**Age-specific estimates and comparisons of youth tri-ponderal mass index and body mass index in predicting adult obesity-related outcomes**

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**Authors' Contributions**

Dr Wu, Dr Magnussen and Dr Pahkala conceptualized and designed the study, performed data analysis, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr Buscot Dr Juonala, and Dr Sabin were involved in the study design, reviewed and revised the manuscript.

Dr Niinikoski, Dr Rovio, Dr Jula and Dr Rönnemaa were responsible for data collection and management and reviewed and revised the manuscript.

Dr Viikari coordinated and supervised data collection and management, contributed to the initial design of the STRIP, and reviewed and revised the manuscript.

Dr Raitakari leads the STRIP and contributed to obtaining funding and to the study design, coordinated and supervised data collection and management, and reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

**Key words:** Youth; body mass index, tri-ponderal index; adult outcomes; cohort

**ABSTRACT**

**Objectives** To estimate and compare tri-ponderal mass index (TMI) and body mass index (BMI) at each age from childhood to young adulthood in the prediction of adulthood obesity-related outcomes.

**Study Design** Participants of this observational study (n=432) were from a 20-year infancy-onset randomized atherosclerosis prevention trial. BMI and TMI were calculated using weight and height measured annually from participants between ages 2 and 20 years. Outcomes were aortic intima-media thickness (at the age of 15, 17 or 19 years), impaired fasting glucose and elevated insulin levels, Homeostasis model assessment of insulin resistance index, serum lipids, and hypertension at the age of 20 years. Poisson regressions, Pearson's correlation, logistic regression and area under the curve (AUC) were used to estimate and/or compare associations and predictive utilities between BMI and TMI with all outcomes.

**Results** The associations and predictive utilities of BMI and TMI with all outcomes were stronger at older ages. BMI had significantly stronger correlations than TMI with insulin (at age 16), systolic blood pressure (age 5 to 20), and triglycerides (age 18). BMI had significantly higher predictive utilities than TMI for insulin resistance (at age 14 to 16; difference in AUC=0.018 to 0.024), elevated insulin levels (age 14 to 16; difference in AUC=0.018 and 0.025) and hypertension (age 16 to 20; difference in AUC=0.017 to 0.022) but they were similar for other outcomes.

**Conclusions** TMI is not superior to BMI at any ages from childhood to young adulthood in the prediction of obesity-related outcomes in young adulthood.

## Introduction

Obesity-related diseases represent a major health burden worldwide[1, 2]. The burden continues to rise, largely due to the escalating rates of overweight and obesity, particularly in children and adolescents (herein referred to as youth)[3]. Screening of youth who are overweight or obese is critically important for implementing early interventions to reduce the risk of developing many obesity-related conditions later in life[4].

Body mass index (BMI) is widely used in clinical guidelines for the screening of youth obesity[4, 5]. However, BMI has limitations in the estimation of youth adiposity because weight scales better with height powers of greater than two during this period of rapid growth. As a result, tri-ponderal mass index (TMI), mass divided by height cubed, has been proposed as an alternate to BMI. In support of this, a recent study has shown that TMI had better accuracy in estimating body fat levels than BMI in adolescents[6]. However, whether youth TMI outperforms BMI in the context of predicting important obesity-related outcomes in adulthood, such as type 2 diabetes (T2D) and hypertension, has remained obscure. Moreover, age may play an important role in estimating the utility of these two adiposity measures in predicting adult outcomes because TMI and BMI changes in a largely different pattern with age[6]. Therefore, using data from a 20-year infancy-onset cohort, we estimated and compared BMI and TMI at each age from childhood to young adulthood in the prediction of adulthood obesity-related outcomes.

## Subjects and methods

### *Participants*

Participants of this study were from the ongoing Special Turku Coronary Risk Factor Intervention Project (STRIP), which is an infancy-onset randomized controlled trial of dietary counseling that aimed to reduce the risk of atherosclerosis. Details of the STRIP have been

described elsewhere[7, 8]. Briefly, at baseline (February 1990 to June 1992) the families of 5-month-old infants were recruited from well-baby clinics in Turku, Finland. These families received detailed information about STRIP when their infants were 6 months old. A total of 1062 infants participated in the study (56.5% of the eligible age cohort) and were randomly assigned to a dietary intervention group (N = 540; 256 girls) or a control group (N = 522; 256 girls) when they were aged 7 months. During the study visits, all children met with a nutritionist and a pediatrician or a nurse. The children in the intervention group received individualised dietary counseling at 1- to 3-month intervals until the age of 2 years and biannually thereafter until 20 years of age. The children in the control group came to the study visits biannually until the age of 7 years and annually thereafter until the age of 20 years. During the study visits, the control group received basic health education similar to the education routinely given at Finnish well-baby clinics and by school health care. Three participants who had type 1 diabetes were excluded in this study. The present observational analysis included 432 participants who had height and weight measured at the age of 2 and 20 years and at least one obesity-related outcome (see below for details) at age 20 years (at age 15, 17 or 19 for a*ortic intima-media thickness (aIMT)*). The number of participants for analyses for each outcome at each age varied from 403 to 423. A flow chart of participation is given in **Figure 1** (online). The study was approved by the Joint Commission on Ethics of the Turku University and the Turku University Central Hospital. Written informed consent was obtained from the parents in the beginning of the study and from the adolescents at 15 and 18 years of age.

