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Faster increase in body mass index between ages 8 and 13 is associated with risk factors for cardiovascular morbidity and mortality

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Abstract *Background and aims:* Excess childhood weight is associated with cardiovascular disease (CVD) in adulthood. Whether this is mediated through adult body mass index (BMI) and associated risk factors such as metabolic derangements remains unclear. The aim was to examine whether childhood BMI velocity (Δkg m^{-2} per year) was associated with adult CVD mortality and to examine how adult BMI and cardiometabolic risk factors contribute to the association.
Methods and results: Subjects were 1924 Icelanders born between 1921 and 1935 and living in Reykjavik when recruited into a longitudinal study from 1967 to 1991. From ages 8–13 years, BMI velocity was calculated to quantify the association between childhood growth and adult CVD mortality. Deaths from recruitment to 31 December 2009 were extracted from the national register. There were 202 CVD deaths among men and 90 CVD deaths among women (mean follow-up: 25.9 years). Faster BMI velocity from ages 8–13 years was associated with CVD mortality when comparing those in the highest versus lowest tertile with corresponding hazard ratio (HR) (95% confidence interval (CI)): 1.49 (1.03, 2.15) among men and 2.32 (1.32, 4.08) among women after adjustment for mid-life BMI and CVD risk factors. Faster childhood BMI velocity was associated with elevated CVD risk factors among men at mid-life but these associations were less pronounced among women.
Conclusion: Faster increase in BMI from ages 8–13 years was associated with an increased CVD mortality risk. Children with early growth spurts coupled with excess weight gain during this transition period from childhood into adolescence should be closely monitored to ensure better health in adulthood.

Excess weight in early life may have health implications such as an increasing risk of cardiovascular disease (CVD) later in life. While small size at birth is recognised as a modest risk factor for CVD [1–4], it appears that the combination of being small at birth and remaining thin during infancy, followed by rapid growth later in childhood, is associated with the greatest risk of coronary heart disease (CHD) in adulthood [5].

Growing evidence, though, suggests that it is the tempo of childhood growth that increases the risk of CVD later in

Abbreviations: BMI, body mass index; CHD, coronary heart disease; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio; SD, standard deviation.

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life regardless of size at birth. Previous studies investigating early growth and adult CVD or CHD risk have focused on the association between a 1-kg m^{-2} or 1-SD increment change in BMI at each age during childhood [6–8]. These findings provide some understanding into how CVD risk develops. However, there is a need to ascertain whether there are changes in risk over a certain phase of growth compared to BMI at a specific age during childhood. This period has been difficult to establish partially due to the close interaction between BMI, both during childhood and adulthood, and CVD risk [9,10]. Mechanistic insight has also been a challenge and there is a need to consider cardiometabolic risk factors simultaneously with childhood growth to determine their contributions to adult disease risk. Thus, in order to quantify whether childhood growth influences later CVD risk, both adult BMI and conventional CVD risk factors need to be taken into consideration. Furthermore, examining the rate of BMI gain over multiple time points during childhood may provide better understanding of when CVD risk changes.

To the best of our knowledge, previous studies investigating childhood BMI velocity and CVD mortality have not taken into account adult body size which is associated with CVD risk factors. In this current analysis, our objective was to determine whether the tempo of childhood growth is associated with CVD mortality while accounting for adult body size. Moreover, the aim was to explore whether any associations between childhood growth and CVD death persist while also considering traditional adult CVD risk factors.

Methods

Study population

The longitudinal Reykjavik Study was initiated by the Icelandic Heart Association in 1967 [11]. The source data consisted of 4601 singletons born in Reykjavik between 1914 and 1935 and who resided there when recruited into the study from 1967 to 1991. Growth measures from ages 8–13 years were recorded at regular intervals from 1929 (birth year $\geq$ 1921) in two main schools in Reykjavik. The 782 subjects born prior to 1921, as well as the 1699 subjects for whom clinical records were unavailable, were excluded from this analysis. Furthermore, 196 subjects had multiple missing growth measures leaving a total of 1924 subjects in our current analyses. At recruitment into the Reykjavik Study (1967–1991), we found small differences between subjects included in our analyses (n = 1924) versus those who were not (n = 2677) with respect to characteristics such as (included vs. not included) birth weight (3743 vs. 3745 g), adult BMI (25.7 vs. 25.7 kg m^{-2}), triglycerides (1.3 vs. 1.2 mmol l^{-1}) and total cholesterol (6.3 vs. 6.4 mmol l^{-1}). It has also previously been shown that the childhood growth measures in this cohort are a fair representation of school children in Iceland during this period when compared to reference data from public schools in Reykjavik [12].

Informed consent was obtained from all participants. The collection of birth and childhood growth measures was approved and released by the Icelandic National Bioethics Committee and the Data Protection Commission.

Anthropometric measures at birth and during growth

At birth, weight was recorded to the nearest ±50 g and birth length from crown to heel (in centimetres) was obtained from midwives' birth records. Childhood growth measures were collected from school health records stored in the National Archives of Iceland.

At each yearly examination from ages 8–13 years, the child's height, weight and date of measurement were recorded by school health professionals. BMI velocity was quantified as the mean change in BMI per year for the period between 8 and 13 years.

Collection of adult data

Methods on data collection from the Reykjavik Study have been previously described [13]. Participants were asked to arrive at the Icelandic Heart Association Heart Preventive Clinic in a fasting state to complete a medical examination, blood sample collection and lifestyle questionnaire. Each participant's height was recorded to the nearest 0.5 cm and weight to the nearest 100 g, without shoes and in light undergarments. Blood samples were drawn after an overnight fast and total cholesterol, triglycerides, glucose and uric acid levels were analysed. Quality control of the lipid and glucose measurements was employed throughout the recruitment period [14]. Blood pressure was measured after a 5-min rest to the nearest 2 mmHg with a mercury sphygmomanometer Erkameter wall model (Erka, Germany) using a cuff size of 12 × 23 cm. The same cuff was used throughout the study. Skinfolds were measured at two sites, subscapular and triceps, with calibrated callipers to the nearest 1.0 mm [15].

Fatal CVD and CHD events

Information on cause of death was collected from files at the Statistical Bureau of Iceland from the time of recruitment (beginning in 1967) to 31 December 2009. Mortality due to CHD was determined if death certificates included the following International Classification of Diseases: code 420 (1967–1970, 7th revision), codes 410–413 (1971–1980, 8th revision) and codes 410–414 (1981–2009, 9th revision).

Statistical analysis

The mean and standard deviation (SD) or proportions were used to describe participant characteristics. The child's BMI z-scores were calculated separately by sex, based on the internal distribution in our cohort. Trend tests for adult characteristics and CVD risk factors were calculated using t-tests for continuous variables and chi-squared tests for categorical variables.