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Association of Non–High-Density Lipoprotein Cholesterol Measured in Adolescence, Young Adulthood, and Mid-Adulthood With Coronary Artery Calcification Measured in Mid-Adulthood

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IMPORTANCE Elevated non–high-density lipoprotein cholesterol (non–HDL-C) is associated with the presence of coronary artery calcification (CAC), a marker of heart disease in adulthood. However, the relative importance of non–HDL-C levels at specific life stages for CAC remains unclear.

OBJECTIVE To identify the relative association of non–HDL-C measured at distinct life stages (adolescence, young adulthood, mid-adulthood) with the presence of CAC measured in mid-adulthood.

DESIGN, SETTING, AND PARTICIPANTS The Cardiovascular Risk in Young Finns Study is a population-based prospective cohort study that started in 1980 with follow-up over 28 years. Participants from 3 population centers (Kuopio, Tampere, and Turku in Finland) represent a convenience sample drawn from the 3 oldest cohorts at baseline (aged 12-18 years in 1980). Data were collected from September 1980 to August 2008. Analysis began February 2020.

EXPOSURES Non–HDL-C levels were measured at 3 life stages including adolescence (aged 12-18 years), young adulthood (aged 21-30 years), and mid-adulthood (aged 33-45 years).

MAIN OUTCOMES AND MEASURES In 2008, CAC was determined from computed tomography and dichotomized as 0 (no CAC, Agatston score = 0) and 1 (presence of CAC, Agatston score ≥1) for analysis. Using a bayesian relevant life course exposure model, the relative association was determined between non–HDL-C at each life stage and the presence of CAC in mid-adulthood.

RESULTS Of 589 participants, 327 (56%) were female. In a model adjusted for year of birth, sex, body mass index, systolic blood pressure, blood glucose level, smoking status, lipid-lowering and antihypertensive medication use, and family history of heart disease, cumulative exposure to non–HDL-C across all life stages was associated with CAC (odds ratio [OR], 1.50; 95% credible interval [CrI], 1.14-1.92). At each life stage, non–HDL-C was associated with CAC and exposure to non–HDL-C during adolescence had the strongest association (adolescence: OR, 1.16; 95% CrI, 1.01-1.46; young adulthood: OR, 1.14; 95% CrI, 1.01-1.43; mid-adulthood: OR, 1.12; 95% CrI, 1.01-1.34).

CONCLUSIONS AND RELEVANCE These data suggest that elevated non–HDL-C levels at all life stages are associated with coronary atherosclerosis in mid-adulthood. However, adolescent non–HDL-C levels showed the strongest association with the presence of CAC in mid-adulthood, and greater awareness of the importance of elevated non–HDL-C in adolescence is needed.

Supplemental content

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Biological processes underlying the causes of heart disease begin years before the emergence of clinical symptoms. Indeed, autopsy studies indicate that aortic and coronary artery atherosclerotic lesions are present among children as young as 2 years old, the prevalence and severity of which rapidly increase during adolescence.[1,2] Moreover, data from ongoing cohort studies suggest adolescent and young adulthood risk factor levels may be better than concurrent measures for predicting increased carotid intima-media thickness and coronary artery calcification (CAC), markers of heart disease in mid to later life.[3,4] Therefore, early-life initiation of primary and primordial prevention strategies represents a potentially compelling opportunity to reduce future heart disease risk. However, heart disease risk is typically managed in middle to later life when symptoms become more apparent and the need for clinical intervention more acute.

Low-density lipoprotein cholesterol (LDL-C) is an important risk factor for heart disease and is the primary target in the management of adult dyslipidemia.[5] Alone, LDL-C does not encompass the full extent of atherogenic risk associated with dyslipidemia.[6] Non-high-density lipoprotein cholesterol (non-HDL-C), which encompasses a greater number of atherogenic lipids and lipoproteins, might provide a better marker of heart disease risk attributable to dyslipidemia.[7] Among children and adults, previous studies have shown that non-HDL-C is at least as good as LDL-C and other lipid measures for predicting future atherosclerotic burden.[8,9] This has led to the National Heart, Lung, and Blood Institute (NHLBI) recommending non-HDL-C for primary screening of dyslipidemia in childhood.[10] Yet, the relative importance of non-HDL-C levels at different life stages for predicting atherosclerotic disease in later life remains unclear. In the present study, we sought to determine the relative association of non-HDL-C levels at different life stages for the presence of CAC in mid-adulthood.