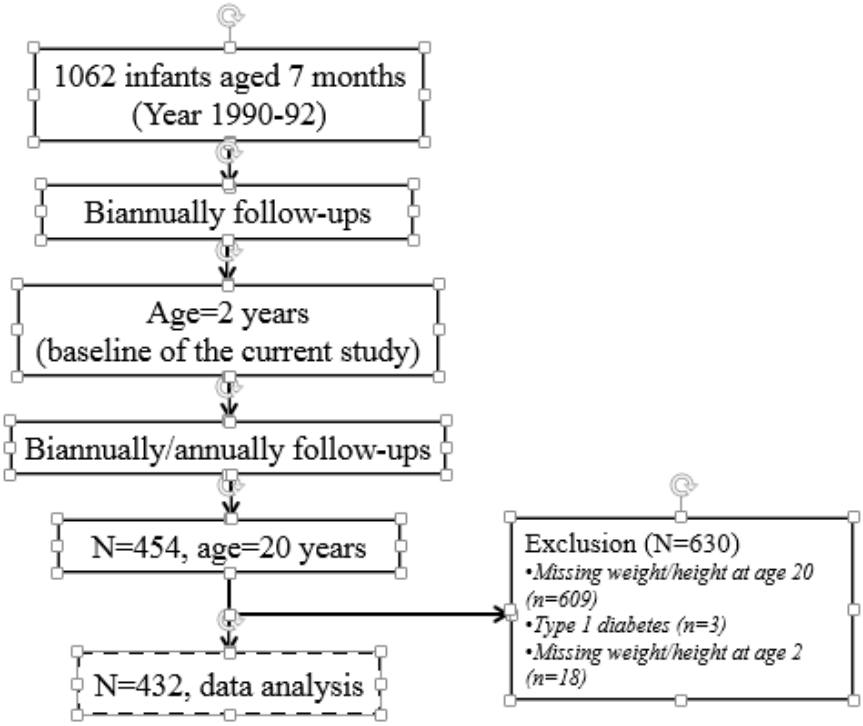


Figure 1.

***Obesity-related outcomes (measured at age 20 unless otherwise stated)***

*aIMT*

aIMT at the age 15, 17 and 19 years was assessed by non-invasive high-resolution ultrasound using highly reproducible standardised techniques as previously used in our laboratory[9, 10]. The latest available aIMT values were used for analyses (93% from age 19 years). High aIMT was defined as having a value ≥ age- and sex-specific 90$^{th}$ percentile.

*Blood pressure*

Sitting blood pressure (BP) (systolic and diastolic) was measured after an appropriate rest of at least 15 minutes using an oscillometric non-invasive BP monitor (Criticon Dinamap Compact T). Proper cuff size according to the size of the participant's right arm was used.

The accuracy of the device was regularly checked against a mercury manometer. BP was measured twice and the average was used in our analysis. According to the latest American College of Cardiology guideline, hypertension was defined as systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg.

*Serum lipids, fasting glucose and insulin*

Fasting serum total and high-density lipoprotein cholesterol (HDL-C) and triglyceride levels/concentrations were measured as previously described[11]. The Friedewald formula was used to calculate serum low-density lipoprotein cholesterol (LDL-C) level/concentration[12]. Low HDL-C, high LDL-C and high triglycerides were defined using cut-offs of <40 mg/dl (1.03 mmol/l), ≥160 mg/dl (4.14 mmol/l) and ≥200 mg/dl (2.26 mmol/l), respectively. As a small number of participants had high LDL-C (n=8), a cut-off of ≥age- and sex-specific 75$^{th}$ percentile was used to define high LDL-C for analyses in the present study.

The fasting venous blood samples were also used to determine serum glucose and insulin levels. The samples were centrifuged immediately, with 15 µl of the enzyme inhibitor Antagosan added to 0.5 ml serum insulin sample. Samples were stored frozen until analysed. Serum insulin levels were measured with a microparticle enzyme immunoassay (Insulin IMX system reagent, Abbott, [Chicago, IL], interassay coefficient of variation [CV] 6.5%) or with a chemiluminescent microparticle immunoassay (ARCHITECT insulin assay, Abbott, USA, interassay CV 1.8%). A correction of analytical level between the methods was used as reported previously[7]. Serum glucose was measured by a hexokinase method (Glucose Olympus System Reagent, Olympus, Ireland, interassay CV 1.8%). Insulin sensitivity was estimated by Homeostatic Model Assessment for Insulin Resistance (HOMA-IR, fasting insulin mU/mL × [fasting glucose (mmol/L)/22.5])[13]. The laboratory of the National Public Health Institute in Turku, Finland performed all serum analyses.

Impaired fasting glucose (IFG) was defined as having a fasting plasma glucose ≥5.6 mmol/L but ≤6.9 mmol/L and T2D as ≥7 mmol/L as well as being diagnosed by physician[14]. Insulin resistance was defined using a previous WHO study where HOMA-IR was ≥ the 75$^{th}$ sex-specific percentile[15]. For consistency, high fasting insulin was dichotomized using the 75th sex-specific percentile.

**Weight and height from the age 2 to 20 years**

Weight was measured annually from the age 2 to 20 years using an S10 electronic scale (Soehnle, Murrhardt, Germany) to the nearest 0.1 kg and height to the nearest 0.1 cm using a Harpender stadiometer (Holtain, Crymych, U.K.). BMI at each age was calculated as weight divided by height squared (kg/m$^2$) and TMI as weight divided by height cubed (kg/m$^3$).

