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# Childhood and long-term dietary calcium intake and adult cardiovascular risk in a population with high calcium intake

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**Abbreviations**: IMT, intima-media thickness; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PWV, arterial pulse wave velocity; CAC, carotid artery compliance; YEM, Young's elastic modulus; SI, stiffness index; BMI, body mass index; 25OHD, 25-hydroxyvitamin D; RR, relative risk; CI, confidence intervals; SD, standard deviation.

## Abstract

**Background & Aims** The influence of dietary calcium intake in childhood on adult cardiovascular health is unknown, particularly in those with long-term high intake. To examine both linear and non-linear associations of childhood and long-term (between childhood and adulthood) dietary calcium intake with adult cardiovascular risk outcomes.

**Methods** A population-based prospective cohort study in Finland (n=1029, aged 3-18 years at baseline). Dietary calcium intake was assessed in childhood (1980, baseline) and adulthood (mean of available data from 2001, 2007 and 2011). Long-term dietary calcium intake was calculated as the mean between childhood and adulthood. Outcomes were measured in 2001, 2007, and/or 2011, and the latest available data were used for analyses, including high carotid intima-media thickness, hypertension, low high-density lipoprotein cholesterol, high low-density lipoprotein cholesterol and triglycerides, arterial pulse wave velocity (PWV), carotid artery compliance (CAC), Young's elastic modulus (YEM), and stiffness index (SI).

**Results** There were no significant non-linear or linear associations between childhood or long-term dietary calcium intake with any adult cardiovascular outcomes, after adjustment for age, sex, and childhood and adulthood confounders (e.g., body mass index, systolic blood pressure, smoking, physical activity, fruit and vegetable consumption).

**Conclusions** Childhood or long-term dietary calcium intake that is higher than the recommended level is not associated with increased cardiovascular risk in adulthood.

**Key words:** pediatric, dietary calcium intake, cardiovascular risk, cohort

## Introduction

Adequate calcium intake is important for bone health throughout the life course. However, the potential detrimental effects of high calcium intake on non-skeletal health outcomes, particularly cardiovascular diseases, have raised major public health concern in the past decade[1-3]. Of note, clinical trials and observational studies have shown that calcium supplement use increased the risk of cardiovascular diseases and related mortality in adults[1, 2, 4]. What is less clear, however, is whether dietary calcium (obtained from food and beverages) is associated with increased cardiovascular risk, particularly among individuals with long-term high intake.

It has been suggested that dietary calcium might have a different role compared to calcium supplements in relation to cardiovascular health[5]. However, previous observational studies have been limited to adulthood with an average low to moderate dietary calcium intake and have shown conflicting findings (detrimental[1, 3], beneficial[3, 6] or no associations[4]). These inconsistent findings may be partly explained by variations in calcium intake (low vs. moderate) and statistical methods (e.g., categorisation of calcium intake vs. nonlinear analysis), but overall suggest a nonlinear association. For example, a dose-response meta-analysis of cohort studies (n=757,304) showed a U-shaped association between dietary calcium intake and cardiovascular mortality, that is, compared with an intake of 800 mg/day, both lower and higher intakes were associated with a higher risk of cardiovascular mortality[3]. Nevertheless, the long-term influence of dietary calcium in childhood on adult cardiovascular health is unknown, particularly in those with high dietary calcium intake. Addressing this evidence gap is important because early life exposures are considered to have profound influences on cardiovascular risk later in life and calcium

intake higher than recommended level is common, particularly in Northern European countries[7].

Therefore, we aimed to describe the association between childhood and long-term (between childhood and adulthood) dietary calcium intake with adult cardiovascular risk in a 31-year cohort study of Finnish participants with a generally high calcium intake. We hypothesised that both higher and lower (vs. an intake of 800 mg/d) childhood or long-term dietary calcium intakes are detrimentally associated with cardiovascular risk in adulthood.

