTF standards is important to consider. Secular change in childhood obesity from the time when the 18-year old 'adults' in the IOTF surveys were themselves children could account for the difference observed. Using the percentage of participants found to be obese at age 18 to define the percentage overweight or obese in concurrent childhood samples gives estimates that are higher than if the data for these 18-year olds as children had been used. This is because the children in the cross-sectional samples have a higher BMI at the same age than did their predecessors when an upward secular trend across the population is occurring. The authors of the IOTF paper have argued that the period in which their survey samples were collected, from 1963-1993, was prior to the upward shift in BMI that has occurred in recent decades.[20] In fact, a modest upturn in prevalence of overweight and obesity in the years during the 1980s and 1990s in the populations from which their samples came was observed.[21] On the other hand, an increase in the prevalence of factors determining development of obesity from childhood to age 18 in the i3C Consortium would mean that more children of lower BMI would become obese in adulthood than if there had been no secular change. In both scenarios the i3C longitudinal data would generally estimate BMI cut-points in childhood lower than would the IOTF cross-sectional data. To take into account the possible effect of birth year on risk of overweight and obesity we conducted additional sensitivity analyses adjusting for year of birth. These cut-points are presented in Supplementary Figures 13 and 14. We found that adjustment for birth year made little difference to the estimates.

It might be suggested that the greater screening validity observed when i3C Consortium cut-points were applied to STRIP Study data than when those from IOTF were used was due to the fact STRIP and i3C included participants from Finland. However, this

seems unlikely, since YFS contributed only 9% of the participants in the i3C dataset used for this analysis, with the majority being from the U.SA.

Based on our cut-points the share of obesity-prone children was higher at younger ages. The models used for defining cut-points are more precise and have less uncertainty the closer the response and the explanatory variable are temporally. Thus, the most precise of our cut-points are the ones defined for teenagers in the models with response being overweight or obesity at age 18. Where the temporal distance between the response and explanatory variable is bigger there is greater uncertainty. In the context of this paper, it appears to lead to lower cut-points and higher prevalence of those who are predicted to be overweight or obese. The phenomena can clearly be seen by looking at the sensitivities, specificities and Youden's J indexes in supplementary tables 5, 6, and 12. Within each table, the Youden's J increases with the age of measurement of explanatory variable, i.e., the smaller the temporal distance between the exposure and response. Accordingly, the cut-points defined with age 18 as response appear to have overall higher Youden's J indexes than the cut-points that were defined with age 18-20 or 21-29 as response. It is inarguable that the cut-points for childhood overweight and obesity vary depending on the adult age range chosen. Partly this is explained by the increasing uncertainty, however, the prevalence of overweight and obesity in the chosen age range also affects them. CARDIA data show the prevalence of obesity increases into the 30s and early 40s.[22] Which adult age group might be the best for comparison is not an issue we have addressed here as our main focus has been on examining what would be obtained with the cohort approach if it was compared to another major internationally used set of standards which were derived from cross-sectional data. Our choice of age 18 was to ensure we were able to make comparisons with IOTF. When we used an older age for our cohort participants for comparison in adulthood (as shown in our analyses using ages 18-20

or 21-29) we found that the estimated cut-points were lower than the cut-points using data from 18-year olds to identify adult obesity.

A major strength of the present study was its ability to utilize longitudinal data on BMI from childhood including different international cohorts. However, as the present analysis was not planned when these cohorts were established, there are some limitations that need to be noted. Most importantly, not all participants in the i3C Consortium cohorts had BMI data at the age of 18 and this meant we were dealing with a subset of the cohorts. Our additional analysis found that the eligible population for the analyses was slightly older and had a higher proportion of females than the original population (Supplementary Table 13). However, since the analyses were conducted stratified by sex and age, these differences should not affect the cut-points. While we found that the 3,779 participants who had BMI measurement at age 18 and those 5,019 who had BMI measurement between ages 18-20 had lower age- and sex-adjusted baseline BMI than those who were excluded from these samples, the participants who had BMI measured between ages 21-29 did not differ from the non-participants in this respect (Supplementary Table 13). An additional limitation of this study is that, in the i3C data there were few participants who had been measured specifically at ages 3-5 and then later in life at age 18 due to which they couldn't be included in the analyses.

Further, when comparing the i3C cut-points to the IOTF cut-points it is important to note that IOTF cut-points were based on populations from countries of different socioeconomic settings and obesity rates (Brazil, Great Britain, Hong Kong, the Netherlands, Singapore and the U.S.A), whereas the i3C population consists of cohorts only from developed and industrialized countries (U.S.A, Finland and Australia). It will be particularly important in the future to determine whether the assessment of standards derived from predominantly non-Hispanic Caucasian populations are generalizable to other racial/ethnic groups. Previous international standards have been developed without an attempt to adjust

analyses for SES, possibly because of the difficulty in specifying what might be an ideal population base from which to derive an expected SES distribution. The i3C database does provide the opportunity for adjusting for SES measurement on individuals. However, the SES measures across cohorts differed to some extent, with missing information on about 30% of the sample. Further, the issue of which base population we might use for comparison remained. Bearing these considerations in mind we felt that we would not advance our understanding about the generalisability of our findings beyond what we had achieved by adjusting for region. In future, particularly where standards have been derived from a sample sourced from a single population, investigators may wish to adjust their results for SES in the particular reference population.

The majority of the i3C participants were children in the period, 1970-1988, and adults approximately twenty years later. IOTF participants were children approximately ten years later on average. Neither have measurements that make the samples 'contemporary'. If the i3C estimates had been obtained from a more recent sample they would be even lower than reported here, given that adult overweight and obesity has increased since the i3C participants were young adults. The cut-points will need to be revised with each opportunity that presents as time passes. What we do suggest is that the approach using cohort data has advantages over that using cross-sectional data and that it results in lower estimated cut-points, identifying a higher proportion of the child population as being at risk of future overweight or obesity. As more recent cohorts are able to produce estimates in the same way then these cut-points should be revised, and because of secular trends in adiposity they are likely to be lower than those we have produced.

CONCLUSIONS

Our analyses of data from multiple pooled longitudinal cohort studies provides childhood BMI cut-points for adult overweight/obesity prediction, using age 18 data for the adult comparison. Compared to existing IOTF data, the present cut-points are lower at each childhood age. Using adult data at an older age lowers the childhood cut-points and would appear to improve prediction of subsequent overweight or obesity in adulthood.

AUTHOR CONTRIBUTORSHIP

TD conceptualised the study, NK analysed the data, TD, RR, and SL guided the data analysis. TD, NK, and RR drafted the manuscript. All authors contributed to the interpretation of data for the work and revised it critically for important intellectual content. All authors have given final approval of the version to be published and agree to be accountable for all aspects of the work.

DECLARATION OF INTERESTS

All authors with the exception of Alison Venn have declared no conflict of interest. Dr. Venn reports grants from National Health & Medical Research Council (Australia), grants from National Heart, Lung & Blood Institute (USA) during the conduct of the study.

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RESEARCH IN CONTEXT

Evidence before this study

The cut-points for defining childhood overweight and obesity have thus far been based on cross-sectional data in childhood from which population-specific percentiles have been derived for children or, alternatively, on inference from concurrent adult data about the percentage of the population who are overweight and applying this percentile to define the cut-point for children from that population.

Added value of this study

This study provides new cut-points using methodologically preferable longitudinal cohort data. We show that these provide better discrimination of those who will become overweight or obese adults than do those previously derived from cross-sectional data.

Implications of all the available evidence

Using the more precisely defined cut-points from this study will allow intervention efforts to more efficiently identify children and adolescents at risk of becoming overweight or obese in adulthood compared to the estimates obtained by use of current standards.