***Statistical analysis***

Mean (standard deviation) or median (interquartile range) was used to describe participants' characteristics at the age of 2 and 20 years. As per previous studies in youth[6, 16], BMI and TMI were standardised by sex for each age (z-scores) for analyses. Univariable Poisson regressions were used to estimate the relative risk (RR) for associations between BMI and TMI z-scores at each age from 2 to 20 years old with all outcomes at 20 years (at the age of 15, 17 or 19 for aIMT). Pearson's correlation coefficients were estimated for BMI and TMI z-scores with all outcomes, which were compared based on Steiger's Z-test using a STATA command 'cortesti' when one or both coefficients at each age were significant[17]. Logistic regression models and area under receiver-operating characteristic curve values were used to estimate and compare the area under the curve (AUC) of BMI and TMI with these outcomes[18]. BMI and TMI did not differ at any ages in the STRIP study groups (intervention/control); therefore, it was not included in the model. Possible effect modification of the STRIP study group and sex for BMI and TMI were analysed by adding an

interaction term (study group/sex*BMI/TMI) in the models separately for each outcome. Stratified analyses by the study groups and sex were conducted for each variable showing significant interaction. Sensitivity analyses were performed for triglyceride and HDL-C by using different cut-offs: ≥age- and sex-specific 75th percentile for high triglyceride and ≤ age- and sex-specific 25th percentile for low HDL-C. Sensitivity analyses were also performed by repeating previous Poisson regressions using inverse probability weighting to account for missing data as previously performed[19], where data were assumed to be missing at random. STATA 15.1 was used for all analyses and a two-tailed p-value of 0.05 was considered statistically significant.

**Results**

The prevalence of outcomes at age 20 years was 4.7% (n=20) for IFG, 25.7% (n=111) for hypertension, 17.1% (n=73) for low HDL-C, and 3.5% (n=15) for high triglyceride levels. None developed type 2 diabetes. Participants' characteristics at the age of 20 years for females and males are shown in **Table 1**. Mean values

**Table 1** Characteristics of the study population at the age of 20 years stratified by sex

| | Females | Males |
|---|---|---|
| Characteristics | n=224 | n=208 |
| Weight (kg) | 64.0 (12.4) | 75.2 (12.4) |
| Height (cm) | 167.5 (6.0) | 181.0 (6.4) |
| Body mass index (kg/m$^2$) | 22.8 (4.2) | 22.9 (3.6) |
| Tri-ponderal mass index (kg/m$^3$) | 13.6 (2.6) | 12.7 (2.1) |
| Glucose (mmol/L) | 4.7 (4.5 to 5.0) | 4.9 (4.7 to 5.1) |
| Insulin (μU/L) | 6.3 (4.9 to 8.7) | 6.3 (4.9 to 8.3) |
| HOMA-IR | 1.32 (1.00 to 1.88) | 1.39 (1.06 to 1.82) |
| Systolic blood pressure (mmHg) | 115 (12) | 127 (12) |
| Diastolic blood pressure (mmHg) | 66 (8) | 66 (8) |
| HDL cholesterol (mg/dl) | 1.50 (0.33) | 1.18 (0.25) |
| LDL cholesterol (mg/dl) | 2.64 (0.69) | 2.46 (0.65) |
| Triglycerides (mg/dl) | 1.0 (0.7 to 1.4) | 0.9 (0.7 to 1.3) |
| aIMT (mm)[a] | 0.509 (0.094) | 0.517 (0.101) |

Data are mean (SD) or median (interquartile range); aIMT, aortic intima-media thickness; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
[a] based on the latest available values from age 15 (n=3), 17 (n=27) and 19 years (n=394).

and 95% confidence intervals for BMI and TMI from the age of 2 to 20 years are shown in **Figure 2**. BMI had a slight decline from the age of 2 to 5 years but increased rapidly thereafter until the age of 20 years. In contrast, the mean levels of TMI declined until about age 10 years and plateaued afterwards.

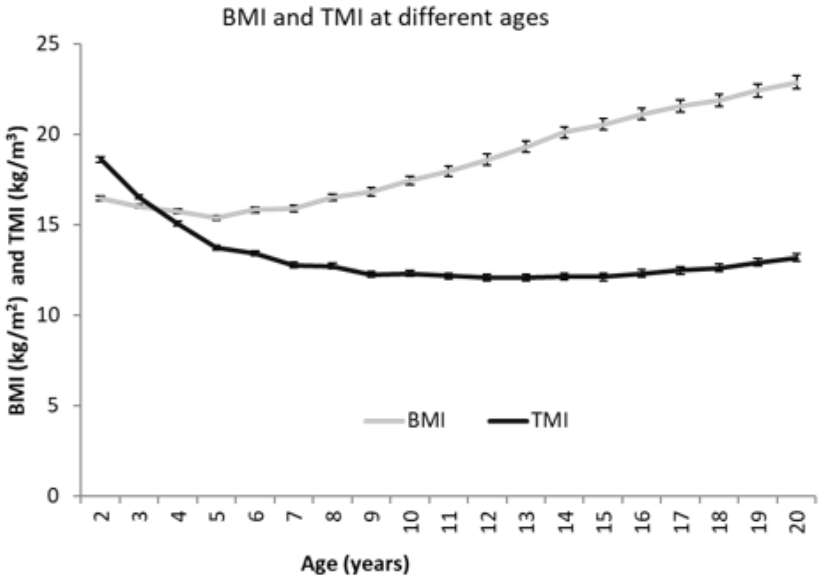


Figure 2.

The associations of BMI and TMI with all outcomes were overall stronger at older ages and became statistically significant at age 3 to 16 years depending on the outcome examined

(**Figure 3; online**). The strongest associations for both BMI and TMI were observed with values measured at the age of 20 years for all outcomes except for aIMT and high triglyceride levels, which had the strongest associations observed from measurements at age 8 and 9 years, respectively (Figure 3; online). Overall, correlation coefficients increased and became significant with increased age (Table 2; online). BMI had significantly stronger correlations than TMI with insulin (age 16), systolic blood pressure (age 5 to 20), and triglycerides (age 18) (Table 2; online).

