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Life-period associations of body mass index with adult carotid intima-media thickness: The Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study

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ABSTRACT

Objective: Child and adult body mass index (BMI) associates with adult carotid artery intima-media thickness (cIMT). However, the relative contribution of BMI at different life-periods on adult cIMT has not been quantified. This study aimed to determine the life-course model that best explains the relative contribution of BMI at different life-periods (childhood, adolescence, and young-adulthood) on cIMT in adulthood.
Methods: BMI was calculated from direct measurements of height and weight at up to seven time-points from childhood to adulthood (1973–2007) among 2485 participants of the Cardiovascular Risk in Young Finns Study (YFS) and 1271 participants in the Bogalusa Heart Study (BHS). BMI measures at three ages representative of childhood (9-years), adolescence (18 years) and young-adulthood (30 years) life-periods were used. B-mode ultrasound was used to measure common cIMT in adulthood (>30 years). Associations were evaluated using the Bayesian relative life-course exposure model.
Results: In both cohorts, cumulative exposure to higher levels of BMI across the life-course was associated with greater cIMT. Of the examined life-periods, BMI in young-adulthood provided the greatest relative contribution towards the development of adult cIMT for YFS (49.9 %, 95 % CrI = 34–68 %) and white BHS participants (48.6 %, 95 % CrI = 9–86 %), whereas BMI in childhood had the greatest relative contribution for black BHS participants (54.0 %, 95 % CrI = 8–89 %).
Conclusion: Although our data suggest sensitive periods in the life-course where prevention and intervention aimed at reducing BMI might provide most benefit in limiting the effects of BMI on cIMT, maintaining lower BMI across the life-course appears to be optimal.

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1. Introduction

Although atherosclerotic cardiovascular disease (CVD) is the primary global cause of mortality and morbidity among middle aged and older adults (Lusis, 2000), risk factors begin impacting the disease process much earlier in life (Berenson et al., 1998; Jacobs et al., 2022), One childhood risk factor shown to associate with atherosclerotic CVD related markers and clinical outcomes in adulthood is excess adiposity, particularly indicated by body mass index (BMI). Longitudinal studies have shown higher levels of BMI at a single time-period in childhood and across the early life-course to associate with higher carotid artery intima-media thickness (cIMT) in adulthood (Li et al., 2003; Raitakari et al., 2003), a marker of early vascular structure,(Lorenz et al., 2007) and more rapid increases in cIMT in adulthood (Juonala et al., 2010b). The causal association between early lifetime BMI with adult cIMT has been confirmed by Mendelian randomization analysis (Kivimäki et al., 2008). While there are data to suggest adolescent BMI is a stronger correlate with adult cIMT than child BMI (Juonala et al., 2010a), there has been no prior attempt to determine the relative contribution of BMI measured at different time-periods with cIMT in adulthood. Using a novel life-course epidemiology approach, the relative contribution of BMI at different life-periods on adult cIMT can be determined (Madathil et al., 2018b; Mishra et al., 2009). This approach compares three theoretical life-course exposure models to identify the hypothesis that best explains the exposure-outcome relationship: (1) an accumulation model, in which BMI measured at each life-period equally associates with adult cIMT; (2) a sensitive period model, where BMI at one or more of the life periods exhibits a greater association with adult cIMT; and (3) a critical period model, where BMI at only one life-period associates with adult cIMT. Identifying the life-course hypothesis that best explains the relationship between BMI and cIMT could help determine when actions to prevent or treat excess adiposity might be most effective as well as when additional intervention targeting mechanisms outside of adiposity reduction may also be required. Therefore, using data collected from childhood to mid-adulthood in the Cardiovascular Risk in Young Finns Study (YFS) and the Bogalusa Heart Study (BHS), we aimed to determine the relative contribution of BMI measured at different life-periods (childhood, adolescence, young adulthood) on adult cIMT.