Supplementary material

Supplementary Table 1 Comparison of participants and non-participants in the STRIP study

	Participants	Non-participants	p-value
% Females	51.6	47.2	0.26
% Intervention group	44.6	55.3	<0.001
Baseline BMI at 7 months: mean (SD)	17.2 (1.4)	17.28 (1.5)	0.16
BMI at 10 years: mean (SD)	17.4 (2.6)	17.50 (2.6)	0.77
SES (%)*	21/32/47	28/29/42	0.08

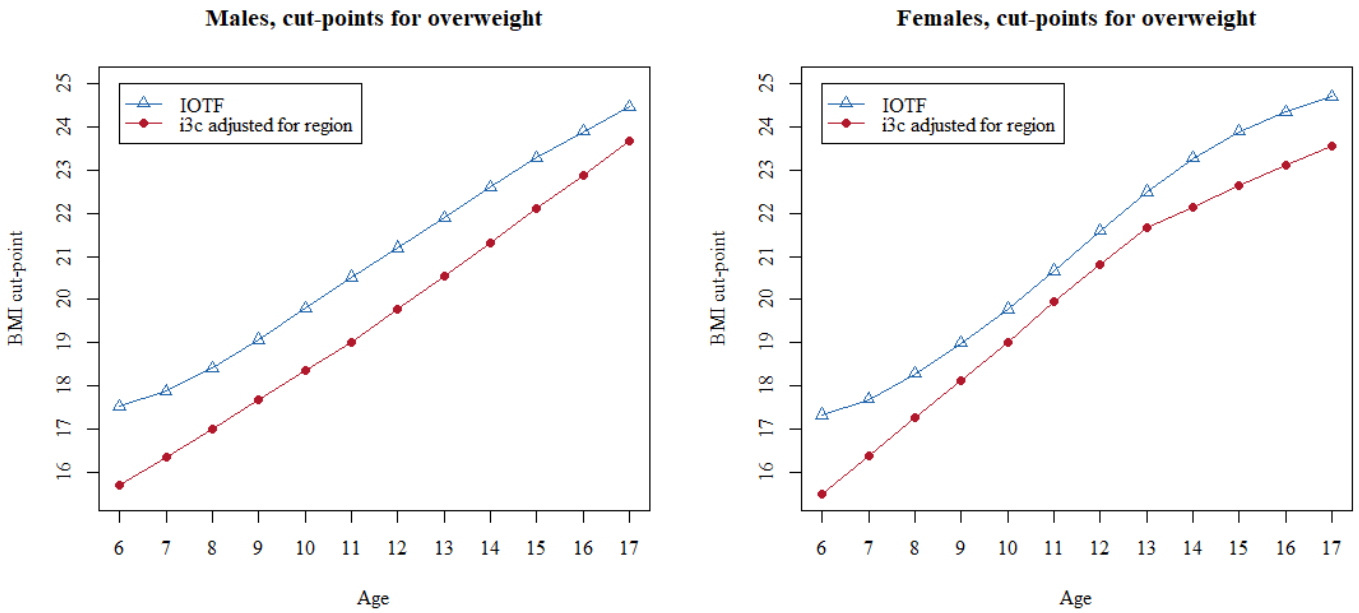
*Parental occupation at age 13 months (Manual/Lower non-manual/Higher non-manual)
Abbreviation: STRIP = The Special Turku Coronary Risk Factor Intervention Project

Additional sensitivity analyses adjusted for region

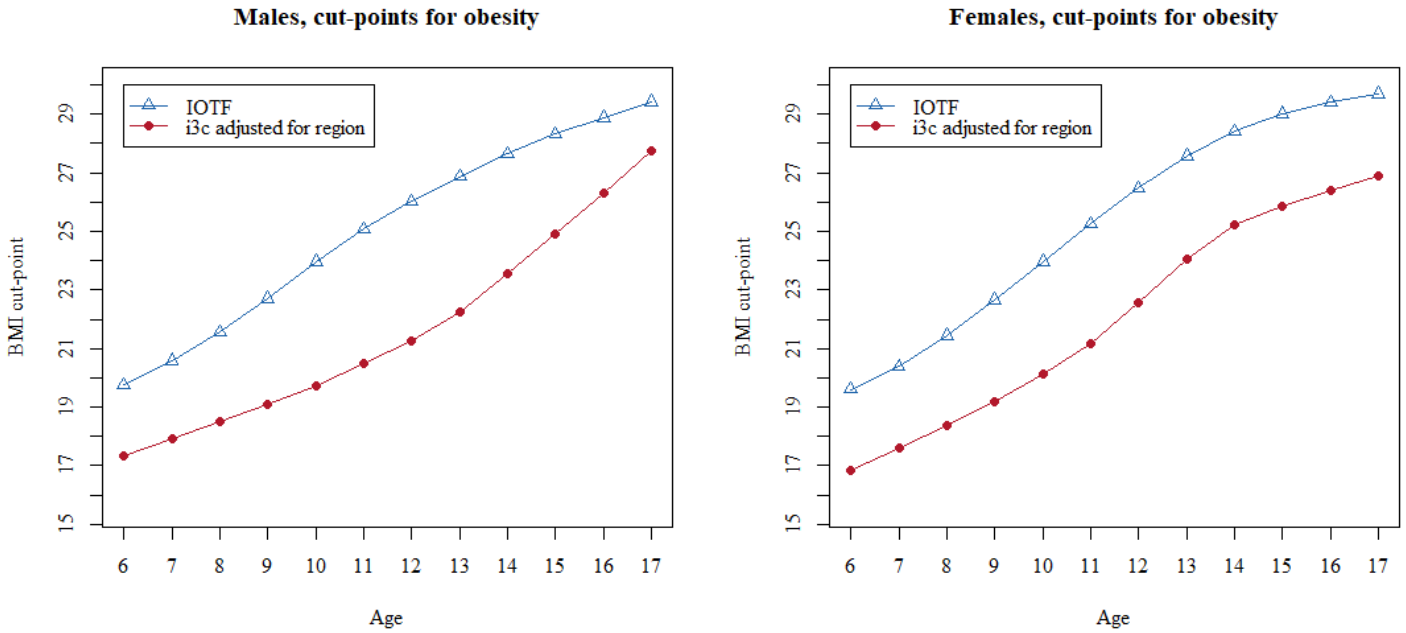
Supplementary Table 2 Cut-points for overweight and obesity at age 18 obtained by adjusting for region (BHS/Midwestern cohorts/YFS)

	Age 18 Overweight		Age 18 Obesity	
Age	**Males**	**Females**	**Males**	**Females**
6	15.69	15.49	17.34	16.82
7	16.34	16.36	17.91	17.61
8	17.01	17.25	18.50	18.39
9	17.67	18.13	19.10	19.18
10	18.34	19.10	19.73	20.12
11	19.02	19.95	20.50	21.19
12	19.77	20.80	21.26	22.56
13	20.53	21.65	22.23	24.05
14	21.31	22.15	23.55	25.22
15	22.10	22.63	24.91	25.83
16	22.88	23.12	26.30	26.40
17	23.67	23.57	27.73	26.91