## Methods

### *Participants*

The prospective Cardiovascular Risk in Young Finns Study (YFS) is an ongoing multi-center population-based cohort study to assess risk factors underlying cardiovascular diseases, which began in 1980 (baseline) and included follow ups in 2001, 2007 and 2011[8]. At baseline, 3596 participants aged 3-18 years were randomly selected from the national register of the study areas in different parts of Finland. At baseline, a 50% random sample of the participants was selected to participate in the dietary recall interview (n=1767). In 2011, 2063 participants were re-examined. Participants who had Type 1 diabetes, were pregnant at each follow-up, or had calcium supplement in 1980 or 2011 were excluded from all analyses. The current analyses used data from 1029 participants who had dietary and risk factor data from baseline, and at least one of the adult cardiovascular outcomes. All participants gave written informed consent, and local ethics committees approved the study.

### *Cardiovascular risk outcomes in adulthood*

Carotid intima-media thickness (cIMT) was measured on the left common carotid posterior wall using Sequoia 512 ultrasound mainframes (Acuson, Mountain View, CA) with a 13.0 MHz linear array transducer[9]. Four or more scans were obtained to calculate the mean cIMT. One reader analysed the scans manually and was blinded to the participant's information. The coefficients of variation were 6.4% for between-visit and 3.4% for intra-observer measurements, in our laboratory[9]. Blood pressure was measured with a random zero sphygmomanometer. Fasting blood samples were drawn from the antecubital vein and serum was separated, aliquoted and stored at −70°C for analysis. Serum levels of triglyceride and cholesterol were measured using enzymatic methods[10]. High-density lipoprotein cholesterol (HDL-c) was analysed after precipitation of very low-density lipoprotein and LDL-c with dextran sulfate 500 000. All above-mentioned measures were assessed in 2001, 2007 and 2011 follow-ups, except that cIMT was not measured in 2011. High cIMT, hypertension and high-risk lipid levels were used for data analyses, defined using the latest available data as[10]: High cIMT, cIMT≥90th percentile for age-, sex-, and study-year-specific values; Hypertension: systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg or self-reported use of blood-pressure-lowering medication; High LDL-c: ≥160 mg/dl (4.14 mmol/l) or reported taking lipid-lowering medication; Low HDL-c: <40 mg/dl (1.03 mmol/l); High triglycerides: ≥200 mg/dl (2.26 mmol/l).

Arterial stiffness was measured by arterial pulse wave velocity (PWV), carotid artery compliance (CAC), Young's elastic modulus (YEM), and stiffness index (SI). PWV was measured in 2007 and the other three stiffness variables were measured in 2001 and 2007. Details have been described previously[11, 12], and the latest available data were used for data analyses.

***Dietary calcium intake***

Diet was measured by trained dietitians, in 1980 and 2001, by a 48-hour dietary recall. The type and amount of food two days prior to the interview were recorded for each participant[13]. In 1980, children aged 3-12 years were interviewed together with their mothers, fathers or another accompanying person. Special computer software[14] was used to calculate dietary calcium intake[13]. The food composition files used in the computing were based mainly on Finnish food composition tables and analytical data obtained from the local food industry, and were supplemented by data from foreign food composition tables when no other data were available[15]. All data on the mineral element composition of foods came from the Mineral Element Study[16] performed in Finland in 1975-1978. In 2007 and 2011, diet was measured by a validated 128-item food frequency questionnaire as described in detail elsewhere[17]. In brief, participants were asked to answer questions about their usual eating habits during the past 12 months, which were presented under 12 subgroups (e.g., dairy products, vegetables, and fruits and berries). The portion sizes were fixed and, if possible, specified using natural units (e.g., glass, slice). The frequency categories ranged from never or seldom to six or more times a day. Dietary calcium intake was measured using the National Food Composition Database in Finland[18]. The calcium intake from FFQ had a correlation of 0.46 for women and 0.53 for men, compared to a 3-day food recall[17]. Adulthood dietary calcium intake was calculated as the mean of available data from 2001, 2007 and 2011. Long-term dietary calcium intake was calculated as the mean value of dietary calcium intake in childhood (1980) and adulthood[19]: [1980 calcium + (2001 calcium + 2007 calcium + 2011 calcium)/3]/2.