2. Methods

2.1. Study Cohorts

The design, sampling, and attrition of participants in the BHS and the YFS have been reported (Pyörälä et al., 1985; Berenson, 1980), and are summarized in Appendix A. Briefly, both population-based cohorts collected measurements on participants first in childhood, who were re-measured in adolescence, and adulthood. The YFS is an ongoing multi-centre study designed to investigate the prevalence, risk factors and origins of cardiovascular disease among the Finnish population. Comprised of 3596 participants at baseline in 1980, aged 3, 6, 9, 12, 15 and 18 years. Six additional follow-up studies occurred in 1983, 1986, 1989, 1992, 2001 and 2007. Data from a subset of 2485 participants who had carotid ultrasound studies performed in the 2001 or 2007 adult follow-ups were considered for this study. The BHS was comprised of 12,164 children measured in a series of cross-sectional surveys spaced

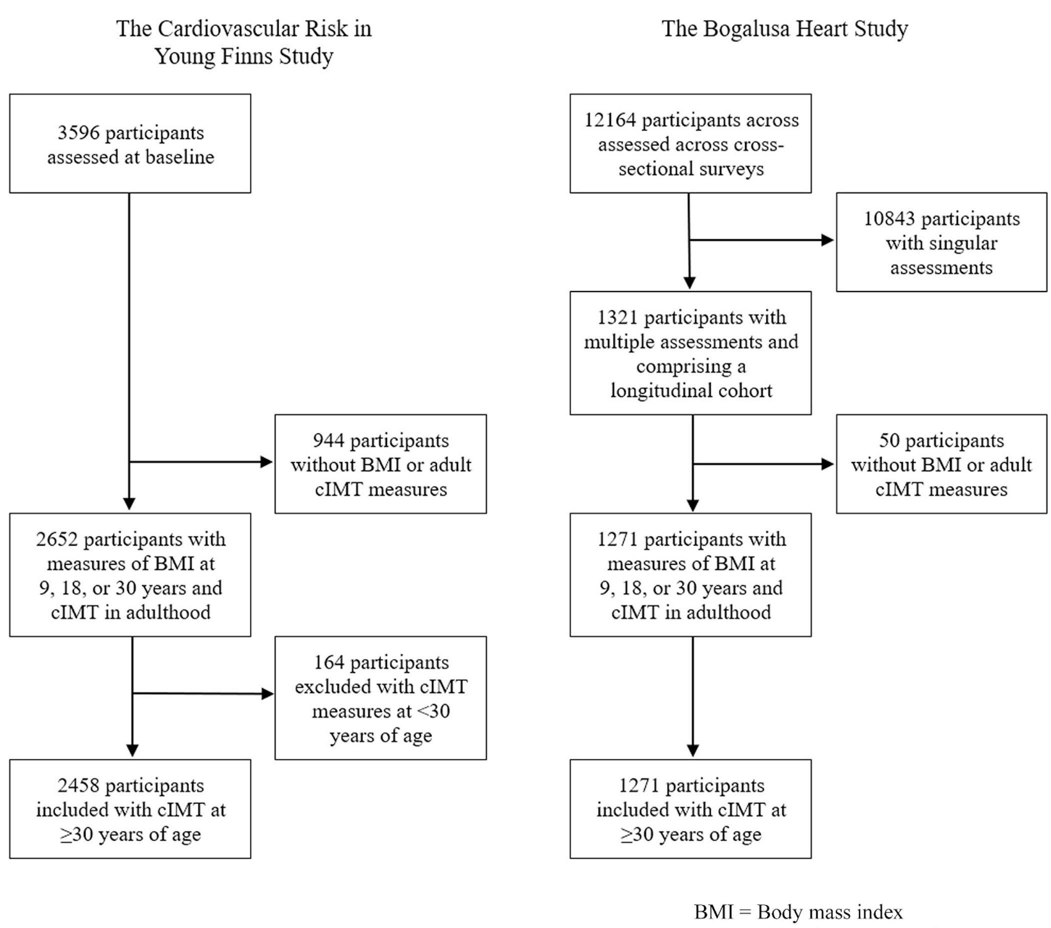

Fig. 1. Flowchart of participant inclusion from the Cardiovascular Risk in Young Finns (Finland) and Bogalusa Heart (United States) studies from childhood to young-adulthood (1973–2007).