Note: Midwestern cohorts = MN, NGHS, PRLS, and Muscatine



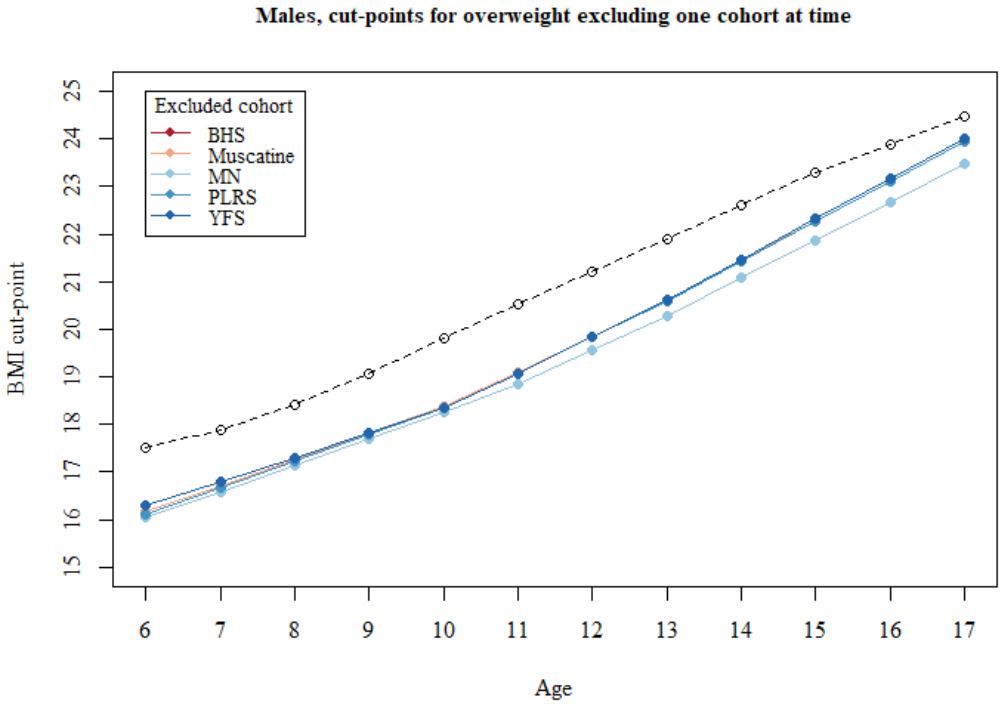
Supplementary Figure 1 Cut-points for overweight at age 18 obtained by adjusting for region (BHS/Midwestern cohorts/YFS). IOTF cut-points for comparison



Supplementary Figure 2 Cut-points for obesity at age 18 obtained by adjusting for region (BHS/Midwestern cohorts/YFS). IOTF cut-points for comparison

Additional sensitivity analyses excluding one cohort at time

Supplementary Figures 3-6 Cut-points for overweight and obesity for males and females obtained by excluding one cohort at time. The black line represents IOTF cut-points for comparison.


Males, cut-points for overweight excluding one cohort at time
Excluded cohort
BHS
Muscatine
MN
PLRS
YFS
BMI cut-point
15
16
17
18
19
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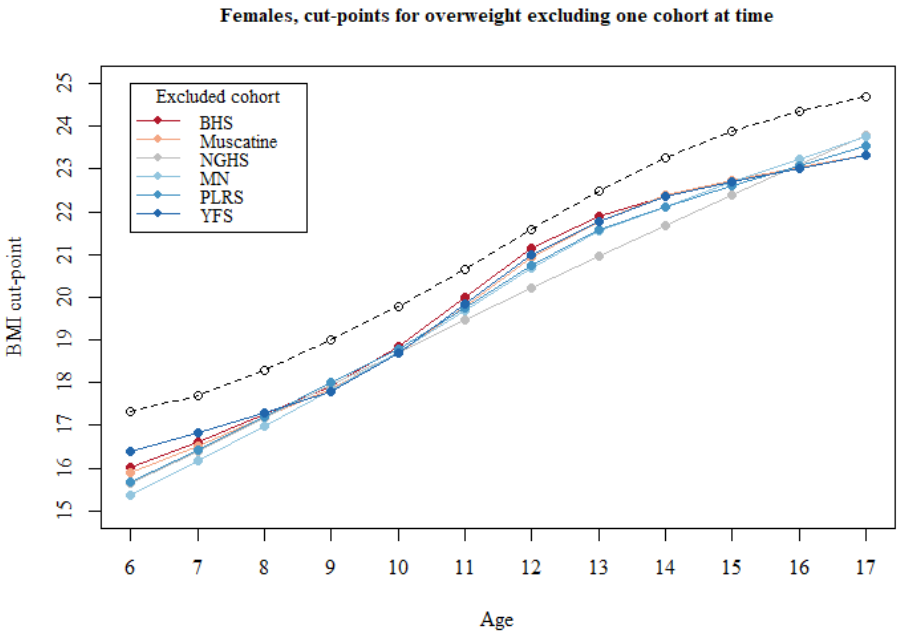
17
Age


Females, cut-points for overweight excluding one cohort at time
Excluded cohort
BHS
Muscatine
NGHS
MN
PLRS
YFS
BMI cut-point
15
16
17
18
19
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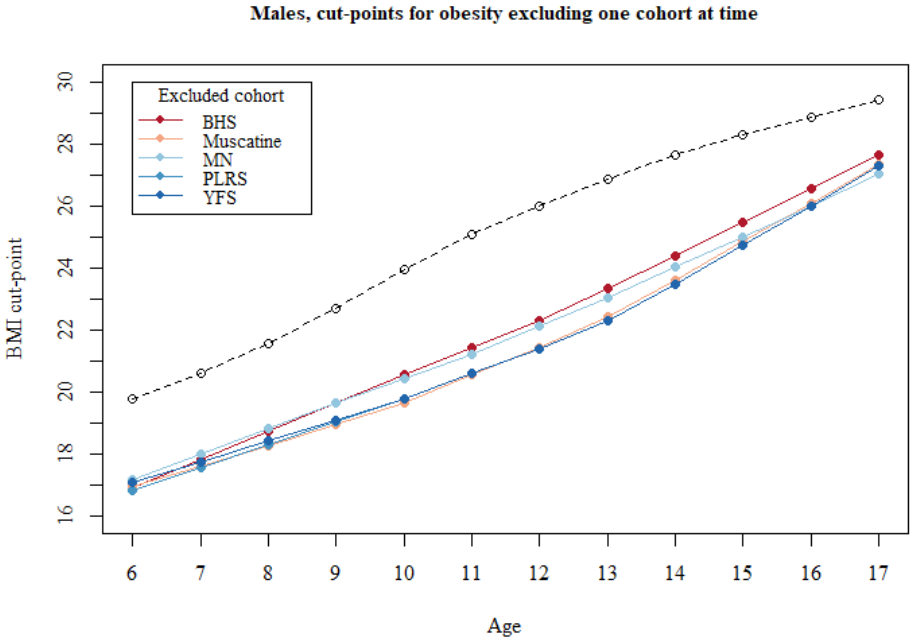
Age


Males, cut-points for obesity excluding one cohort at time
Excluded cohort
BHS
Muscatine
MN
PLRS
YFS
BMI cut-point
16
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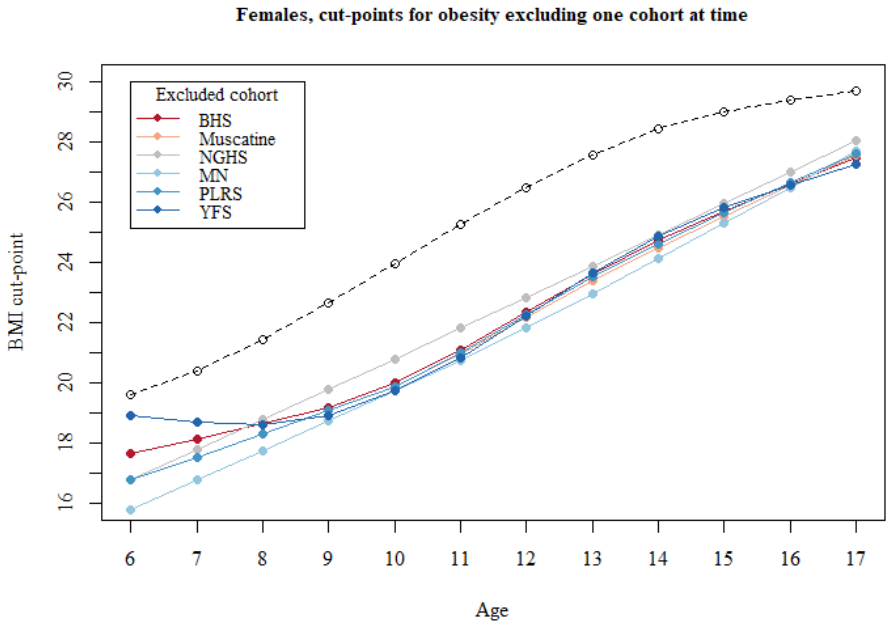
Age