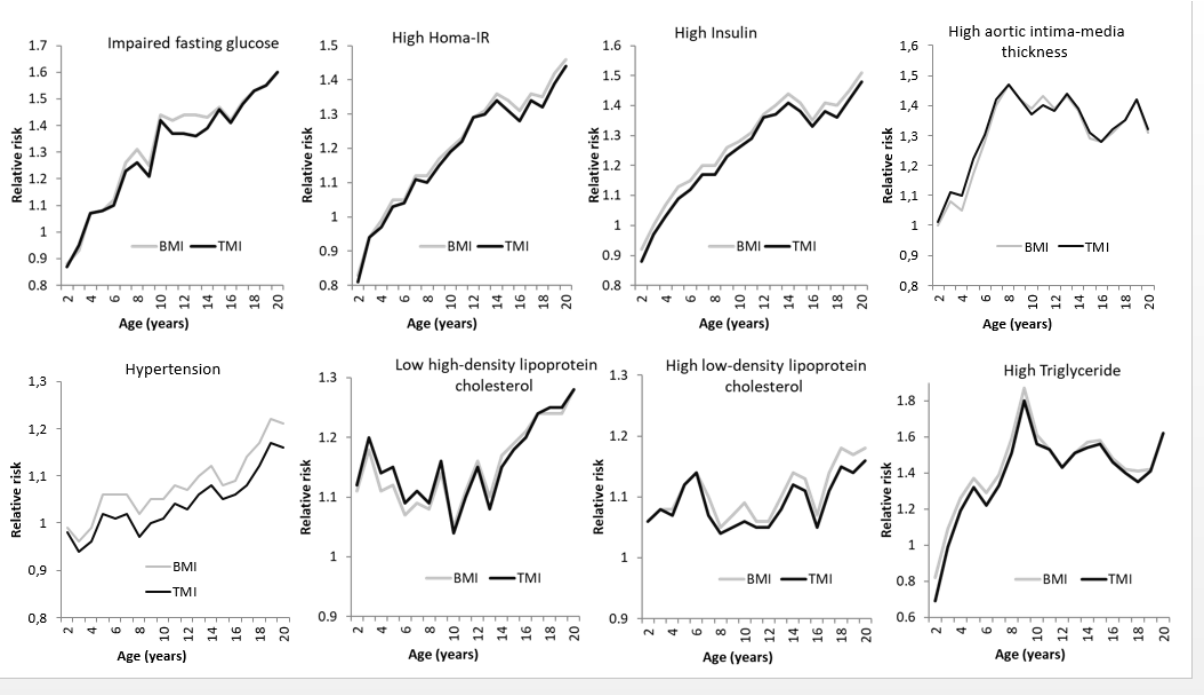


Figure 3:

The predictive utilities of both BMI and TMI were also overall larger at older ages (**Figure 4** and **Table 3; online**). BMI had significantly higher predictive utilities than TMI for insulin resistance (at age 14 to 16; difference in AUC=0.018 to 0.024), elevated insulin levels (age 14 to 16; difference in AUC=0.018 and 0.025) and hypertension (age 16 to 20; difference in

AUC=0.017 to 0.022) but they were similar for all other outcomes (**Table 3; online**).

Number of participants for above analyses are shown in **Table 4 (online)**.

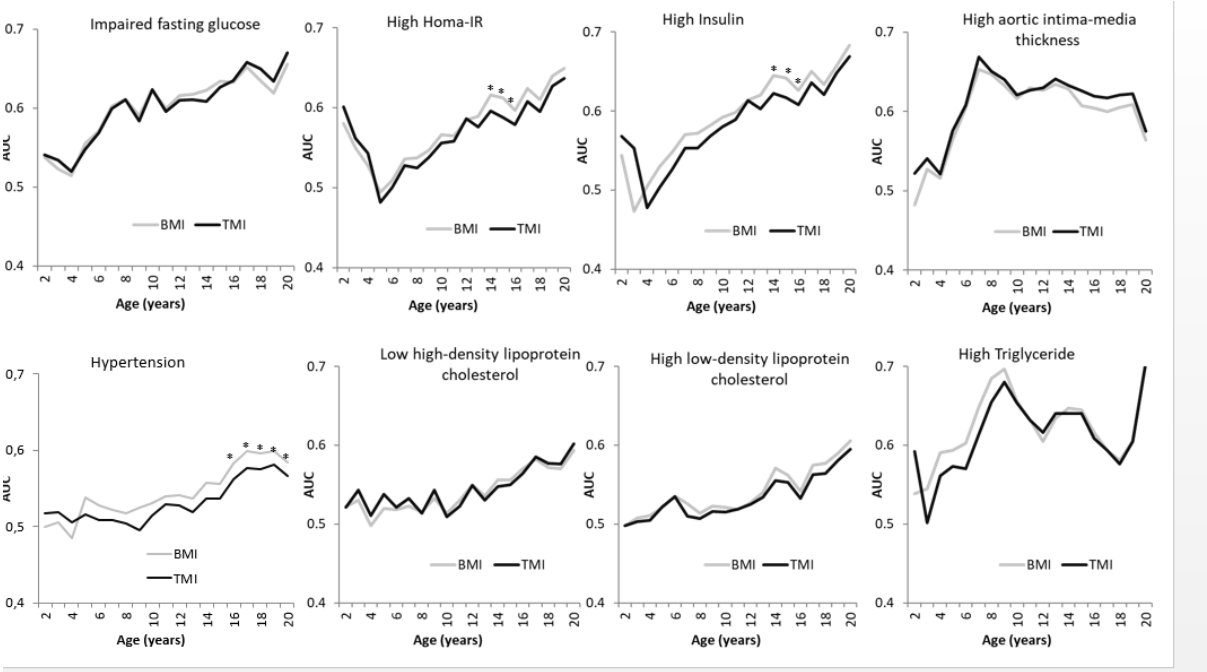


Figure 4.