every two to three years apart – only 1321 formed a long-term cohort with follow-up through to mid adulthood. A subset of 1271 participants with a BMI measure at childhood, adolescence, and adulthood time-points and carotid ultrasound studies performed in adulthood were considered in this study (1973–2003). A flowchart of participant inclusion is presented in Fig. 1. Within both cohorts informed consent was obtained by study participants or their guardians. Ethical approval was granted for the YFS by the local Ethics Committee of the Hospital District of Southwest Finland, and for the BHS by the Louisiana State University and Tulane University Medical Center ethics and research committees. Both studies accorded to the Declaration of Helsinki.

2.2. Measures

Detailed methods regarding the measurement of cIMT, height, weight, physical activity, diet, smoking, alcohol consumption, and socioeconomic status are provided in Appendix A. The primary exposure measure, BMI, was determined from direct measures of body mass (kg) and height (m), as body mass (kg)/ [height (m)^2]. At the 2001 and 2007 adult follow-ups of YFS participants, B-mode ultrasound scans was used to measure mean cIMT at the posterior wall of the left common carotid artery ~10 mm proximal to the beginning of the bifurcation as the greatest distance between the media-adventitia and the internal lumen-intima interface. cIMT observation at the final follow-up (2001 or 2007) was used if data from both time-points was available. Similarly, cIMT for BHS participants was assessed at the latest available follow-up. cIMT mean maximum measurement in the BHS was performed on the far-wall of the left common carotid, 0–10 mm proximal to the bifurcation at 1 mm intervals. In both studies, measurements of cIMT were performed in correspondence with ECG determined end-diastole. In both studies, high cIMT was defined at age-, sex-, race- (BHS only), and study year-specific cIMT ≥90th percentile (Buscot et al., 2018b; Magnussen, 2017).

2.3. Statistical analysis

2.3.1. Participant characteristics

Participant characteristics at each life period are presented as number of participants (proportion) for categorical variables and mean (standard deviation, SD) for continuous variables and were determined using Stata (version 15.1; StataCorp, College Station, TX, USA).

2.3.2. Bayesian relevant life-course model

The Bayesian relevant life-course exposure model (BRLM) is a life-course epidemiology approach that quantifies the relative contribution (defined as relative weights) of BMI at each examined life-period (in our case, childhood, adolescent, young adulthood) on continuous and dichotomous (high) cIMT in young adulthood. Additional detail outlining this approach is presented elsewhere (Madathil et al., 2018b; Madathil et al., 2018a). In short, the BRLM allows estimation of the degree in which BMI contributes to the association with cIMT depending on when in the life course it was measured. The joint distribution of the relative weights helps identify the life course hypothesis (accumulation, critical or sensitive period models) that the data best supports. The model estimates an overall (total) effect for *lifetime* exposure to BMI, in our case indicating the full effect of BMI accumulated across the considered life periods on cIMT in adulthood. Life period-specific effects (a combination of the overall effect and relative weights) can also be estimated.

Three different life periods were considered (i.e., childhood (BHS =3–12 years; YFS = 6–12 years), adolescence (13–21 years) and young-adulthood (22–36 years)). For each considered life-period, a representative measure of BMI from a certain age (childhood: 9 years; adolescent: 18 years; young adulthood: 30 years) was used and considered in the BRLM. As a per unit increase in BMI does not represent an equal portion of the distribution at each life period, for each cohort we standardized BMI at each life period.