Females, cut-points for obesity excluding one cohort at time
Excluded cohort
BHS
Muscatine
NGHS
MN
PLRS
YFS
BMI cut-point
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Age

Sensitivity analysis with early adulthood and later adulthood responses

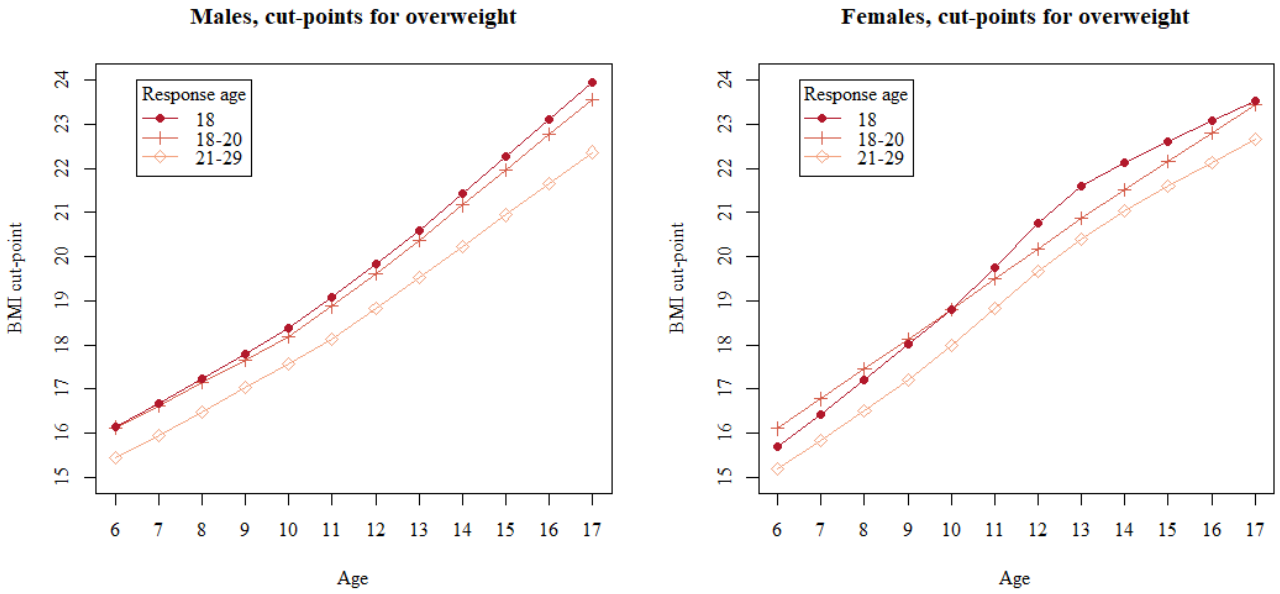
Additional cut-points were calculated using the same methods for the original cut-points. The young adulthood response indicates whether the participant was overweight or obese during the ages 18-20; and the later adulthood response indicates whether the participant was overweight or obese during the ages 21-29.

Supplementary Table 3 Cut-points defined with response being overweight or obese at young adulthood (ages 18-20). In total, N=5,019 participants had BMI measurements in childhood and during ages 18-20.

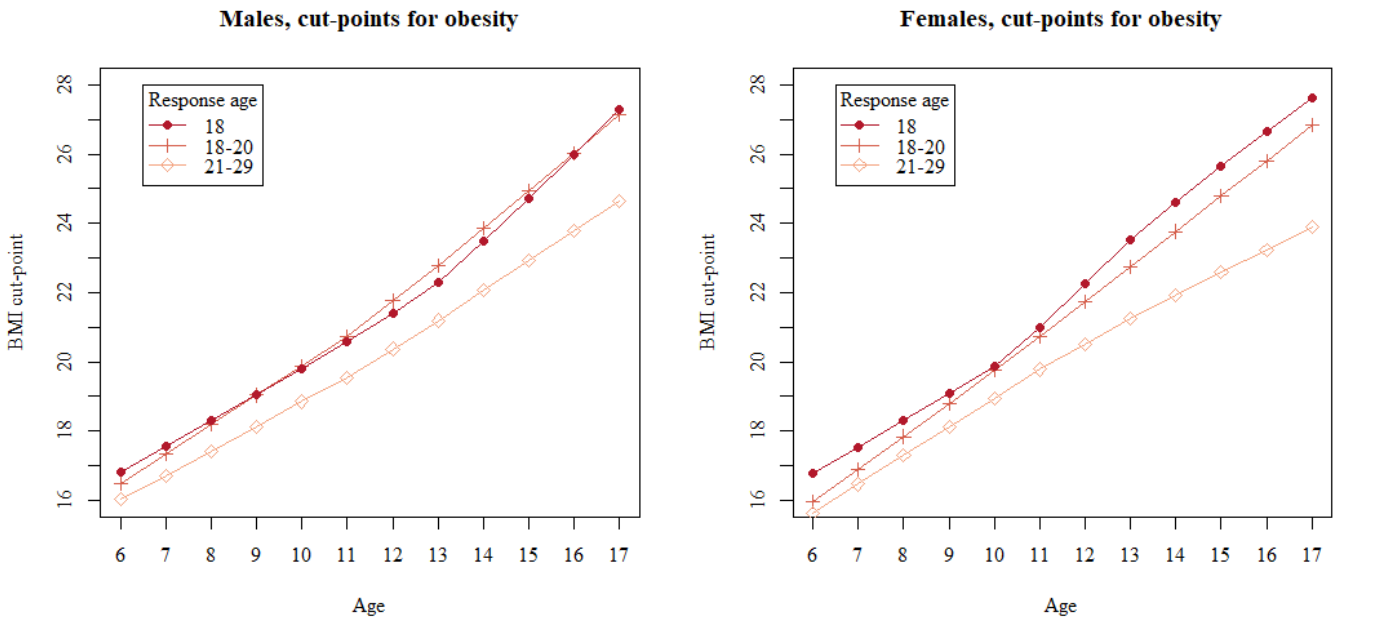
	Age 18-20 Overweight		Age 18-20 Obesity	
Age	**Males**	**Females**	**Males**	**Females**
6	16·12	16·10	16·47	15·96
7	16·62	16·77	17·33	16·89
8	17·14	17·44	18·18	17·83
9	17·66	18·12	19·03	18·79
10	18·19	18·80	19·88	19·75
11	18·87	19·50	20·73	20·73
12	19·62	20·18	21·76	21·74
13	20·37	20·86	22·78	22·75
14	21·16	21·51	23·87	23·77
15	21·96	22·16	24·95	24·79
16	22·76	22·81	26·04	25·81
17	23·56	23·45	27·14	26·83

Supplementary Table 4 Cut-points defined with response being overweight or obese at later young adulthood (ages 21-29). In total, N=9,039 participants had BMI measurements in childhood and during ages 21-29.

	Age 21-29 Overweight		Age 21-29 Obesity	
Age	**Males**	**Females**	**Males**	**Females**
6	15·43	15·18	16·02	15·62
7	15·95	15·84	16·71	16·46
8	16·48	16·51	17·41	17·29
9	17·03	17·20	18·13	18·12
10	17·58	17·98	18·84	18·94
11	18·14	18·82	19·55	19·78
12	18·83	19·66	20·37	20·51
13	19·52	20·39	21·19	21·25
14	20·23	21·04	22·06	21·92
15	20·94	21·59	22·92	22·58
16	21·65	22·15	23·79	23·24
17	22·36	22·67	24·66	23·89



Supplementary Figure 7 Cut-points for overweight for males and females using different response age categories.



Supplementary Figure 8 Cut-points for obesity for males and females using different response age categories.