Key Points

Question What is the relative association of non–high-density lipoprotein cholesterol (non–HDL-C) levels in adolescence, young adulthood, and mid-adulthood with coronary artery calcification in mid-adulthood?

Findings In this 28-year cohort study of 589 participants, the presence of coronary artery calcification in mid-adulthood was associated with exposure to non–HDL-C in adolescence, young adulthood, and mid-adulthood. However, adolescent non–HDL-C levels showed the strongest association with coronary artery calcification.

Meaning The odds for the presence of coronary atherosclerosis attributable to non–HDL-C begins early in life, and greater awareness of the importance of elevated non–HDL-C in adolescence is needed.

Methods

Participants

The first (baseline) survey of the Cardiovascular Risk in Young Finns Study conducted in 1980 included 3596 participants aged 3, 6, 9, 12, 15, and 18 years who were representative of the underlying population at the time. Subsequent follow-ups of baseline participants were conducted in 1983, 1986, 1989, 1992, 2001, and 2007 when many of the original, as well as new, measures were made.[11] In August 2008, a convenience sample of 711 participants from the 3 oldest birth cohorts (aged 12, 15, and 18 years in 1980) residing in the locales of 3 population centers (Kuopio, Tampere, and Turku in Finland) were invited to participate in a cardiac computed tomography (CT) study to measure CAC. Of those invited, 589 individuals (80%) attended, then aged 40 to 46 years. Notably, the presence of CAC at this age would be considered premature. Yet, studies have shown that the presence of CAC in this age group is highly predictive of future cardiovascular mortality.[12,13] Study protocols were approved by the Ethics Committee of the Hospital District of Southwest Finland. Written informed consent was obtained from the parent/guardian until the participant was old enough to provide independent consent, after which written informed consent was obtained from the participant.

Primary Predictors: Non–HDL-C

Blood samples were collected from the antecubital vein of participants who had observed an overnight fast. Standard methods were used to determine total cholesterol and HDL-C concentrations at each survey.[14] Because of changes in reagents or methods during the study period between 1980 and 2007, values from different survey years were calibrated according to a correction factor as previously described.[15] Non–HDL-C was calculated as total cholesterol minus HDL-C and was available in 3-year increments for individuals aged 12 to 45 years. Where data were incomplete, individual-level data were derived via individual growth curve analysis performed over the ages between observed measurements. Briefly, when analyzing longitudinal data, it is possible to determine linear or nonlinear individual growth trajectories using multilevel regression modeling. Using this approach, it is possible to quantify changes in non–HDL-C over time at the individual level, which can be used to interpolate over the ages with missing data. In the present study, the growth trajectory of non–HDL-C was best described by a quartic age polynomial with the inclusion of sex and CAC as modifiers (eMethods in the Supplement). Life stage averaged values for non–HDL-C were then calculated as the mean values between ages 12 and 18 years for adolescence, 21 and 30 years for young adulthood, and 33 and 45 years for mid-adulthood.

Outcome: CAC in Mid-Adulthood

In 2008, CAC was determined via CT scans performed at the 3 population centers in Finland (Kuopio, Tampere, and Turku). In Kuopio, CT scans were performed using a Siemens Somatom Sensation 16-slice CT system (Siemens Healthcare); in Tampere, a Philips Brilliance 64-slice CT system (Philips Medical Systems); and in Turku, a GE Discovery VCT 64-slice CT/positron emission tomography system (GE Healthcare). To assess the consistency between the 3 CT scanners at each study location, an imaging phantom with deposits of known calcium concentration was scanned twice using 3 projections at all study locations. The CAC

scores from these phantom scans were compared and the coefficient of variation between all phantom scans was 3.9%. The coefficient of variation for interobserver measurements was 4%. Using the Agatston method,[16] CAC scores for each coronary artery (including left main, left anterior descending, circumflex, and right coronary artery and its branches) were determined by a trained radiographer at each study center. Coronary artery calcification scores were dichotomized as 0 (no CAC, Agatston score = 0) and 1 (presence of CAC, Agatston score ≥1) for analysis.