**Table 3** Area under the curve (AUC) and 95 % confidence intervals (CI) for youth BMI and TMI in predicting adult HOMA-IR, insulin and hypertension (age 20 years)

| | High HOMA-IR | | High Insulin | | Hypertension | |
|---|---|---|---|---|---|---|
| Age (yr) | BMI AUC (95% CI) | TMI AUC (95% CI) | BMI AUC (95% CI) | TMI AUC (95% CI) | BMI AUC (95% CI) | TMI AUC (95% CI) |
| 2 | 0.58 (0.51, 0.65) | 0.60 (0.54, 0.67) | 0.54 (0.48, 0.61) | 0.57 (0.50, 0.63) | 0.50 (0.44, 0.56) | 0.52 (0.45, 0.58) |
| 3 | 0.55 (0.48, 0.62) | 0.56 (0.50, 0.63) | 0.47 (0.41, 0.54) | 0.55 (0.49, 0.61) | 0.51 (0.44, 0.57) | 0.52 (0.46, 0.58) |
| 4 | 0.53 (0.46, 0.60) | 0.54 (0.48, 0.61) | 0.51 (0.44, 0.57) | 0.48 (0.41, 0.54) | 0.49 (0.42, 0.55) | 0.51 (0.44, 0.57) |
| 5 | 0.49 (0.43, 0.56) | 0.48 (0.41, 0.55) | 0.53 (0.46, 0.60) | 0.50 (0.44, 0.57) | 0.54 (0.47, 0.61) | 0.52 (0.45, 0.58) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 6 | 0.51 (0.44, 0.58) | 0.50 (0.43, 0.56) | 0.55 (0.48, 0.62) | 0.53 (0.46, 0.59) | 0.53 (0.46, 0.59) | 0.51 (0.45, 0.57) |
| 7 | 0.54 (0.47, 0.61) | 0.53 (0.46, 0.60) | 0.57 (0.50, 0.64) | 0.55 (0.49, 0.62) | 0.52 (0.46, 0.59) | 0.51 (0.44, 0.57) |
| 8 | 0.54 (0.47, 0.61) | 0.53 (0.46, 0.59) | 0.57 (0.51, 0.64) | 0.55 (0.49, 0.62) | 0.52 (0.45, 0.58) | 0.50 (0.44, 0.57) |
| 9 | 0.55 (0.48, 0.62) | 0.54 (0.47, 0.61) | 0.58 (0.51, 0.65) | 0.57 (0.50, 0.64) | 0.52 (0.46, 0.59) | 0.50 (0.43, 0.56) |
| 10 | 0.57 (0.50, 0.63) | 0.56 (0.49, 0.62) | 0.59 (0.53, 0.66) | 0.58 (0.51, 0.65) | 0.53 (0.47, 0.59) | 0.52 (0.45, 0.58) |
| 11 | 0.57 (0.50, 0.63) | 0.56 (0.49, 0.63) | 0.60 (0.53, 0.67) | 0.59 (0.52, 0.66) | 0.54 (0.48, 0.60) | 0.53 (0.47, 0.59) |
| 12 | 0.59 (0.52, 0.66) | 0.59 (0.52, 0.66) | 0.61 (0.55, 0.68) | 0.61 (0.55, 0.68) | 0.54 (0.48, 0.61) | 0.53 (0.47, 0.59) |
| 13 | 0.59 (0.52, 0.66) | 0.58 (0.51, 0.65) | 0.62 (0.55, 0.69) | 0.60 (0.53, 0.67) | 0.54 (0.47, 0.60) | 0.52 (0.46, 0.58) |
| 14 | 0.62 (0.55, 0.69) | **0.60 (0.53, 0.67)** | 0.65 (0.58, 0.71) | **0.62 (0.55, 0.69)** | 0.56 (0.49, 0.62) | 0.54 (0.47, 0.60) |
| 15 | 0.61 (0.54, 0.68) | **0.59 (0.52, 0.66)** | 0.64 (0.57, 0.71) | **0.62 (0.55, 0.69)** | 0.56 (0.49, 0.62) | 0.54 (0.48, 0.60) |
| 16 | 0.60 (0.53, 0.67) | **0.58 (0.51, 0.65)** | 0.63 (0.56, 0.69) | **0.61 (0.54, 0.68)** | 0.58 (0.52, 0.64) | **0.56 (0.50, 0.62)** |
| 17 | 0.62 (0.56, 0.69) | 0.61 (0.54, 0.68) | 0.65 (0.58, 0.72) | 0.64 (0.57, 0.70) | 0.60 (0.54, 0.66) | **0.58 (0.52, 0.64)** |
| 18 | 0.61 (0.54, 0.68) | 0.60 (0.52, 0.67) | 0.63 (0.56, 0.70) | 0.62 (0.55, 0.69) | 0.60 (0.53, 0.66) | **0.58 (0.51, 0.64)** |
| 19 | 0.64 (0.57, 0.71) | 0.63 (0.56, 0.70) | 0.66 (0.59, 0.73) | 0.65 (0.58, 0.72) | 0.60 (0.53, 0.66) | **0.58 (0.52, 0.64)** |
| 20 | 0.65 (0.58, 0.72) | 0.64 (0.57, 0.71) | 0.68 (0.61, 0.75) | 0.67 (0.60, 0.74) | 0.58 (0.52, 0.65) | **0.57 (0.50, 0.63)** |

BMI, body mass index; TMI, tri-ponderal mass index.

BMI and TMI were standardised with the strata of sex and age.

Bold denotes statistical significance for comparing with the AUC of BMI for the same outcome at the same age, $p<0.05$.