Supplementary Table 5 Sensitivity, specificity and Youden's J (YJ) index for each of the cut points presented in Supplementary Table 3

	Age 18-20 Overweight						Age 18-20 Obesity					
	Males			Females			Males			Females		
age	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ
6	0.71	0.89	0.60	0.52	0.84	0.36	0.80	0.87	0.67	0.58	0.79	0.38
7	0.64	0.80	0.43	0.69	0.76	0.45	0.80	0.89	0.69	0.65	0.92	0.57
8	0.78	0.73	0.51	0.63	0.86	0.49	0.77	0.85	0.61	0.83	0.79	0.62
9	0.76	0.79	0.55	0.71	0.85	0.56	0.90	0.81	0.70	0.79	0.87	0.66
10	0.83	0.80	0.63	0.78	0.80	0.58	0.83	0.82	0.65	0.87	0.82	0.69
11	0.88	0.75	0.63	0.80	0.81	0.60	0.81	0.94	0.75	0.90	0.80	0.70
12	0.88	0.79	0.67	0.87	0.74	0.61	0.93	0.91	0.84	0.91	0.77	0.68
13	0.82	0.85	0.67	0.81	0.85	0.66	0.90	0.84	0.74	0.83	0.89	0.72
14	0.87	0.84	0.71	0.86	0.84	0.70	0.92	0.88	0.80	0.81	0.91	0.72
15	0.90	0.83	0.73	0.88	0.84	0.72	0.93	0.94	0.87	0.91	0.87	0.79
16	0.86	0.88	0.75	0.85	0.88	0.73	0.98	0.93	0.91	0.88	0.91	0.79
17	0.92	0.88	0.81	0.92	0.85	0.77	1.00	0.96	0.96	0.91	0.94	0.84

Supplementary Table 6 Sensitivity, specificity and Youden's J (YJ) index for each of the cut points presented in Supplementary Table 4

	Age 21-29 Overweight						Age 21-29 Obesity					
	Males			Females			Males			Females		
age	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ
6	0.63	0.74	0.37	0.70	0.66	0.36	0.74	0.68	0.42	0.71	0.68	0.39
7	0.75	0.61	0.36	0.70	0.70	0.40	0.56	0.89	0.45	0.69	0.78	0.47
8	0.58	0.77	0.35	0.73	0.75	0.48	0.76	0.78	0.54	0.78	0.72	0.50
9	0.77	0.66	0.43	0.75	0.72	0.47	0.84	0.69	0.53	0.75	0.80	0.55
10	0.72	0.75	0.47	0.71	0.76	0.47	0.81	0.78	0.59	0.70	0.84	0.55
11	0.72	0.77	0.50	0.69	0.84	0.53	0.88	0.73	0.61	0.77	0.80	0.57
12	0.72	0.80	0.51	0.74	0.79	0.53	0.79	0.81	0.60	0.80	0.78	0.58
13	0.81	0.72	0.53	0.76	0.79	0.56	0.81	0.79	0.60	0.81	0.78	0.59
14	0.73	0.82	0.55	0.80	0.79	0.58	0.87	0.78	0.65	0.79	0.83	0.62
15	0.80	0.76	0.56	0.78	0.79	0.57	0.81	0.83	0.64	0.84	0.79	0.64
16	0.81	0.78	0.59	0.77	0.79	0.56	0.85	0.82	0.67	0.85	0.81	0.66
17	0.76	0.82	0.58	0.76	0.85	0.60	0.84	0.85	0.68	0.85	0.84	0.69

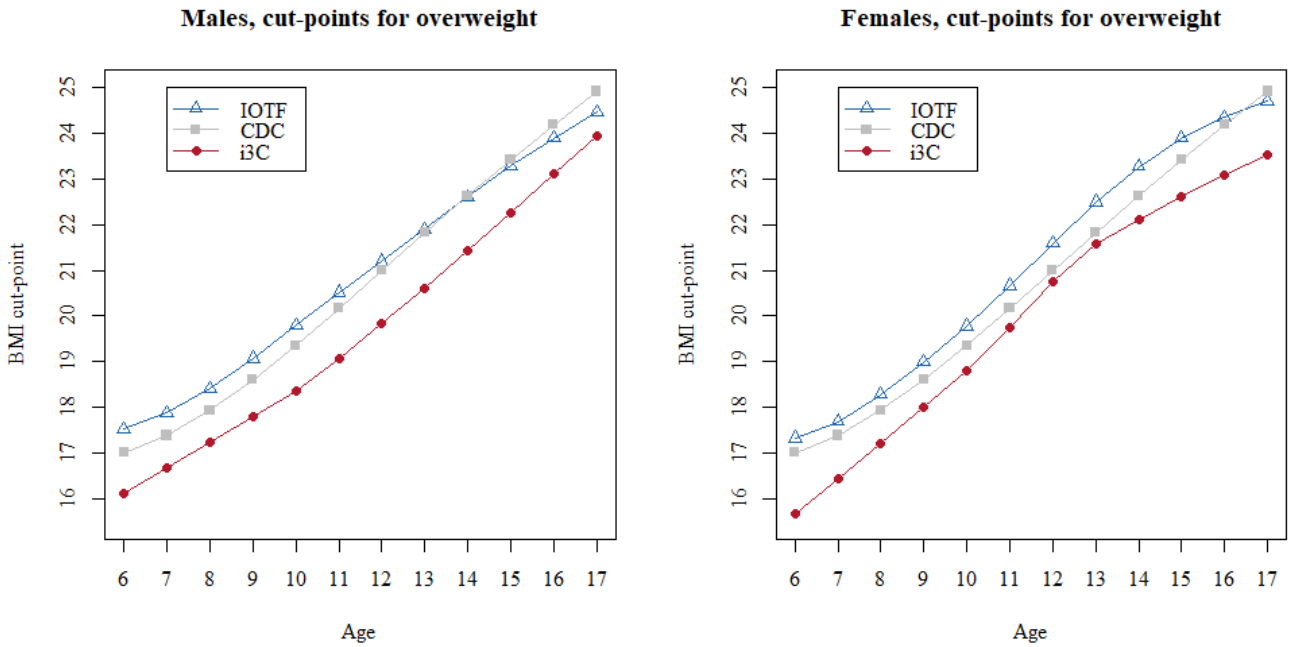
Additional comparisons in the STRIP Study validation data between the i3C and CDC cut-points

The cut-points defined based on CDC's percentile approach are also higher than the i3C cut-points. We compared the predictive ability of these cut-points to those derived from the longitudinal i3C data using ROC curves. The areas under the ROC curves were higher for the i3C cut-points. The areas under the ROC curves for both sets of cut-points are presented in supplementary Tables 8 and 9 with the p-values for comparisons between i3C cut-points and CDC cut-points.
The i3C cut-points have larger AUROCs in all of the analyses, even though the differences between the two cut-points are mostly insignificant.

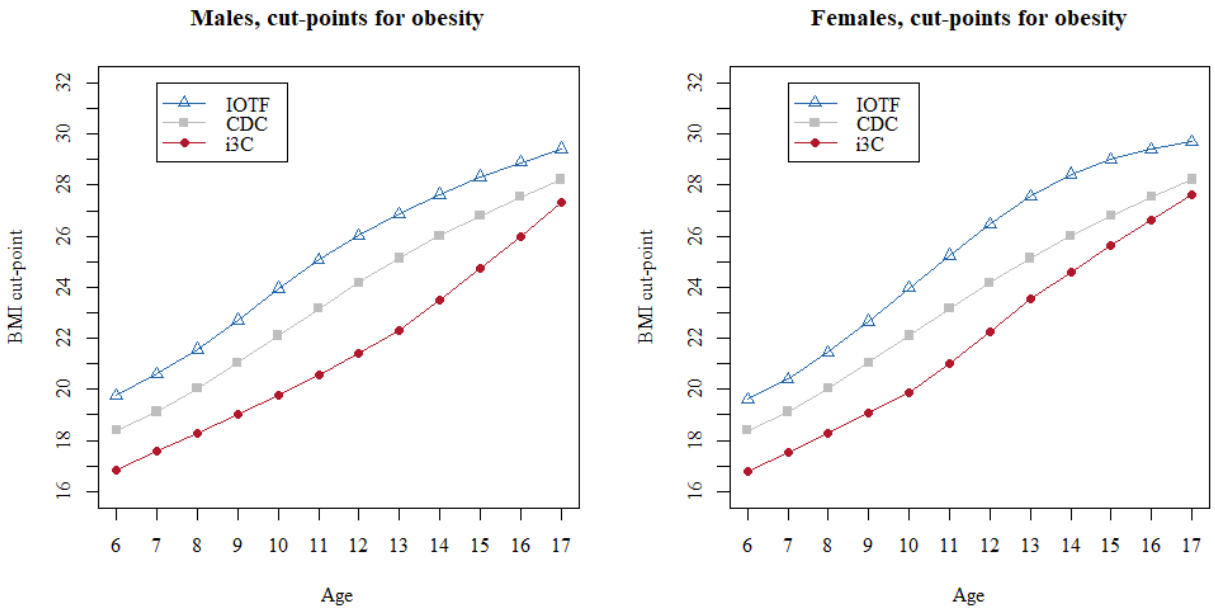
Supplementary Table 7 CDC cut-points for overweight and obesity