In cases where cIMT assessment was only performed prior to the age of 30 years, participants were excluded from analysis to ensure exposure assessment occurred prior to that of the outcome (BHS: $n = 0$; YFS: $n = 168$) (age of cIMT assessment detailed in Appendix A, Table A2). Where a participant was missing a specific measure of BMI for a given life-period, the missing BMI data were derived from Individual Growth Curve (IGC) models. Mean differences between observed BMI and IGC derived BMI for each representative age in each life-period was low and fell within the thresholds of acceptance determined a priori, it was determined that both derived and observed BMI exposure variables were equivalent and IGC derived BMI may be included in the BRLM in place of missing data; Additional detail explaining this approach is outlined in Appendix A and Table A1. The BRLM was then used to examine the association of BMI measured at different periods at the chosen representative age for each for three life periods (childhood, adolescence, young adulthood) with continuous and high cIMT in young adulthood. For all analyses, a non-informative Dirichlet prior [~(1,1,1)] was used for the weights and a Cauchy prior [~ (0,2.5)] was used for the lifetime effect and covariates (Appendix A). Posterior distributions were used to compute β-coefficients (continuous cIMT outcome), odds ratio (OR) (categorical high cIMT outcome, see Appendix A for definition) and 95 % credible intervals (CrI) for the lifetime effect and the mean (95 % CrI) relative weights, interpreted as the relative contribution of BMI at each of the respective life periods in relation to cIMT in adulthood; cumulative and life-period specific effects (95 % CrI) between BMI and cIMT were estimated. Posterior probability of the observed life course hypothesis (accumulation, critical or sensitive period model) were also calculated (Chumbley et al., 2021). Two models were considered: Model 1 adjusted for sex and year of birth (to account for secular effects of differing birth periods); Model 2 additionally included potential confounding variables: physical activity, diet (YFS only), alcohol, smoking, and socioeconomic status (SES). As we were interested in the direct effects of BMI at different life stages on cIMT, we did not adjust for risk factors that might be on the pathway between BMI and cIMT, such as lipids, blood pressure, and measures of glucose homeostasis. As time-variant covariates are not accommodated in the BRLM, life-course averages for standardized diet (YFS only), physical activity and SES were used. Preliminary analysis of BHS participants found the contribution of BMI across the life-course to adult cIMT to differ by race. As interactions are not currently able to be fit within the BRLM, all analysis of the BHS cohort were stratified by race. Analyses were run in R (version 3.5.3; R Foundation for Statistical Computing, Vienna, Austria) and RStudio (version 1.2.1511; RStudio, Inc., Boston, MA, USA) using the package rstan 2.18.2.

2.4. Sensitivity analysis

Two sensitivity analyses were performed. First, the BRLM was repeated for the binary outcome of high cIMT in adulthood. Second, the primary BRLM was stratified by sex for 2362 YFS participants (1294 males; 1068 females) and stratified by sex and race for 836 BHS participants (99 black and 262 white males; 162 black and 313 white females) who had all covariates for Model 2.

3. Results

3.1. Participant characteristics

Characteristics of participants are displayed in Table 1. In childhood (9 years), mean observed BMI was greatest among white BHS participants (17.3 kg/m), compared to black BHS (16.7 kg/m^2) and YFS participants (16.6 kg/m^2). During adolescence (18 years), black BHS participants had the highest BMI of 23.6 kg/m^2 (white BHS = 22.2 kg/m^2; YFS = 21.4 kg/m^2). In adulthood (30 years) observed BMI was largest among black BHS participants (21.4 kg/m^2) compared to white BHS (26.1 kg/m^2) and YFS (25.1 kg/m^2) participants. cIMT was greater

Table 1
Characteristics of participants in the Cardiovascular Risk in Young Finns (Finland) and Bogalusa Heart (United States) studies from childhood to adulthood (1973–2007).