Statistical Analyses

Detailed methods relating to the bayesian relevant life course exposure model (BRLM) have previously been published.[17,18] To summarize, the BRLM assumes relative weights for non-HDL-C measured in adolescence, young adulthood, and mid-adulthood. These weights determine the relative importance of non-HDL-C at each of the 3 life stages for the presence of CAC in mid-adulthood. The relative weights, in combination with the joint posterior distribution of the weight parameters, help determine the life course model best supported by the data. In the case of an accumulation life course model, non-HDL-C measured at each life stage is equally associated with the presence of CAC. Under a sensitive period model, non-HDL-C at 1 life stage is more strongly associated with the presence of CAC than other life stages. If the exposure at only 1 life stage is associated with the presence of CAC, then this indicates a critical period model. The BRLM also estimates the lifetime odds using non-HDL-C measured over all life stages, herein referred to as the accumulated odds. Using the accumulated odds and the relative weights for non-HDL-C, it is possible to determine the life stage–specific odds. In the present study, a Dirichlet noninformative prior was used so that the exposure at each life stage is weighted equally, and the life course model is determined by the data alone. A weakly informative Cauchy prior was used for the accumulated odds and covariates. All statistical analyses were performed in R, version 3.6.1 (R Foundation) and the R package rstan was used to fit bayesian models in the statistical programing language, Stan (R Foundation).[19] Analysis began February 2020.

Covariate selection was based on previous associations in the Young Finns Study with our main exposures and outcome variables.[20,21] Covariates were year of birth, sex, and lifetime averaged values for body mass index, systolic blood pressure, and ever a daily smoker. Ever a daily smoker was a binary (yes/no) variable, where a positive lifetime smoking status (yes) was defined as individuals who had ever reported being a daily smoker (smokes once per day or more often) during their lifetime. In a subset of 546 participants, data were available for lipid-lowering and antihypertensive medication use, family history of heart disease (collected in mid-adulthood), and lifetime averaged values for fasting plasma glucose levels, and these variables were included in the fully adjusted model. Notably, plasma glucose data were only collected in 1986, 1989, 2001, and 2007. Family history of heart disease was defined as myocardial infarction or coronary heart disease diagnosed before age 55 years for the father or age 65 years for the mother.[22]

Results

Participant Characteristics

Of 589 participants, 327 (56%) were female. Participant characteristics at each life stage are presented in **Table 1**. Total