	Overweight cut-point CDC		Obesity cut-point CDC	
Age years (months)	**Males**	**Females**	**Males**	**Females**
6 (72mo)	17·00	17·08	18·39	18·80
7 (84mo)	17·38	17·60	19·12	19·64
8 (96mo)	17·93	18·29	20·03	20·65
9 (108mo)	18·60	19·08	21·05	21·77
10 (120mo)	19·36	19·95	22·11	22·93
11 (132mo)	20·16	20·83	23·17	24·09
12 (144mo)	20·99	21·72	24·19	25·21
13 (156mo)	21·82	22·54	25·14	26·26
14 (168mo)	22·63	23·31	26·01	27·22
15 (180mo)	23·42	24·02	26·81	28·09
16 (192mo)	24·18	24·64	27·53	28·88
17 (204mo)	24·91	25·18	28·22	29·60

Note: Since the CDC obesity cut-points are defined monthly for mid-month points, the final values for cut-points for exact months were calculated as the mean of two midpoints. For example, the cut-point for 72 months was calculated from the mean of 71.5 months and 72.5 months.



Supplementary Figure 9 Comparison of CDC, IOTF and i3C cut-points for overweight



Supplementary Figure 10 Comparison of CDC, IOTF and i3C cut-points for obesity

Supplementary Table 8 The performance of i3C cut-points as presented in Table 3 and CDC cut-points for prediction of overweight in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC CDC [95% Wald CI]	p
6	0·75 [0·70 ; 0·80]	0·69 [0·63 ; 0·76]	0·08
7	0·73 [0·67 ; 0·79]	0·72 [0·65 ; 0·78]	0·49
8	0·78 [0·72 ; 0·84]	0·76 [0·69 ; 082]	0·29
9	0·78 [0·72 ; 0·84]	0·71 [0·65 ; 0·77]	0·01
10	0·79 [0·73 ; 0·84]	0·75 [0·68 ; 0·81]	0·08
11	0·80 [0·75 ; 0·86]	0·78 [0·72 ; 0·84]	0·26
12	0·78 [0·73 ; 0·84]	0·75 [0·69 ; 0·82]	0·14
13	0·81 [0·75 ; 0·86]	0·75 [0·68 ; 0·81]	0·02
14	0·81 [0·75 ; 0·86]	0·79 [0·73 ; 0·85]	0·41
15	0·84 [0·79 ; 0·90]	0·80 [0·74 ; 0·86]	0·06
16	0·87 [0·83 ; 0·92]	0·82 [0·76 ; 0·87]	0·02
17	0·88 [0·84 ; 0·93]	0·83 [0·77 ; 0·89]	0·03

Abbreviations: STRIP = The Special Turku Coronary Risk Factor Intervention Project, CDC = Centers for Disease Control and Prevention, i3C = International Childhood Cardiovascular Cohort, CI = Confidence Interval, AUROC = Area Under Receiver Operating Curve

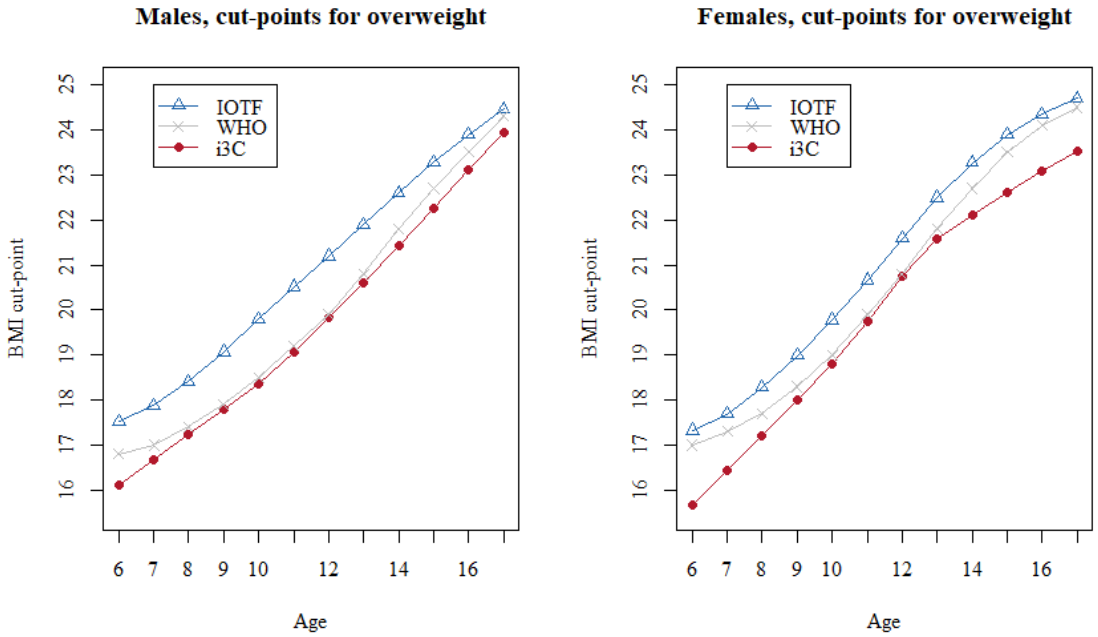
Supplementary Table 9 The performance of i3C cut-points as presented in Table 4 and CDC cut-points for prediction of obesity in adulthood in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC CDC [95% Wald CI]	p
6	0·88 [0·83 ; 0·94]	0·70 [0·58 ; 0·82]	0·002
7	0·87 [0·80 ; 0·95]	0·66 [0·55 ; 0·78]	0·0004
8	0·84 [0·75 ; 0·93]	0·65 [0·54 ; 0·76]	0·002
9	0·85 [0·76 ; 0·94]	0·73 [0·62 ; 0·85]	0·04
10	0·86 [0·78 ; 0·93]	0·74 [0·62 ; 0·86]	0·05
11	0·85 [0·77 ; 0·94]	0·80 [0·69 ; 0·91]	0·30
12	0·86 [0·78 ; 0·95]	0·83 [0·72 ; 0·94]	0·44
13	0·85 [0·76 ; 0·95]	0·86 [0·76 ; 0·96]	0·72
14	0·90 [0·82 ; 0·98]	0·88 [0·78 ; 0·98]	0·62
15	0·89 [0·80 ; 0·98]	0·80 [0·68 ; 0·92]	0·07
16	0·88 [0·79 ; 0·98]	0·81 [0·70 ; 0·92]	0·11
17	0·86 [0·76 ; 0·96]	0·76 [0·64 ; 0·88]	0·04