***Anthropometric, lifestyle and clinical factors***

All measures were for childhood unless otherwise stated. Height and weight were measured in 1980 (baseline), 2001, 2007 and 2011 and body mass index (BMI) calculated as weight/(height$^2$) (kg/m$^2$). The latest available adult BMI was used. Baseline serum 25-hydroxyvitamin D (25OHD) levels were measured as previously described[20]. Smoking habits were asked during a medical examination in a solitary room. For those aged 12-18 years at baseline, smoking was defined as regular cigarette smoking on a weekly basis (or more often). Smoking for participants aged <12 years at baseline was defined as smoking daily, using follow-up data in 1983, 1986, 1989 and 1992 when they were aged between 12 and 18 years. An age-standardised physical activity index was calculated as previously described[21]. A parent-completed physical activity questionnaire was used for participants aged 3 and 6 years, while self-completed questionnaires were used for children aged 9 to 18 years. This physical activity measure has been shown to be reliable and valid[22] and has a theoretical range from 5 to 14. The consumption of fruits and vegetables was assessed by a questionnaire asking about habitual dietary choices during the past month (1=daily or more often, 2=almost daily, 3=a couple of times per week, 4= once a week, 5=a couple of times per month, and 6=more seldom or not at all). Questionnaires were used to obtain information on parental years of education and history of diabetes. Childhood serum HDL-c and LDL-c levels[23] and systolic blood pressure were measured as previously described[8]. Adult smoking, physical activity and calcium supplement use (2011) were measured using questionnaires and the latest available data from the 2001, 2007 or 2011 follow-ups were used. Smoking was defined as smoking daily and a physical activity index was calculated with a higher score indicating a higher activity level (ranged from 5 to 15)[22].

**Statistical analysis**

Mean (standard deviation) and number (%) were used, as appropriate, to describe variables. Energy-adjusted childhood and long-term dietary calcium intake was generated using the residual method and used for the following analyses. Univariable and multivariable modified Poisson regression models (using a robust error variance) were used to estimate the relative risk (RR) and 95% confidence intervals (CI) for the association between dietary calcium intake and the risk of adult outcomes. We did not stratify by sex because we observed no significant interactions between sex and childhood/long-term dietary calcium intake with any of the adulthood outcomes. Model 1 estimated unadjusted RRs. Model 2 adjusted for age, sex and childhood factors (BMI, serum 25OHD levels, parental history of diabetes, HDL-c, LDL-c, systolic blood pressure, fruit and vegetable consumption, smoking, physical activity, and parental education years). Model 3 additionally adjusted for adult factors (BMI, smoking and physical activity). We used restricted cubic splines to examine the potential non-linear associations between calcium intake and outcomes[24]. Three knots (at the $10^{th}$, $50^{th}$, and $90^{th}$ percentiles) were used as recommended[25]. Non-linearity was tested by comparing the log-likelihood of the new model with that of the linear model. A reference point of 800 mg/d (the median of recommended intake for childhood aged 6-17 years in Finland) was used to estimate the RR (95%CIs) for each categorical outcome at different calcium intakes. Missing data of long-term calcium intake (n=196) were imputed using multiple imputation (20 datasets imputed). We assumed all values were missing at random. All analyses were performed in Stata version 15.1 (Stata Corporation, Texas, USA). A two-tailed p value $<0.05$ was considered statistically significant.

**Results**

Of the 1029 participants (49% female), 199 (19.4%) developed hypertension, 163 (16.0%) high LDL-c, 205 (20.0%) low HDL-c and 125 (12.2%) high triglycerides. Participants' characteristics in childhood and adulthood are presented for females and males (Table 1). Baseline mean (SD) dietary calcium intake was 1020 (341) in females and 1283 (512) mg/d in males. The long-term mean intake was 1142 (295) in females and 1380 (387) mg/d in males.

We found no evidence for non-linear associations between childhood/long-term dietary calcium intake with any outcomes in adulthood (all p for non-linearity >0.05, Supplemental **Figure 1 and 2**). In linear analyses without adjustment (**Table 2 and 3**), childhood or long-term dietary calcium intake was not associated with any cardiovascular outcomes in adulthood except that long-term dietary calcium intake was positively associated with CAC (**Table 3**). However, this association was reduced and no longer significant after adjustment for childhood and adulthood risk factors (**Table 3**, Model 3). No other associations were found in unadjusted or adjusted analyses (**Table 2 and 3**).

**Discussion**

This is the first study that examined the long-term association of dietary calcium intake in childhood and between childhood and adulthood with adult cardiovascular risk. We found no evidence for non-linear or linear associations between childhood or long-term calcium intake with adult cardiovascular outcomes.