Table 1. Characteristics of Participants

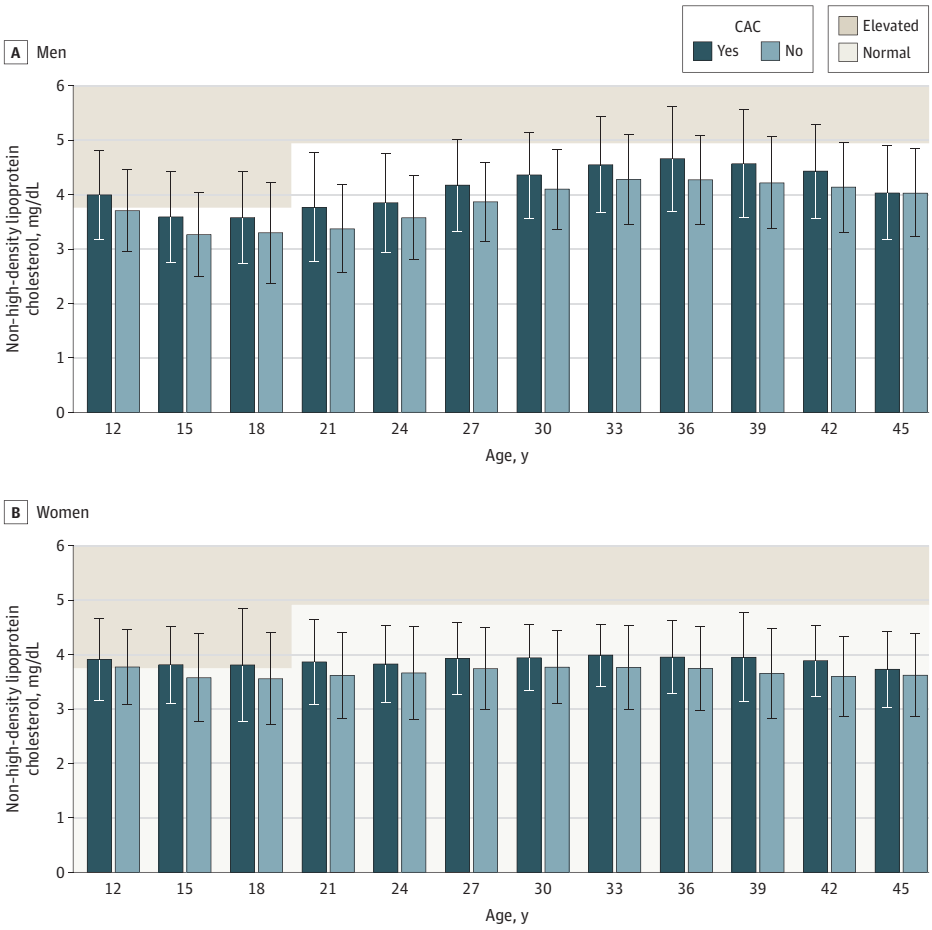
Clinical value	Life stage, mean (SD)		
	Adolescence	Young adulthood	Mid-adulthood
Age, y	15.9 (2.3)	24.2 (2.9)	38.8 (3.9)
Weight, kg	56.5 (12.5)	68.4 (13.5)	78.2 (17.1)
Height, cm	165.8 (10.4)	172.2 (8.9)	171.5 (8.7)
BMI	20.3 (3.0)	22.9 (3.4)	26.4 (4.9)
Blood pressure, mm Hg			
Systolic	118.1 (11.0)	120.8 (11.7)	121.2 (15.0)
Diastolic	68.9 (9.4)	70.5 (9.6)	75.3 (11.8)
Glucose, mg/dL	82.88 (7.21)	84.68 (19.82)	95.50 (14.41)
Ever daily smoker, No. (%)[a]	146 (24.8)	178 (30.2)	131 (22.2)
Cholesterol, mg/dL			
Total	193.05 (38.61)	196.91 (38.61)	204.63 (38.61)
LDL	123.55 (34.75)	123.55 (34.75)	127.41 (34.75)
HDL	61.78 (11.58)	57.92 (15.44)	50.19 (11.58)
Non-HDL cholesterol, mg/dL	139.00 (30.89)	146.72 (30.89)	154.44 (30.89)
Non-HDL cholesterol status, No. (%)			
Normal	369 (62.6)	550 (93.4)	529 (89.8)
Elevated	220 (37.4)	39 (6.6)	60 (10.2)
Family history of heart disease, No. (%)	NA	NA	110 (20.1)
Lipid-lowering medication use, No. (%)	NA	NA	19 (3.3)
Presence of coronary calcium, No. (%)	NA	NA	113 (19.2)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; LDL, low-density lipoprotein; NA, not applicable.

SI conversion factor: To convert cholesterol to millimoles per liter, multiply by 0.0259; glucose to millimoles per liter, multiply by 0.0555.

[a] Ever daily smoker was defined as individuals who had ever reported being a daily smoker (smokes once per day or more often) during each life stage.

Figure 1. Non-High-Density Lipoprotein Cholesterol Trajectories From Age 12 to 45 Years in Men and Women Stratified by Coronary Artery Calcium (CAC) Status



Data are reported as mean and SD. Shaded area represents current guideline-recommended thresholds for elevated non-high-density lipoprotein cholesterol in adolescence (≥144.79 mg/dL) and adulthood (≥189.58 mg/dL).

cholesterol, LDL-C, and non-HDL-C levels increased from adolescence to mid-adulthood while HDL-C levels decreased. Of 589 participants, 113 (19.2%) had CAC in mid-adulthood of which 73 (12.4%) were men and 40 (6.8%) were women (χ^2_1 = 22.9 [N = 589]; P < .001). Characteristics of participants and non-HDL-C age trajectories by CAC status stratified by sex are presented in **Figure 1**. Briefly, among individuals who had evidence of CAC in mid-adulthood, non-HDL-C was higher at every observed age compared with those without CAC (Figure 1). In women compared with men, non-HDL-C was, on average, more stable with advancing age, higher in adolescence, and lower in mid-adulthood (Figure 1). Characteristics of participants stratified by sex are reported in eTable 1 in the Supplement.