**Table 4** Number of participants for analyses for each outcome at each age

| | aIMT | IFG | High HOMA-IR | High Insulin | Hypertension | Low HDL-C | High LDL-C | High Triglyceride |
|---|---|---|---|---|---|---|---|---|
| Age (yr) | n | n | n | n | n | n | n | n |
| 2 | 420 | 423 | 420 | 420 | 428 | 423 | 423 | 423 |
| 3 | 409 | 412 | 409 | 409 | 417 | 412 | 412 | 412 |
| 4 | 415 | 418 | 415 | 415 | 423 | 418 | 418 | 418 |
| 5 | 414 | 417 | 414 | 414 | 422 | 417 | 417 | 417 |
| 6 | 413 | 416 | 413 | 413 | 420 | 416 | 416 | 416 |
| 7 | 409 | 411 | 408 | 408 | 416 | 411 | 411 | 411 |
| 8 | 406 | 409 | 406 | 406 | 414 | 409 | 409 | 409 |
| 9 | 403 | 406 | 403 | 403 | 411 | 406 | 406 | 406 |
| 10 | 408 | 411 | 408 | 408 | 416 | 411 | 411 | 411 |
| 11 | 408 | 411 | 408 | 408 | 416 | 411 | 411 | 411 |
| 12 | 404 | 407 | 404 | 404 | 412 | 407 | 407 | 407 |
| 13 | 412 | 415 | 412 | 412 | 420 | 415 | 415 | 415 |
| 14 | 411 | 414 | 411 | 411 | 418 | 414 | 414 | 414 |
| 15 | 411 | 414 | 411 | 411 | 418 | 414 | 414 | 414 |
| 16 | 413 | 416 | 413 | 413 | 421 | 416 | 416 | 416 |
| 17 | 410 | 413 | 410 | 410 | 418 | 413 | 413 | 413 |
| 18 | 410 | 411 | 408 | 408 | 415 | 411 | 411 | 411 |
| 19 | 406 | 408 | 405 | 405 | 412 | 408 | 408 | 408 |
| 20 | 420 | 423 | 420 | 420 | 428 | 423 | 423 | 423 |

aIMT, aortic intima-media thickness; IFG, impaired fasting glucose; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Significant study group*BMI/TMI interactions were found for IFG, high HOMA-IR, high insulin, hypertension and aIMT at only a few ages (p for all <0.05; **Table 5; online**). Associations were stronger for both BMI and TMI in the intervention group for all outcomes except for IFG; however, the associations of BMI or TMI with the outcomes were largely similar in each study group. Similar patterns were found for the results of analyses stratified by females and males (**Table 6; online**).

**Table 5** Relative risk (RR) and 95 % confidence intervals (CI) for the association between youth BMI and TMI and adult (age 20-year) outcomes by intervention groups

| | | | BMI | | | TMI | |
|---|---|---|---|---|---|---|---|
| | | | Intervention | | Control | Intervention | Control |
| | Age (yr) | n | RR (95% CI) | n | RR (95% CI) | RR (95% CI) | RR (95% CI) |
| IFG | 8 | 184 | 0.85 (0.50, 1.47) | 225 | **1.62 (1.19, 2.22)** | 0.92 (0.62, 1.36) | **1.55 (1.10, 2.17)** |
| High HOMA-IR | 19 | 184 | **1.63 (1.36, 1.96)** | 221 | **1.32 (1.18, 1.48)** | **1.65 (1.37, 1.98)** | **1.28 (1.13, 1.45)** |
| High Insulin | 13 | 188 | **1.59 (1.29, 1.97)** | 224 | **1.29 (1.10, 1.51)** | **1.60 (1.34, 1.92)** | **1.24 (1.06, 1.46)** |
| | 15 | 184 | **1.68 (1.40, 2.02)** | 227 | **1.30 (1.14, 1.48)** | **1.64 (1.39, 1.95)** | **1.26 (1.10, 1.45)** |
| | 16 | 185 | **1.57 (1.33, 1.85)** | 228 | **1.27 (1.11, 1.44)** | **1.54 (1.33, 1.79)** | **1.24 (1.08, 1.41)** |
| | 17 | 185 | **1.66 (1.39, 1.98)** | 225 | **1.31 (1.16, 1.48)** | **1.62 (1.38, 1.91)** | **1.27 (1.12, 1.44)** |
| | 19 | 184 | **1.69 (1.40, 2.04)** | 221 | **1.34 (1.21, 1.49)** | **1.72 (1.43, 2.07)** | **1.30 (1.16, 1.46)** |
| Hypertension | 3 | 190 | **1.60 (0.88, 2.90)** | 227 | 0.84 (0.57, 1.24) | 1.51 (0.89, 2.54) | 0.70 (0.47, 1.04) |
| | 19 | 187 | **1.96 (1.44, 2.66)** | 225 | **1.36 (1.08, 1.71)** | **1.90 (1.42, 2.53)** | 1.26 (0.99, 1.62) |
| aIMT | 17 | 184 | **1.79 (1.21, 2.65)** | 226 | 1.04 (0.74, 1.47) | **1.85 (1.25, 2.72)** | 1.04 (0.77, 1.40) |
| | 18 | 184 | **2.00 (1.37, 2.93)** | 226 | 1.06 (0.75, 1.49) | **2.12 (1.42, 3.15)** | 1.06 (0.79, 1.42) |

IFG, impaired fasting glucose; BMI, body mass index; TMI, tri-ponderal mass index; aIMT, aortic intima-media thickness (based on latest available data from age 15, 17 and 19 years).
Number of participants were the same for BMI and TMI in each group; BMI and TMI were standardised with the strata of sex and age.
Bold denotes statistical significance, $p<0.05$.