No previous studies have investigated the long-term association of dietary calcium intake in childhood on adult health outcomes, particularly in those with long-term high intake (e.g. mean > 1000 mg/d). This is important as calcium requirement may differ by age and outcomes assessed[1, 3]. Therefore, our study is of high originality

and clinical importance by assessing both the linear and nonlinear associations of dietary calcium intake at an early stage of life with multiple cardiovascular outcomes in adulthood. Our data showed no evidence of linear or non-linear associations between childhood or long-term calcium intake with adult outcomes. These findings provide new evidence to suggest that high childhood dietary calcium intake that is below the tolerable upper intake levels is unlikely to confer harms to cardiovascular health in adulthood.

Although studies have generally shown detrimental effect of calcium supplementation on cardiovascular diseases and mortality in adults[2, 5], conflicting results have been found about calcium intake from diet[3, 6, 26], with studies showing positive[6, 27], U-shaped[1, 3] or no associations[4, 6, 26]. For example, a meta-analysis conducted in 2014 showed a U-shaped association of dietary calcium intake with cardiovascular mortality, with intakes lower or higher than 800 mg/d being associated with a gradually increased risk[3]. This is supported by a more recent study in a Korean population with low dietary calcium intake (mean (SD) calcium intake: 461 (253) mg/d in men and 426 (256) mg/d in women), where higher calcium intake was associated with a reduced risk of incident cardiovascular disease among women[6], but not men[6]. Moreover, recent data from the Multi-Ethnic Study of Atherosclerosis showed that higher dietary calcium intake was associated with lower risk of coronary artery calcification, though the association was not statistically significant[26].

The exact mechanisms for the detrimental association between calcium intake from supplement and cardiovascular health in previous studies remain unclear, but Reid et al. discussed that circulating calcium levels could directly affect vascular calcification and play a role in clotting and also platelet function via the calcium-sensing receptor[5]. Although circulating calcium levels measured in the fasting state are

considered to be independent of calcium intake from either diet or supplement, serum calcium levels do increase immediately following calcium ingestion, with higher increases observed in individuals receiving calcium from citrate supplement compared with that from a dairy-rich meal[28]. In contrast, high calcium intake from diet may have minimum impact on serum calcium concentrations due to reduced efficiency of intestinal absorption and increased urinary calcium excretion[29]. This may explain the lack of association between dietary calcium intake and cardiometabolic outcomes in the current study.

This study has the strength of using unique data from a long-term population-based cohort, enabling the assessment of the influence of early life exposures on adult health outcomes. We also assessed the nonlinear association using restricted cubic splines rather than in an approach of using pre-specified cut-offs. This avoids the risk of missing any potential associations and cut-offs and maximises the statistical power when no cut-off exists (which is the case in the current study). We could not examine the role of calcium supplement use due to the low rate of supplementation (<0.5% in childhood and 8% in adulthood) and future studies in childhood with a high proportion using supplements are warranted. The intra-individual variability of calcium intake in childhood was limited by the 48-hour recall method. However, the long-term dietary calcium intake was calculated using four measurements (two of which were food frequency questionnaires examining intake over the previous year), accounting for long-term intra-individual variability. Loss to follow-up is an inherent issue of cohort studies, but missing data of long-term calcium intake were accounted for by multiple imputation and the study sample has been previously shown to be representative of the original cohort[10, 19, 30].

In conclusion, childhood and long-term dietary calcium intake higher than the recommended level (but lower than the tolerable upper intake levels) is not associated with increased cardiovascular risk in adulthood. This needs to be considered when making suggestions of increasing calcium intake in childhood for improving calcium-related health outcomes.

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Statement of Authorship: F.W. and C.G.M were involved in study design. M.J., N.P., A.J., T.L., K.P, N.H., M.K., T.L., J.S.A.V., and O.T. R. were responsible for data collection and management. F.W. performed data analysis and drafted the manuscript. All authors revised manuscript content and approved the final manuscript and had access to the data. J.S.A.V. contributed to the initial design of Young Finns. O.T.R. leads Young Finns and contributed to obtaining funding and to the study design. C.G.M. and O.T.R. are the guarantors of the study and accept full responsibility for the finished article, had access to any data, and controlled the decision to publish.