Association of Non–HDL-C

In an unadjusted model, the accumulated odds for CAC in mid-adulthood were 1.7 (95% credible interval, 1.36-2.14) times higher for each 1-unit increase in non-HDL-C. Adjustment for sex in the model slightly attenuated the accumulated odds for CAC (**Table 2**) and the highest life stage-specific odds was provided from non-HDL-C exposure in adolescence. In a fully adjusted model (adjusted for year of birth, sex, body mass index, systolic blood pressure, blood glucose level, smoking status, lipid-lowering and antihypertensive medication use, and family history of heart disease), there was 1.5 times higher accumulated odds for CAC for each 1-unit increase in non-HDL-C (Table 2 and **Figure 2**). Furthermore, in the fully adjusted model, the association between non-HDL-C and CAC was best described by a relaxed accumulation life course model, and the highest life stage-specific odds was provided from adolescent exposure (Figure 1). Results using non-HDL-C as a categorical exposure are presented in the eResults and eTable 2 in the Supplement. Briefly, the accumulated odds for the presence of CAC in mid-adulthood was 2.7 times higher for individuals with dyslipidemia and the highest life stage-specific odds was provided from adolescent dyslipidemia exposure. Additional sex stratified analyses can be found in eTables 3 and 4 in the Supplement. Although there was some variation with the estimated odds ratios between men and women, the conclusion drawn on the relevant life-course model were the same. That is, the association between non-HDL-C and CAC was best described by an accumulation life-course model. Comparisons of posterior probabilities between life stages can be found in the eResults in the Supplement.

Table 2. Life Stage–Specific Associations of Non–HDL-C for the Presence of Coronary Artery Calcium in Mid-Adulthood

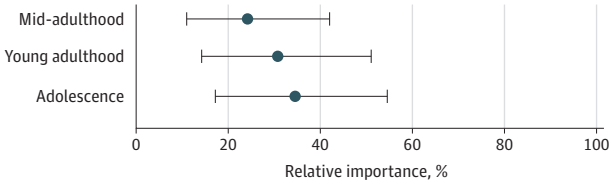
Life stage[a]	OR (95% CrI)[b]	Relative importance (95% CrI)
Model 1 (n = 589)		
Accumulated odds	1.59 (1.25-1.99)	NA
Adolescence	1.18 (1.01-1.49)	0.36 (0.03-0.78)
Young adulthood	1.18 (1.01-1.48)	0.34 (0.03-0.78)
Mid-adulthood	1.15 (1.01-1.40)	0.29 (0.02-0.71)
Model 2 (n = 546)		
Accumulated odds	1.50 (1.14-1.92)	NA
Adolescence	1.16 (1.01-1.46)	0.37 (0.04-0.79)
Young adulthood	1.14 (1.01-1.43)	0.34 (0.03-0.78)
Mid-adulthood	1.12 (1.01-1.34)	0.29 (0.02-0.70)

Abbreviations: CrI, credible interval; HDL-C, high-density lipoprotein cholesterol; NA, not applicable; OR, odds ratio.

[a] Model 1 is adjusted for sex, and model 2 is adjusted for year of birth, sex, body mass index, systolic blood pressure, ever daily smoker, lipid-lowering and antihypertensive medication use, glucose, and family history of heart disease.

[b] Odds ratios represent the likelihood of developing coronary artery calcification in mid-adulthood per 38.61-mg/dL increase in non–HDL-C.

Figure 2. Relative Importance of Non–High-Density Lipoprotein Cholesterol in Adolescence, Young Adulthood, and Mid-Adulthood for Coronary Artery Calcium in Mid-Adulthood



Data are reported as medians with 50% credible intervals (brackets). Adolescence is categorized by age 12 to 18 years; young adulthood, page 21 to 30 years; and mid-adulthood, age 33 to 45 years.