	Young Finns study		Bogalusa heart study			
			White		Black	
Characteristic	N	Statistic	N	Statistic	N	Statistic
	2485		883		388	
Sex (male), n (%)		1132 (45.6)		397 (45.0)		156 (40.2)
Observed BMI, kg/m^2						
Childhood (9 years)	1084	16.6 (2.2)	173	17.3 (2.7)	95	16.7 (2.6)
Adolescence (18 years)	1224	21.4 (2.7)	232	22.2 (4.2)	113	23.6 (4.8)
Young-adulthood (30 years)	791	25.1 (4.5)	124	26.1 (6.7)	54	30.1 (6.9)
Predicted BMI, kg/m^2						
Childhood (9 years)	1401	17.0 (1.8)	710	17.2 (2.8)	293	17.3 (2.9)
Adolescence (18 years)	1261	21.2 (1.8)	651	22.9 (4.6)	275	23.3 (4.9)
Young-adulthood (30 years)	1694	24.9 (4.1)	759	27.1 (5.9)	334	28.2 (6.9)
Carotid intima-media thickness, µm	2485	623.7 (97)	883	646.5 (199)	388	685.0 (217)
High, n (%)		286 (11.3)		89 (10.1)		60 (15.4)
Alcohol						
Consumption, portions/day*	2471	0.9 (1.4)				
Behaviours, n (%)			575		261	
Never				434 (75.5)		168 (64.4)
Only childhood or adolescence				11 (1.9)		3 (1.1)
Only young-adulthood				120 (20.9)		83 (31.8)
Childhood, adolescence and Young-adulthood				10 (1.7)		7 (2.7)
Smoking						
Consumption, packs/year	2388	3.8 (7.3)				
Behaviours, n (%)			575		261	
Never				189 (32.9)		86 (32.9)
Only childhood or adolescence				144 (25.0)		54 (20.7)
Only in adulthood				110 (19.1)		55 (21.1)
Childhood, adolescence and Young-adulthood				132 (23.0)		66 (25.3)
Physical activity						
Life-course index of duration, Intensity and occurrence	2485	8.9 (1.4)				
Adult rating of activity			575	3.0 (1.0)	261	3.0 (1.2)
Socioeconomic status						
Parent and participant maximum Years of education, z-score	2452	0.03 (0.8)				
Parent and participant maximum Education level			575	4.1 (0.9)	261	3.53 (0.9)
Diet, z-score	2485	−0.01 (0.5)				

Statistics are mean (standard deviation) for continuous variables or n (proportion) for categorical variables.
BMI = body mass index.
* Alcohol consumption only assessed in adulthood.

among BHS participants (black = 646.5 µm; white = 685.0 µm; mean assessment age = 41 years) compared to YFS participants (623.7 µm; mean assessment age = 34 years).

3.2. Life-course body mass index and carotid intima-media thickness in adulthood

The association between BMI and continuous cIMT in both cohorts is presented in Table 2. In the YFS, a standard deviation (SD) higher cumulative BMI across the three life-periods was associated with a 19.7 µm higher adult cIMT (95 %CrI = 16.4–23.0 µm). The greatest relative contribution was observed for BMI measured in young-adulthood (64.2 %, 95 %CrI = 49–79 %), with a one SD higher BMI in young-adulthood associated with a 12.6 µm higher adult cIMT (95 %CrI = 9.2–16.0 µm). In the BHS, a one SD higher cumulative BMI across the three life-periods was associated with higher adult cIMT in whites (β = 25.5 µm; 95 % CrI = 14.0–37.1 µm) and blacks (β = 37.5 µm; 95 %CrI = 18.3–56.8 µm). Among whites, the greatest relative contribution (53.2 %, 95 %CrI = 10–89 %) for BMI was observed in young-adulthood with a 13.9 µm higher cIMT (95 %CrI = 2.0–13.5 µm). Among black BHS participants, BMI in childhood had the greatest relative contribution (48.2 %, 95 % CrI = 8–85 %) with a one SD higher BMI in childhood associated with higher adult cIMT (β = 18.5 µm; 95 %CrI = 2.3–38.4). Results remained similar after adjustment for covariates (Table 2, Model 2).

3.3. Sensitivity analyses

Results using high cIMT as the outcome were consistent with those observed for continuous cIMT (Appendix A, Table A3).

Sensitivity analyses that further stratified by sex (YFS) and sex and race (BHS) are shown in Appendix A, Table A4. Consistent with the main analyses, a young-adulthood sensitive period was observed in both males (relative contribution = 69.4 %, 95 %CrI = 49–86 %) and females (relative contribution = 49.9 %, 95 %CrI = 29–70 %) of the YFS. We observed little difference in the relative contributions between young-adulthood and the other life-periods in both black and white males of the BHS, suggesting an accumulation model. The race difference observed in the main analyses for the BHS was observed only among females with a childhood sensitive-period observed among black females (relative contribution = 50.3 %, 95 %CrI = 8–87 %) and a young-adulthood sensitive-period among white females (relative contribution = 56.7 %, 95 %CrI = 11–91 %).