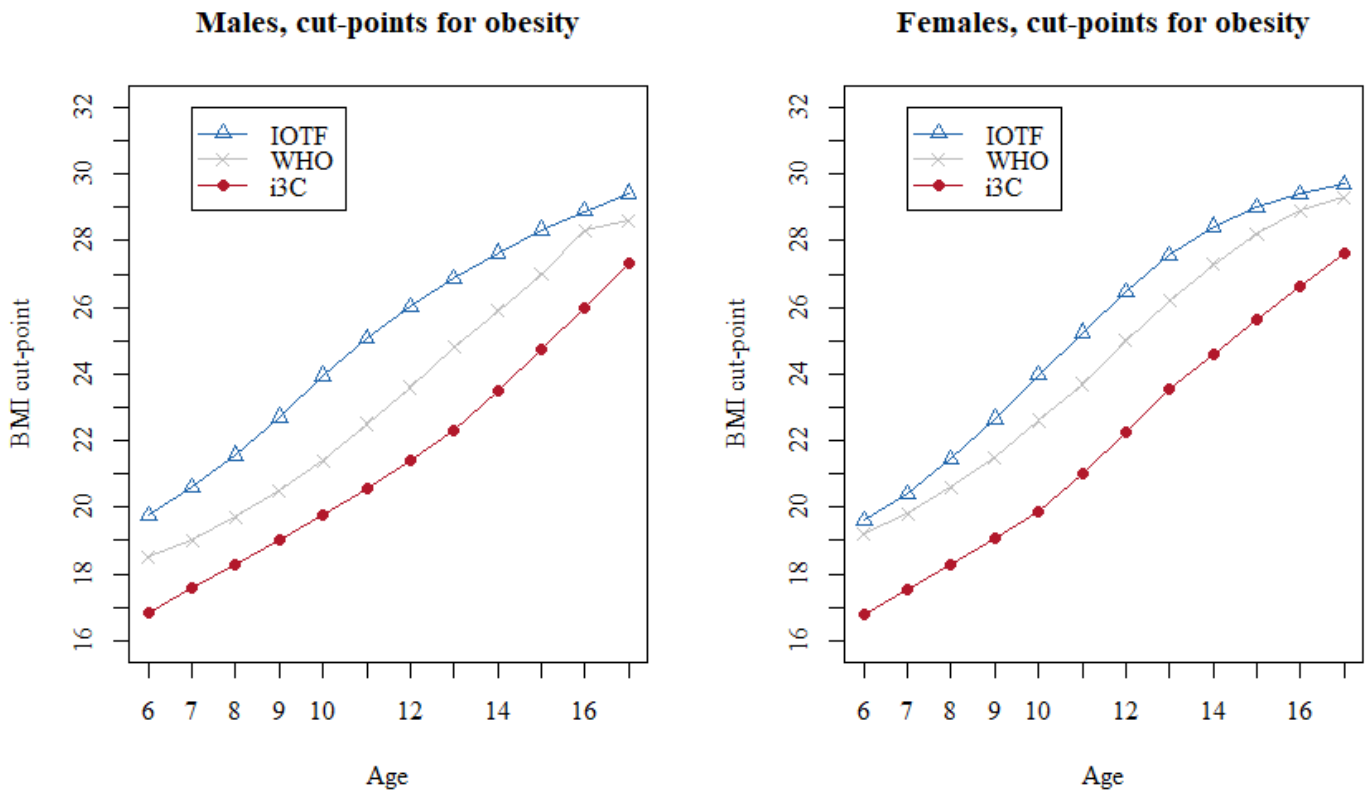
Abbreviations: STRIP = The Special Turku Coronary Risk Factor Intervention Project, CDC = Centers for Disease Control and Prevention, i3C = International Childhood Cardiovascular Cohort, CI = Confidence Interval, AUROC =Area Under Receiver Operating Curve

Additional comparisons in the STRIP Study validation data between the i3C and WHO cut-points

The cut-points defined by WHO are higher that the i3C cut-points for obesity and slightly higher or similar to the i3C cut-points for overweight. These cut-points are presented in Supplementary Figures 11 and 12, with additional reference line to the IOTF cut-points.
Similarly as for CDC, we compared the predictive abilities of WHO and i3C cut-points using ROC curves. These comparisons are presented in Supplementary Tables 10 and 11. The differences between WHO and i3C cut-points are not as remarkable as the differences between i3C cut-points and IOTF or CDC cut-points.



Supplementary Figure 11 Comparison of i3C, IOTF and WHO cut-points for overweight



Supplementary Figure 12 Comparison of i3C, IOTF and WHO cut-points for obesity

Supplementary Table 10 The performance of i3C cut-points as presented in Table 3 and WHO cut-points for prediction of overweight in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC WHO [95% Wald CI]	p -value
6	0·75 [0·70 ; 0·80]	0.72 [0.66 ; 0.78]	0.36
7	0·73 [0·67 ; 0·79]	0.76 [0.70 ; 0.82]	0.003
8	0·78 [0·72 ; 0·84]	0.77 [0.71 ; 0.82]	0.39
9	0·78 [0·72 ; 0·84]	0.75 [0.69 ; 0.81]	0.10
10	0·79 [0·73 ; 0·84]	0.78 [0.72 ; 0.84]	0.53
11	0·80 [0·75 ; 0·86]	0.80 [0.74 ; 0.85]	0.50
12	0·78 [0·73 ; 0·84]	0.79 [0.73 ; 0.85]	0.05
13	0·81 [0·75 ; 0·86]	0.81 [0.75 ; 0.86]	0.95
14	0·81 [0·75 ; 0·86]	0.83 [0.77 ; 0.88]	<0.001
15	0·84 [0·79 ; 0·90]	0.82 [0.76 ; 0.87]	0.13
16	0·87 [0·83 ; 0·92]	0.83 [0.78 ; 0.89]	0.058
17	0·88 [0·84 ; 0·93]	0.88 [0.83 ; 0.93]	0.63

Abbreviations: STRIP = The Special Turku Coronary Risk Factor Intervention Project, i3C = International Childhood Cardiovascular Cohort, WHO=World Health Organization, CI = Confidence Interval, AUROC = Area Under Receiver Operating Curve

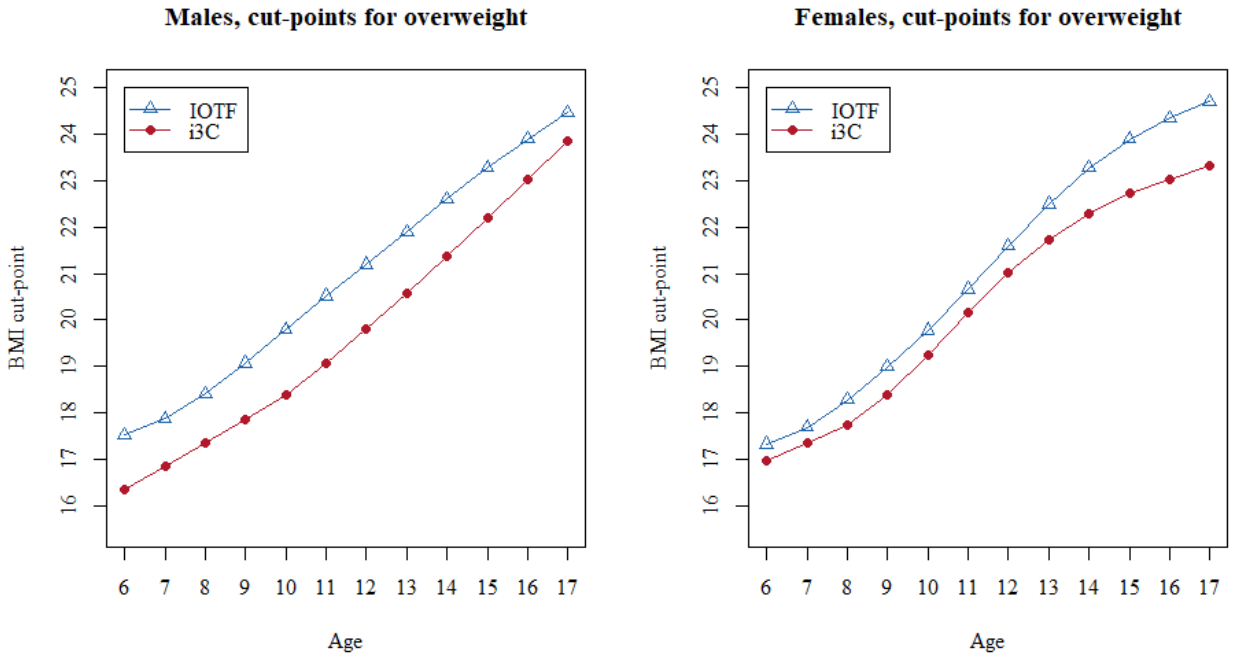
Supplementary Table 11 The performance of i3C cut-points as presented in Table 4 and WHO cut-points for prediction of obesity in adulthood in the STRIP Study population