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**Table 1** Participant characteristics in childhood (1980) and adulthood in the YFS (n=1,029)

| | Females (n=505) | Males (n=524) |
|---|---|---|
| **Childhood** | | |
| Age (year) | 10.7 (5.0) | 10.3 (5.0) |
| BMI (kg/m$^2$) | 17.6 (2.9) | 17.6 (3.1) |
| 25OHD (nmol/L) | **51.0 (15.6)** | **53.3 (14.9)** |
| Dietary calcium intake (mg/d) | **1020 (341)** | **1283 (512)** |
| Energy intake (kcal/d) | **1741 (459)** | **2286 (781)** |
| Physical activity index (z score) [b] | **-0.22 (0.85)** | **0.28 (1.05)** |
| Parental history of diabetes, n (%) | 13 (2.6) | 6 (1.2) |
| Fruit consumption (>6 times/week), n (%) | **416 (82)** | **397 (76)** |
| Vegetable consumption (>6 times/week), n (%) | 194 (38) | 174 (33) |
| Smokers, n (%) | 100 (20) | 113 (22) |
| Parental years of education | 9.9 (3.3) | 10.2 (3.2) |
| LDL-c (mmol/l) | 3.48 (0.81) | 3.32 (0.75) |
| HDL-c (mmol/l) | 1.57 (0.30) | 1.56 (0.32) |
| Systolic blood pressure (mmHg) | 111.6 (11.3) | 112.7 (12.9) |
| **Adulthood [a]** | | |
| Age (year) | 41.7 (5.0) | 41.3 (5.0) |
| BMI (kg/m$^2$) | **25.5 (5.1)** | **26.9 (4.5)** |
| Smokers, n (%) | **92 (18)** | **122 (24)** |
| Physical activity index [b] | 8.9 (1.9) | 8.9 (2.0) |
| Long-term dietary calcium intake (mg/d) [c] | **1142 (295)** | **1380 (387)** |
| Energy intake (kcal/d) | **2053 (608)** | **2570 (825)** |

Data are mean (standard deviation) unless otherwise stated.

Abbreviations: BMI, body mass index; 25OHD, 25-hydroxyvitamin D; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol.

[a] all variables used data from the latest available values in adulthood (from 2001, 2007 and 2011).

[b] an index without unit and a higher value indicates that the participant is more physically active (theoretical range from 5-14 for childhood and 5-15 for adulthood).

[c] Long-term calcium intake was calculated as the mean value of dietary calcium intake in childhood (1980) and adulthood (mean of 2001, 2007 and 2011).

Bold denotes significant difference between females and males, $p<0.05$.

**Table 2** Associations of childhood and long-term dietary calcium intake with cardiovascular outcomes in adulthood in the YFS

| | | | Childhood calcium | Long-term calcium [b] |
|---|---|---|---|---|
| Outcomes | | Cases/total number | RR (95% CI) [a] | RR (95% CI) [a] |
| High cIMT | Model 1 | 116/974 | 1.04 (0.87 to 1.25) | 1.10 (0.92 to 1.30) |
| | Model 2 | 116/974 | 1.05 (0.88 to 1.25) | 1.09 (0.92 to 1.29) |
| | Model 3 | 114/952 | 1.07 (0.90 to 1.28) | 1.09 (0.92 to 1.29) |
| Hypertension | Model 1 | 199/1027 | 1.04 (0.91 to 1.18) | 0.99 (0.87 to 1.13) |
| | Model 2 | 199/1027 | 1.07 (0.96 to 1.20) | 1.02 (0.90 to 1.15) |
| | Model 3 | 191/996 | 1.09 (0.97 to 1.21) | 1.06 (0.94 to 1.18) |
| High LDL-c | Model 1 | 163/1020 | 0.92 (0.80 to 1.05) | 0.92 (0.80 to 1.07) |
| | Model 2 | 163/1020 | 0.94 (0.83 to 1.07) | 0.95 (0.83 to 1.09) |
| | Model 3 | 159/990 | 0.93 (0.82 to 1.06) | 0.95 (0.83 to 1.08) |
| Low HDL-c | Model 1 | 205/1026 | 0.96 (0.84 to 1.10) | 0.99 (0.87 to 1.13) |
| | Model 2 | 205/1026 | 0.96 (0.85 to 1.08) | 0.98 (0.87 to 1.10) |
| | Model 3 | 197/996 | 0.93 (0.84 to 1.04) | 0.97 (0.87 to 1.08) |
| High triglycerides | Model 1 | 125/1026 | 1.01 (0.84 to 1.20) | 0.92 (0.77 to 1.10) |
| | Model 2 | 125/1026 | 1.01 (0.86 to 1.20) | 0.92 (0.77 to 1.09) |
| | Model 3 | 119/996 | 1.00 (0.86 to 1.17) | 0.94 (0.81 to 1.10) |