4. Discussion

Our study found that BMI in all life periods contributed to adult cIMT, reinforcing that exposure to excess BMI should be minimised across the lifecourse. However, we also identified certain periods in life when exposure to higher BMI levels had a stronger association with

Table 2
Associations of body mass index in childhood, adolescence, and young-adulthood with continuous carotid intima-media thickness measured in young adulthood among the Cardiovascular Risk in Young Finns (Finland) and Bogalusa Heart (United States) studies (1973–2007).

	Model 1			Model 2		
	N	β (95 %CrI)	Weight (95 %CrI)	N	β (95 %CrI)	Weight (95 %CrI)
Young Finns study						
Total effect	2485	19.7 (16.4–23.0)		2362	20.5 (17.1–23.9)	
Life-period contribution						
Childhood (9 years)		2.5 (0.2–5.9)	12.8 % (1–29)		2.8 (0.3–6.4)	13.8 % (1–30)
Adolescence (18 years)		4.5 (0.9–8.4)	23.0 % (4–42)		4.5 (0.8–8.5)	21.7 % (4–41)
Young-adulthood (30 years)		12.6 (9.2–16.0)	64.2 % (49–79)		13.2 (9.6–16.7)	64.5 % (49–80)
Bogalusa heart study – Whites						
Total effect	883	25.5 (14.0–37.1)		575	29.0 (14.2–43.8)	
Life-period contribution						
Childhood (9 years)		3.9 (2.2–11.0)	16.0 % (1–44)		3.9 (0.2–11.1)	14.1 % (1–41)
Adolescence (18 years)		7.7 (0.5–19.8)	30.8 % (2–75)		8.4 (0.5–4.8)	30.1 % (2–75)
Young-adulthood (30 years)		13.9 (2.0–13.5)	53.2 % (10–89)		16.7 (2.2–33.4)	55.8 % (11–91)
Bogalusa heart study – Blacks						
Total effect	388	37.5 (18.3–56.8)		261	27.3 (5.2–49.1)	
Life-period contribution						
Childhood (9 years)		18.5 (2.3–38.4)	48.2 % (8–85)		14.4 (0.5–34.7)	49.2 % (7–88)
Adolescence (18 years)		10.0 (0.6–26.5)	27.4 % (2–69)		7.4 (0.2–21.4)	28.4 % (2–72)
Young-adulthood (30 years)		9.0 (0.5–23.9)	24.4 % (2–61)		5.5 (0.2–16.5)	22.3 % (1–61)

β = β-coefficient for cIMT (μm) per 1 standard deviation higher body mass index specific to the life-period. CrI = Credible Interval; N = number of participants.
Model 1 adjusted for sex and year of birth.
Model 2 included Model 1 covariates plus physical activity, diet (Young Finns only), alcohol, smoking and socioeconomic status.

adult cIMT.

Direct comparison of our results with those from others is difficult because our study is the first to use life-course modelling in this area (Sun et al., 2021). However, conventional longitudinal studies provide a point of reference. Several studies, including the BHS and YFS, have shown higher levels of BMI in childhood and adolescence to associate with increased adult cIMT (Li et al., 2003; Raitakari et al., 2003), with evidence suggestive of possible sensitive periods in this relationship. For example, pooled data from the International Childhood Cardiovascular Cohort Consortium found that the association between BMI and cIMT differed by age (Juonala et al., 2010a), with a one SD higher BMI at adolescent ages (12, 15, or 18 years) more strongly associated with adult cIMT measured 22 years later than an equivalent higher BMI at childhood ages (3, 6, or 9 years). Furthermore, examination of BMI trajectories from age 6 to 49 years in the YFS indicated that the divergence between more- and less-healthy trajectories tended to occur in adolescence (Buscot et al., 2018a). Despite these data suggesting a sensitive period in adolescence in the relationship between BMI and cIMT (Anderson et al., 2019), our results suggest a young-adulthood sensitive period for most of our data, with the suggestion of a childhood sensitive period for black females in the BHS.