Age	AUROC i3C [95% Wald CI]	AUROC WHO [95% Wald CI]	p-value
6	0·88 [0·83 ; 0·94]	0.68 [0.56 ; 0.79]	0.0007
7	0·87 [0·80 ; 0·95]	0.67 [0.56 ;0.78]	0.0005
8	0·84 [0·75 ; 0·93]	0.71 [0.59 ;0.82]	0.02
9	0·85 [0·76 ; 0·94]	0.82 [0.70 ;0.93]	0.45
10	0·86 [0·78 ; 0·93]	0.76 [0.64 ;0.88]	0.09
11	0·85 [0·77 ; 0·94]	0.83 [0.72 ;0.93]	0.53
12	0·86 [0·78 ; 0·95]	0.85 [0.75 ;0.95]	0.75
13	0·85 [0·76 ; 0·95]	0.86 [0.76 ; 0.96]	0.75
14	0·90 [0·82 ; 0·98]	0.88 [0.78 ; 0.98]	0.60
15	0·89 [0·80 ; 0·98]	0.80 [0.68 ; 0.92]	0.07
16	0·88 [0·79 ; 0·98]	0.79 [0.67 ; 0.90]	0.05
17	0·86 [0·76 ; 0·96]	0.79 [0.67 ; 0.90]	0.10

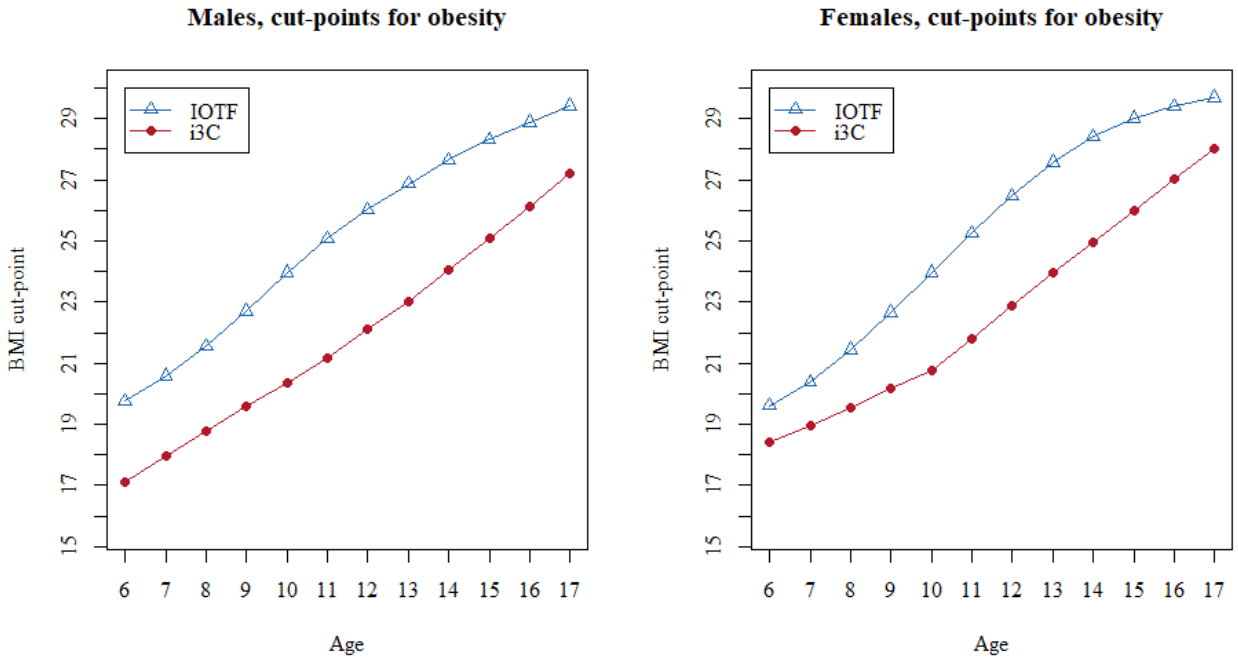
Abbreviations: STRIP = The Special Turku Coronary Risk Factor Intervention Project, i3C = International Childhood Cardiovascular Cohort, WHO=World Health Organization, CI = Confidence Interval, AUROC =Area Under Receiver Operating Curve

Additional analyses adjusting for birth year

As an additional sensitivity analysis, we adjusted the cut-point analyses for birthyear. Resulting cut-points are presented in supplementary Figures 13 and 14 with comparison to the IOTF cut-points.



Supplementary Figure 13 i3C cut-points for overweight adjusted for birth year compared to the IOTF cut-points



Supplementary Figure 14 i3C cut-points for obesity adjusted for birth year compared to the IOTF cut-points

Supplementary Table 12 Sensitivity, specificity and Youden's J index for each of the cut points presented in Table 2

	Age 18 Overweight						Age 18 Obesity					
	Males			Females			Males			Females		
age	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ	Sensitivity	Specificity	YJ
6	0.74	0.89	0.63	0.83	0.65	0.48	1.00	0.80	0.80	0.71	0.76	0.48
7	0.68	0.78	0.46	0.72	0.76	0.47	0.81	0.88	0.68	0.73	0.91	0.64
8	0.75	0.80	0.55	0.67	0.82	0.49	0.83	0.91	0.74	0.89	0.78	0.68
9	0.84	0.73	0.57	0.83	0.75	0.58	0.88	0.95	0.83	0.83	0.86	0.68
10	0.89	0.77	0.66	0.74	0.90	0.64	0.82	0.86	0.68	0.92	0.82	0.73
11	0.90	0.81	0.71	0.79	0.86	0.65	0.87	0.97	0.84	0.95	0.81	0.76
12	0.90	0.80	0.70	0.81	0.83	0.64	0.92	0.92	0.84	0.91	0.85	0.76
13	0.88	0.84	0.71	0.86	0.83	0.69	0.92	0.86	0.78	0.89	0.88	0.77
14	0.89	0.84	0.73	0.88	0.87	0.74	0.93	0.87	0.80	0.86	0.92	0.78
15	0.91	0.82	0.73	0.87	0.89	0.76	0.99	0.91	0.90	0.91	0.94	0.85
16	0.91	0.86	0.77	0.92	0.89	0.81	0.98	0.93	0.91	0.91	0.94	0.85
17	0.92	0.93	0.84	0.95	0.88	0.83	1.00	0.97	0.97	0.95	0.94	0.89

Supplementary Table 13 Comparison of participants and non-participants in the i3C study

	Response at age 18			Response at ages 18-20			Response at ages 21-29		
	Participants	Non-participants	p	Participants	Non-participants	p	Participants	Non-participants	
N	3779	37307		5019	36067		9039	32047	
% females	56.2	49.7	<0.001	57.3	49.3	<0.001	57.3	48.3	<0.001
Age, mean (SD)	10.6 (2.9)	9.4 (3.3)	<0.001	10.5 (3.0)	9.4 (3.3)	<0.001	10.0 (3.4)	9.4 (3.3)	<0.001
BMI, adjusted for age and sex, mean* (SE)	17.7 (0.05)	18.0 (0.02)	<0.001	17.8 (0.04)	18.0 (0.02)	0.0004	17.9 (0.02)	18.0 (0.03)	0.24

Abbreviation: i3C = International Childhood Cardiovascular Cohort

* LSMEANS adjusted for age and sex.