**Table 6** Relative risk (RR) and 95 % confidence intervals (CI) for the association between youth BMI and TMI and adult (age 20-year) outcomes by sex

| | | | BMI | | | TMI | |
|---|---|---|---|---|---|---|---|
| | | | Females | | Males | Females | Males |
| | Age (yr) | n | RR (95% CI) | n | RR (95% CI) | RR (95% CI) | RR (95% CI) |
| High HOMA-IR | 2 | 216 | 1.10 (0.84, 1.43) | 204 | **0.64 (0.52, 0.79)** | 1.03 (0.76, 1.39) | **0.65 (0.52, 0.81)** |
| | 3 | 208 | 1.14 (0.95, 1.37) | 201 | **0.76 (0.60, 0.97)** | 1.10 (0.88, 1.38) | 0.80 (0.63, 1.01) |
| | 5 | 211 | **1.22 (1.06, 1.41)** | 203 | 0.83 (0.63, 1.09) | **1.19 (1.00, 1.41)** | 0.86 (0.66, 1.11) |
| High Insulin | 2 | 216 | 1.21 (0.98, 1.49) | 204 | **0.68 (0.54, 0.86)** | 1.15 (0.90, 1.47) | **0.68 (0.54, 0.86)** |
| | 3 | 208 | **1.18 (1.01, 1.37)** | 201 | 0.81 (0.63, 1.05) | 1.12 (0.91, 1.37) | 0.83 (0.65, 1.06) |
| | 4 | 214 | **1.21 (1.05, 1.39)** | 201 | 0.91 (0.71, 1.16) | 1.15 (0.95, 1.40) | 0.90 (0.71, 1.15) |
| | 5 | 211 | **1.27 (1.13, 1.44)** | 203 | 0.91 (0.70, 1.20) | **1.23 (1.07, 1.42)** | 0.92 (0.70, 1.19) |
| Hypertension | 19 | 215 | **1.44 (1.17, 1.78)** | 197 | 1.12 (0.96, 1.31) | **1.40 (1.13, 1.74)** | 1.06 (0.91, 1.25) |
| | 20 | 222 | **1.43 (1.14, 1.79)** | 206 | 1.10 (0.94, 1.29) | **1.40 (1.12, 1.77)** | 1.05 (0.89, 1.23) |
| Low HDL-C | 2 | 217 | **1.77 (1.28, 2.45)** | 206 | 1.01 (0.84, 1.22) | **1.80 (1.23, 2.64)** | 1.01 (0.84, 1.23) |
| | 3 | 209 | **1.51 (1.19, 1.91)** | 203 | 1.09 (0.90, 1.32) | **1.49 (1.06, 2.08)** | 1.12 (0.93, 1.35) |
| | 4 | 215 | **1.51 (1.17, 1.94)** | 203 | 1.03 (0.85, 1.25) | **1.56 (1.22, 2.01)** | 1.05 (0.87, 1.28) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | 5 | 212 | **1.51 (1.12, 2.03)** | 205 | 1.02 (0.84, 1.25) | **1.52 (1.11, 2.07)** | 1.05 (0.87, 1.27) |
| High LDL-C | 2 | 217 | **1.31 (1.13, 1.50)** | 206 | 0.85 (0.67, 1.07) | **1.26 (1.05, 1.51)** | 0.90 (0.70, 1.15) |
| | 3 | 209 | **1.23 (1.10, 1.39)** | 203 | 0.90 (0.71, 1.15) | **1.19 (1.01, 1.39)** | 0.97 (0.76, 1.22) |
| | 4 | 215 | **1.21 (1.07, 1.37)** | 203 | 0.92 (0.74, 1.16) | 1.16 (0.98, 1.39) | 0.97 (0.77, 1.22) |
| | 15 | 210 | **1.28 (1.09, 1.51)** | 204 | 0.97 (0.79, 1.20) | **1.24 (1.05, 1.47)** | 0.96 (0.78, 1.19) |
| | 16 | 216 | **1.23 (1.03, 1.46)** | 200 | 0.91 (0.74, 1.13) | 1.19 (0.99, 1.43) | 0.91 (0.74, 1.13) |
| | 17 | 213 | **1.29 (1.09, 1.52)** | 200 | 0.98 (0.80, 1.19) | **1.24 (1.05, 1.47)** | 0.97 (0.80, 1.18) |

IFG, impaired fasting glucose; BMI, body mass index; TMI, tri-ponderal mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
Number of participants were the same for BMI and TMI in each group; BMI and TMI were standardised with the strata of sex and age.
Bold denotes statistical significance, $p<0.05$.

Results of sensitivity analyses for HDL-C or triglyceride or using weighted data remained largely similar for all estimates except that no significant associations were found for triglyceride (data not shown).

**Discussion**

This infancy-onset study showed that BMI at older ages had significantly higher predictive utilities than TMI for elevated insulin resistance and insulin levels and hypertension but they were similar for other outcomes. Both BMI and TMI at older ages had stronger associations with obesity-related outcomes in adulthood. These findings suggest that youth TMI is no better than BMI in the prediction of obesity-related outcomes in adulthood, although TMI may have better accuracy in estimating youth fat levels in adolescents (likely due to the lack of adjustment of age for BMI, which changes substantially with age)[6].

Age is highly associated with the change in body fat in youth and the risk of adult obesity-related outcomes. The novelty of this study is the age-specific comparison of youth BMI and

TMI in the prediction of clinically important outcomes in adulthood, which provides new insights into the long-term utility of BMI versus TMI. Our previous study conducted using the data from the Cardiovascular Risk in Young Finns Study is the only prior study that has specifically examined this topic[20]. In that study we showed that youth BMI was equal to or better than TMI in the prediction of adult outcomes[21]. However, we did not rule out the impact of age because of its wide range (3-18 years old) and the lack of long-term repeated measures of youth weight and height in a short time-interval[21]. While confirming our previous findings, this study leveraging an infancy-onset cohort further demonstrated that youth BMI at only late adolescence or early adulthood might be better than TMI in the prediction of high insulin resistance, elevated insulin levels and hypertension. A potential explanation is that the trajectory of youth BMI tends to be more distinct at older ages, which has been associated with health outcomes in adulthood[22]. In contrast, TMI may have a less degree of variation because it could be largely stable in relation to age after 8 years[6]. In addition, our previous study showed that youth BMI is better than TMI in predicting adult T2D but this difference was no longer apparent when age was included in the model[21]. As such, a reasonable assumption is that BMI is likely to be partly a mediator of some age-related factors that may explain adult obesity-related outcomes in addition to TMI. For example, both BMI and smoking prevalence tend to increase with age in youth[23], and childhood smoking has been associated with an increased cardiovascular risk in adulthood[9].