Abbreviations: RR, relative risk; CI, confidence interval; cIMT, carotid intima-media thickness; LDL-c, low-density lipoprotein cholesterol; HDL-c, high-density lipoprotein cholesterol.

Bold denotes statistical significance, $p<0.05$.

[a] relative risk for every sex-specific standard deviation higher dietary calcium intake.

[b] Long-term dietary calcium intake was calculated as the mean between childhood and adulthood.

Model 1, unadjusted; Model 2, adjusted for age, sex and childhood factors (body mass index, serum 25OHD levels, parental history of diabetes, HDL-c, LDL-c, systolic blood pressure, fruit and vegetable consumption, smoking, physical activity, and socioeconomic status); Model 3, model 2 + adulthood factors (body mass index, smoking and physical activity).

**Table 3** Associations of childhood and long-term dietary calcium intake with arterial stiffness outcomes in adulthood in the YFS

| | | Females | | |
|---|---|---|---|---|
| | | | Childhood calcium | Long-term calcium [b] |
| Outcomes | | n | β (95% CI) [a] | β (95% CI) [a] |
| PWV (m/s) | Model 1 | 666 | -0.080 (-0.191 to 0.032) | -0.096 (-0.205 to 0.014) |
| | Model 2 | 666 | -0.029 (-0.132 to 0.073) | -0.029 (-0.129 to 0.072) |
| | Model 3 | 657 | -0.028 (-0.129 to 0.074) | -0.034 (-0.133 to 0.066) |
| CAC (%/10 mm Hg) | Model 1 | 779 | 0.027 (-0.022 to 0.075) | **0.056 (0.008 to 0.104)** |
| | Model 2 | 779 | -0.003 (-0.048 to 0.043) | 0.029 (-0.017 to 0.075) |
| | Model 3 | 770 | -0.004 (-0.049 to 0.042) | 0.025 (-0.020 to 0.071) |
| YEM (mm Hg·mm) | Model 1 | 779 | -14.0 (-41.8 to 13.8) | -16.7 (-44.4 to 11.0) |
| | Model 2 | 779 | -4.8 (-31.9 to 22.4) | -7.3 (-34.5 to 19.8) |
| | Model 3 | 770 | -3.4 (-30.5 to 22.7) | -6.0 (-33.1 to 21.1) |
| SI | Model 1 | 779 | -0.163 (-0.555 to 0.230) | -0.195 (-0.586 to 0.196) |
| | Model 2 | 779 | -0.080 (-0.467 to 0.308) | -0.101 (-0.489 to 0.286) |
| | Model 3 | 770 | -0.068 (-0.457 to 0.322) | -0.087 (-0.477 to 0.303) |

Abbreviations: CI, confidence interval; PWV, pulse wave velocity; CAC, carotid artery compliance; YEM, Young's elastic modulus; SI, stiffness index; CI, confidence interval.

[a] relative risk for every sex-specific standard deviation higher dietary calcium intake.

[b] Long-term dietary calcium intake was calculated as the mean between childhood and adulthood.