The likelihood of a young-adulthood sensitive period is not so surprising. For example, although the BMI trajectory group identified by Buscot et al. (2018b) who resolved their child overweight or obesity status by adulthood had a residual increased risk of adult high cIMT, this group only comprised a very small proportion of the observed population ($N = 43$, 1.6 %). Moreover, in prior YFS studies the association of child and adolescent BMI on cIMT were reported to decrease substantially when adult BMI was entered into the same multivariable model, suggesting that child BMI was having an indirect effect on adult cIMT that was operating through adult BMI (Juonala et al., 2006). This is supported by meta-analysis showing overweight and obesity determined from BMI tracks strongly from childhood and adolescence to adulthood (Simmonds et al., 2016). The BRLM only models the direct effect of exposure at each life stage—showing when risk factors, such as BMI, might be having the greatest direct contribution on an outcome. While our results suggest the greatest benefit for most participants might be achieved by targeting prevention and intervention efforts in young-adulthood, it does not consider that BMI tracks strongly from childhood (Juhola et al., 2011); that BMI trajectories leading to adult obesity are determined very early in life (Buscot et al., 2018a); and once overweight or obesity develops, it is very difficult to resolve (Buscot et al., 2018b; Juonala et al., 2011; Woo et al., 2020). Irrespective of the sensitive period occurring in young-adulthood for most participants in our study, we observed that prior BMI in childhood and adolescence also directly contributed to adult cIMT. These findings are consistent with a recent study examining fatal and non-fatal CVD events (Kartiosuo et al., 2024). Collectively, these data reinforce that exposure to excess BMI at any life-period should be limited.

Although our models were based on a standardized increase in BMI at the respective life-periods, it is possible that lower overall levels of BMI in childhood compared with young-adulthood might explain our observation of a young-adult sensitive period in most participants. It is possible disparities in BMI distribution between life-periods, for example a shift to the right from earlier to latter time-points (as illustrated in Fig. A1 and Table A5, Appendix A) is owing to the accumulative nature of excess adiposity and the secular changes that have occurred while these populations have aged. Both YFS and BHS studies had baseline and childhood assessment in the 1970–80s when the prevalence of overweight and obesity was lower (James, 2008). The global prevalence of obesity has since escalated, with adolescence and young-adulthood follow-ups of the BHS and YFS being performed during a period when secular changes such as a decline in muscular fitness and physical activity alongside increases in sedentary behaviours (Tomkinson, 2007) and changes in dietary habits and energy intake (Kant and Graubard, 2006) influenced BMI levels. Considering these secular changes, it is possible that if we repeated our analysis using a contemporary cohort of children that we might observe greater contributions to the life-course association from BMI measured in childhood and adolescent life-periods. The presence of a young-adult sensitive period may be partially explained by the alignment of the period with a number of key lifestyle and health behaviour transitions shown to influence BMI (Winpenny et al., 2018). These transitions, encompassing living arrangement, education and employment, partnering, parenting, and social behaviours, alter health behaviours such as diet, alcohol consumption, physical activity, sleep, and smoking (Viner et al., 2015; Winpenny et al., 2018; Smith et al., 2017).