In contrast to the findings of insulin resistance and insulin levels, there was no significant difference between BMI and TMI, even at older ages, in predicting IFG. The small number of outcome cases (n=20) in this study may in part explain this. Indeed, even fewer people would have been defined as having IFG when a cut-off of 6.1 mmol/L was used (n=5) and they could have a similar risk of developing T2D with those who had a normal glucose level (<5.6 mmol/L). Another explanation is that fasting glucose levels could remain normal in people at

early developmental stages of T2D due to increased insulin production and hyperinsulinemia as a compensate of muscle tissue, fat tissue and liver becoming insulin-resistant[24]. Therefore, some people who had normal glucose level could also have a higher risk of developing IFG and T2D. From this perspective, our findings for IFG are in line with those of insulin resistance and insulin levels. Moreover, our previous study showed that youth BMI is better than TMI in predicting T2D (AUC=0.682 vs 0.562), although age was not considered[21]. Therefore, it is unclear whether our findings will remain in the future analyses on the STRIP cohort with longer follow-up, older cohort and consequently higher prevalence of T2DM. In addition, consistent results have shown that BMI and TMI had comparable predictive utilities to measures of dyslipidemia. Nevertheless, longer follow-up to older age is needed to confirm these findings and to broaden the outlook into clinical cardiovascular outcomes, such as stroke and cardiovascular mortality.

The increased magnitude of associations and predictive utilities with age is not surprising. Childhood BMI has only a modest predictive utility to the adult BMI, even when genetic factors are considered[25]. Large cohort studies have previously shown that overweight/obesity at a later stage of youth and early adulthood is more important to the risk of developing cardiometabolic diseases in young adulthood and midlife[26-28]. Therefore, youth who are overweight/obese at late adolescence are more likely to have an increased risk of adult diseases even if their overweight is normalised in adulthood. Moreover, a recent study has shown that resolving elevated childhood BMI by the age of 13 years but not in young adulthood (age 17 to 26 years) had similar risk of adult T2D compared to those who were never overweight[26]. Therefore, to some extent, the association of childhood overweight/obesity with adulthood obesity-related outcomes could be largely dependent on the subsequent overweight/obesity status and could be reduced if their childhood overweight/obesity are resolved at an age approaching early adulthood.

Strengths of our study include a birth-cohort design and annually measured weight and height for 20 years, which enables the age-specific examinations. Limitations include small sample size and defining adulthood outcomes at relatively young age leading to a small number of IFG and none of T2D. However, we have large enough numbers of insulin resistance, high insulin levels and aIMT. Nevertheless, further follow-up data will include more cases of IFG and T2D to confirm our present findings. This study used participants from an educational intervention trial. Therefore, their health behaviours and characteristics may be different from those of a general pediatric population and the results may be more applicable to a population with healthier lifestyle behaviours and health profile. It should also be noted that participants in our study were, in general, normal weight (obese: <1% at age 2 and 4.6% at age 20); therefore, further studies in an obese pediatric cohort may be warranted. Loss-to-follow-up is an innate problem of longitudinal studies, particularly for those with long-term, intense follow-up such as in the STRIP. However, our sample is likely to be generalisable to the original cohort after repeated comparisons have shown no systematic differences between participants who were lost to follow-up and those who were not[8]. In line with this, our sensitivity analyses using inverse probability weighting did not show any noteworthy differences to the main results presented.

In conclusion, both BMI and TMI at older ages had stronger associations with obesity-related outcomes in adulthood. Youth TMI, at any ages, is no better than BMI in the prediction of obesity-related outcomes in adulthood. Further studies are needed to confirm these findings using outcomes in middle or older adulthood and assess the predictive utilities of combining repeated measures of those adiposity measures.

**Abbreviations:** TMI, tri-ponderal mass index; BMI, body mass index; T2DM, type 2 diabetes mellitus; IFG, impaired fasting glucose; NFG, normal fasting glucose; STRIP,

Special Turku Coronary Risk Factor Intervention Project; IMT, intima-media thickness; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol, LDL-C, low-density lipoprotein cholesterol; CV, coefficient of variation; HOMA-IR, Homeostatic Model Assessment for Insulin Resistance; AUC, area under the curve; OR, odds ratio; CI, confidence interval; SD, standard deviation; RCT, randomized controlled trial.

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**Figure Legends**

**Figure 1 Online** Flowchart of study participants.

**Figure 2** Mean values and 95 % confidence intervals for body mass index (BMI) and tri-ponderal index (TMI) from the age of 2 to 20 years.

**Figure 3 (online)** Relative risk for the association of youth body mass index (BMI) and tri-ponderal index (TMI) with adult obesity-related outcomes.

**Figure 4** Comparisons of the area under the curve (AUC) between youth body mass index (BMI) and tri-ponderal index (TMI) in predicting adult obesity-related outcomes (see Supplemental Table 3 for 95 % confidence intervals for HOMA-IR, insulin and hypertension). Asterisk denotes statistical significance for comparing AUCs of BMI and TMI at that age, $p<0.05$.