Discussion

In the present study, adolescent non-HDL-C, as opposed to more contemporary measures, showed the strongest association with the presence of CAC in mid-adulthood. Our results add to the growing evidence base underscoring the importance of early-life cardiovascular risk factors and provide new information regarding the relative association of non-HDL-C at different life stages with the presence of CAC. Altogether, early screening, identification, and management of elevated non-HDL-C levels may represent an important goal toward reducing the burden of heart disease in adulthood.

The prevalence of cardiovascular disease has been declining since the 1970s, but recent trends suggest that the decline is slowing.[23,24] Thus, there is a need for a renewed and focused effort to improve primary and primordial prevention strategies. Adult cardiovascular risk factors are well established but comparatively, little attention is given to early-life cardiovascular risk factor levels. In the 1970s and 1980s, several large population-based cohort studies were launched, and although still ongoing, these studies have already provided important insight into the associations between early-life risk factor levels and future cardiovascular risk.[25] In the Muscatine Study,[26] only childhood and adolescent (aged 8-18 years) weight were associated with the presence of CAC in young adulthood. However, in the Coronary Artery Risk Development in Young Adults (CARDIA) study,[3] risk factors in young adulthood, including LDL-C levels, were more strongly associated with CAC in mid-adulthood than concurrent levels. Similarly, Hartiala et al[21] have shown that LDL-C in adolescents is associated with the presence of CAC almost 30 years later. Associations have also been observed between childhood and adolescent non-HDL-C levels and carotid intima-media thickness in adulthood.[8,27] Altogether, exposure to cardiovascular risk factors early in life are associated with the presence of future atherosclerosis and may even be superior to risk factor levels measured later in life.

Early screening and diagnosis of cardiovascular risk factors may be important for reducing future heart disease risk. However, previous studies suggest early-life risk factors may be frequently underdiagnosed in clinical practice.[28,29] Although there is a dearth of data on the prevalence of undiagnosed dyslipidemia, familial hypercholesterolemia is frequently underdiagnosed.[30] Furthermore, de Ferranti et al[29] have shown that adherence to guideline recommendations is suboptimal among pediatric clinicians. Indeed, 70% of pediatric clinicians do not screen for dyslipidemia among individuals aged 9 to 17 years, contrary to guideline recommendations.[29] The underdiagnosis of cardiovascular risk factors in early life may stem from a lack of consistency in the guidelines. In 2011, the NHLBI recommended universal screening of lipid levels in individuals aged between 9 and 11 years and 17 and 19 years.[10] Conversely, the US Preventive Services Task Force does not recommend universal pediatric lipid screening, citing insufficient evidence demonstrating its effectiveness.[31] Since 1992, the American Academy of Pediatrics (AAP) has recommended a targeted or individual approach to pediatric lipid screening based on family history of high cholesterol level or premature cardiovascular disease.[32] Although the most recently published AAP guidelines (2008) do not recommend a universal (populationwide) approach to pediatric lipid screening,[33] the AAP is indirectly in favor of universal screening, having endorsed the 2011 NHLBI guidelines.[10] It should be noted that both the AAP and the NHLBI recommend pharmacologic intervention for individuals starting at ages 8 and 10 years, respectively, but only when LDL-C levels remains elevated (≥189.58 mg/dL) despite efforts to modify lifestyle factors.[10,33] Additionally, pharmacologic intervention may be initiated earlier if individuals have severe primary hyperlipidemia or other high-risk conditions (eg, LDL-C levels ≥401.54 mg/dL).[10]

Between 1999 and 2016, there have been favorable trends in youth cholesterol levels, but there remains a high proportion (25%) of young individuals with adverse cholesterol levels.[34] From an early age and through the teenage years, individuals go through important growth phases comprising high developmental plasticity. We found life course exposure to non-HDL-C was best described by a relaxed accumulation

model and the strongest association with the presence of CAC in mid-adulthood was provided from adolescent non-HDL-C exposure. These findings most closely align with the AAP-endorsed guideline recommendations set by the NHLBI, insofar that, some form of lipid screening before individuals reach young adulthood could be clinically valuable, although this was not directly tested in the present study. Recent trends showing a plateau in the decline of cardiovascular disease is a cause for concern.[23,35] However, early initiation of primordial prevention may provide an important opportunity to improve adult heart health by setting individuals on a favorable trajectory from an early age.