We observed apparent differences by race and sex in the life-course hypothesis that best explained the BMI-cIMT relationship. However, these findings should be interpreted cautiously as we were not powered to look at differences by race/sex strata which is reflected in the low sample size and large overlap in credible intervals for these analyses. Thus, being the first to examine these associations using the BRLM, replication of our race and sex stratified findings is required in other cohorts. There is at least a precedent for this finding in the BHS where cumulative childhood BMI vs. cumulative adult BMI was more strongly associated with adult pulse-wave velocity and cIMT in blacks compared with whites, but there was no statistical evidence for significant BMI*race or BMI*sex interactions (Fan et al., 2022). If we interpret the results on face value, the reasons for the divergence by race among females in the BHS are not obvious but data from the BHS have suggested race- and sex-specific metabolic and physiological differences (Chen et al., 2008; Fan et al., 2022; Li et al., 2007). The BMI distribution for black and white BHS females at each life stage tended to be similar in childhood, with the distribution for black females tending to shift further to the right of the white female distribution with age (Appendix A, Fig. A1), which does not suggest the severity of obesity or high BMI was greater for black females in childhood. Further, research into areas of early-life exposures and CVD has been limited by the low representation of racially diverse parents/families. As such, we have a modest understanding of racial disparities in early life programming of CVD outcomes. Racially and ethnically diverse babies have been shown to have greater CVD risk (Basu et al., 2017), associated with the increased rates of maternal diabetes during pregnancy (Hedderson et al., 2012). Moreover, genetics represents a portion of CVD risk that is understudied in diverse populations (Bayne et al., 2023). Therefore, our findings need further consideration, particularly in regard to pre- and peri-natal exposures, to better understand the mechanisms that might be underlying a potential difference in the life-course model best explaining the association of BMI with cIMT.

This study had limitations. Bias due to differential loss to follow-up in long-term cohort studies is possible. Given that the BRLM estimates the cumulative and life-stage specific contributions of exposures over the life-course, missing data from higher-risk individuals at any life stage could bias both the total and specific life-stage effects. While multiple imputation may mitigate reductions in sample size, the incorporation of such methods into the BRLM technique is not readily available. Our examination of differences by race/sex strata were not sufficiently powered and should be interpreted with caution. As BMI measurements coinciding with important pre- and peri-natal growth periods were not available in our cohorts, we recommend similar life-course analyses be examined among studies that have collected these data. Consideration for time-varying confounding is not possible within the current framework for the BRLM. We have previously found that alternate approaches of covariate adjustment provide similar results (Fraser et al., 2021). Finally, although we present the life-course exposure model that best described the relationship between BMI and cIMT in these data, we are unable to infer causality. However, Mendelian randomization findings suggest a role of life-course BMI with cIMT (Kivimäki et al., 2008). Strengths were the inclusion of participants from two diverse and well-phenotyped cohorts that expands the generalizability of our findings; and the use of IGC to derive values for missing exposure measures that agreed well with actual measurements and meant a larger proportion of the sample was retained for analysis.

5. Conclusions

Although we found BMI in childhood, adolescence, and young-adulthood each were directly associated with young-adult cIMT, we identified certain periods in life when higher BMI levels may have the greatest impact. Further, these lifecourse models highlight periods in which modifications to BMI may yield little reduction in atherosclerotic CVD risk, thus indicating a need for additional intervention addressing mechanisms outside of adiposity reduction. However, findings also present key sensitive periods, in which prevention and intervention might provide most benefit in limiting the effects of BMI on cIMT. These findings suggest that the potential burden to atherosclerotic CVD via adult cIMT might be minimised by maintaining lower BMI across the life-course and initiating prevention efforts prior to sensitive periods.

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Disclosures

None declared.

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Jack T. Evans: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Marie-Jeanne Buscot:** Writing – review & editing, Methodology, Formal analysis, Conceptualization. **Brooklyn J. Fraser:** Writing – review & editing. **Markus Juonala:** Writing – review & editing. **Yajun Guo:** Writing – review & editing. **Camilo Fernandez:** Writing – review & editing. **Mika Kähönen:** Writing – review & editing. **Matthew A. Sabin:** Writing – review & editing. **Matthew K. Armstrong:** Writing – review & editing. **Jorma S.A. Viikari:** Writing – review & editing. **Lydia A. Bazzano:** Writing – review & editing. **Olli T. Raitakari:** Writing – review & editing, Conceptualization. **Costan G. Magnussen:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Anonymized data are available on reasonable request from the Young Finns Study research group. Anonymized data are available on reasonable request from the Bogalusa Heart Study Steering Committee.

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Appendix A. Supplementary data

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