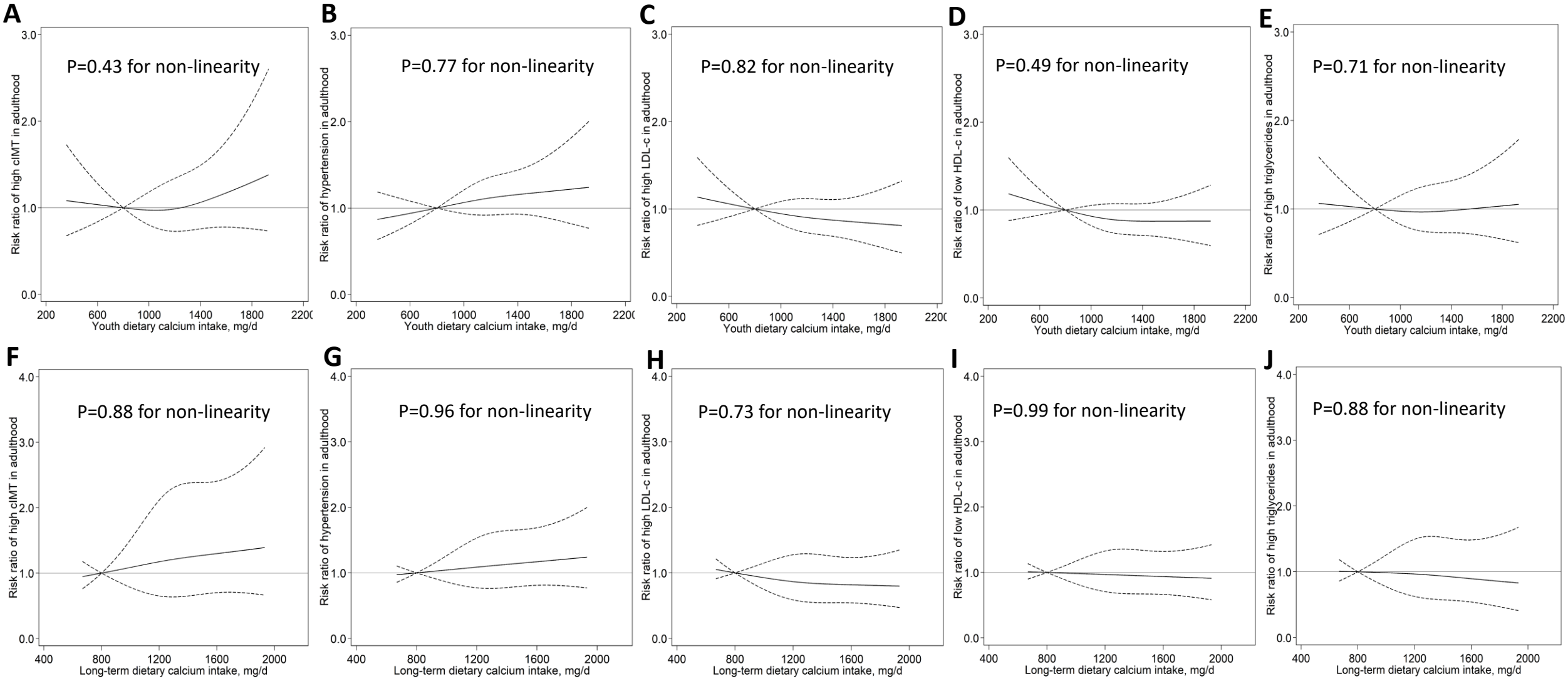
Model 1, unadjusted; Model 2, adjusted for age, sex and childhood factors (body mass index, serum 25OHD levels, parental history of diabetes, HDL-c, LDL-c, systolic blood pressure, fruit and vegetable consumption, smoking, physical activity, and socioeconomic status); Model 3, model 2 + adulthood factors (body mass index, smoking and physical activity).

## Figure Legend

**Supplemental Figure 1** Restricted cubic splines for the non-linear associations between childhood (A to E) and long-term (F to J) dietary calcium intake and adult binary cardiovascular outcomes in the YFS. A calcium intake of 800 mg/d was used as the reference to estimate the relative risks. Solid lines denote relative risks and dashed lines the corresponding 95% confidence intervals.

**Supplemental Figure 2** Restricted cubic splines for the non-linear associations between childhood (A to D) and long-term (E to H) dietary calcium intake and adult continuous cardiovascular outcomes (arterial stiffness measures) in the YFS. A calcium intake of 800 mg/d was used as the reference to estimate the relative risks. Solid lines denote relative risks and dashed lines the corresponding 95% confidence intervals.

# Supplemental Figure 1



# Supplemental Figure 2