Yet, cholesterol levels have been shown to be, in large part, dependent on genetics, with between 61% and 83% heritability observed for LDL-C.[36] Moreover, previous work by our colleagues suggests that lipid-associated risk alleles influence lipid life course trajectories beginning as early as age 3 years and are associated with lipid levels at all ages.[37] In this regard, lipid tracking from childhood to adulthood is, in part, caused by preprogrammed genetic factors.[37] That said, it has been shown that lifestyle modification, including increasing physical activity, healthy diet, and cessation of smoking, elicits clinically important changes in serum lipid levels.[10,38-41] In this regard, tracking of lipid levels throughout the life course may stem from persistent environmental factors. This is exemplified by recent data from the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP) study,[42] in which participants who received individualized dietary counselling from age 7 months to 20 years were more likely to have ideal total cholesterol levels 6 years later (at age 26 years) compared with controls. Moreover, shorter (2-year) family-based interventions may also be effective, as highlighted by findings from the Physical Activity and Nutrition in Children (PANIC) study,[43] in which individuals receiving physical activity and dietary interventions saw reductions in LDL-C levels compared with controls. These data align with our previous work showing that body mass index may be a key determinant of lipid and lipoprotein tracking.[44] That is, favorable changes in body mass index have the potential to shift individuals with high-risk lipid and lipoproteins levels to low risk.[44] Altogether, both genetic and lifestyle factors likely determine an individual's lipid levels throughout life, although only the latter is modifiable.

Strengths and Limitations

A strength of the present study was the 28-year follow-up and the ability to assess the relative importance of exposure to non-HDL-C at each life stage. However, this study is not without limitations. First, because of constraints of the BRLM used in the present study, it was not possible to adjust for life stage-specific or time-varying covariates, and lifetime averaged values were used instead. However, in a subanalysis we used an alternate approach that regressed body mass index and systolic blood pressure on non-HDL-C at each life stage and used the residuals from these regression models as the main exposure in the BLRM. The results, presented in eTable 5 in the Supplement, were essentially similar to those shown in Table 2 and did not change our overall conclusions as to the best life course model supported by the data. It would have been ideal to also examine our outcome of CAC on a continuous scale, which would have helped better determine dose-response associations at each point. Yet, when expressed as a continuous variable (ie, as tomographic density) CAC is nonnormally distributed and heavily zero inflated, particularly in this relatively young-aged adult cohort. Using more traditional approaches, zero-inflated negative binomial regression models have been used to address the issue of zero inflation. Nevertheless, a formal solution to this issue has not yet been implemented in the BRLM and is currently a limitation of this novel modeling approach. We determined the presence of CAC as an Agatston score 1 or higher (CAC score ≥1 indicative of low risk), whereas an Agatston score of 4 (CAC score ≥400 indicative of high risk) is also a commonly used threshold, particularly for guiding clinical decision-making.[45] It was not possible to examine the influence of risk factor levels measured in childhood (aged <12 years). However, it has been shown that adolescent risk factor levels are associated more strongly with preclinical markers of cardiovascular risk than measures collected earlier in life.[4] Among women, the prevalence of CAC in mid-adulthood was low (6.8%), which may reduce our power to derive precise estimates in sex-stratified analyses; nevertheless, results for sex-stratified analyses were similar. In analyses using non-HDL-C as a binary exposure (ie, presence or absence of dyslipidemia), our results may be sensitive to the definition of dyslipidemia. However, dyslipidemia was defined using guideline recommended cutoffs and our conclusions from these analyses were consistent with those using continuous non-HDL-C as the exposure. Lastly, changes in the use of statins and dietary intake of trans fats have changed over the last 30 years and our conclusions may not entirely translate to a more contemporary cohort.

Conclusions

Our results suggest that exposure to non-HDL-C at all life stages (adolescence, young adulthood, and mid-adulthood) is associated with the presence of CAC in mid-adulthood. However, non-HDL-C levels measured in adolescence may be more strongly associated with CAC than measures made in adulthood. As our credible intervals were wide and overlapped, our estimates need to be confirmed and extended to other cardiovascular outcomes of interest.

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