

Cluster patterns of behavioural risk factors among children: longitudinal associations with adult cardio-metabolic risk factors

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Abstract

Much of what is known about childhood clusters of cardiovascular disease behavioural risk factors (RFs) comes from cross-sectional studies, providing little insight into the long-term health impacts of different behavioural cluster profiles. This study aimed to establish the longitudinal relationship between cluster patterns of childhood behavioural RFs and adult cardio-metabolic RFs.

Data were from an Australian prospective cohort study of 1,265 participants measured in 1985 (ages 9-15yrs), and in 2004-06 (ages 26-36yrs). At baseline, children self-reported smoking status, alcohol consumption, physical activity (PA), dietary behaviour and psychological well-being. At follow-up, participants completed questionnaires and attended study clinics where the following component indicators of the metabolic syndrome (MetS) score were measured: waist circumference, blood pressure, fasting blood glucose and lipids. TwoStep cluster analyses were carried out to identify clusters in childhood. Linear regression was used to examine the longitudinal associations between cluster patterns of childhood behavioural RFs and adult cardio-metabolic RFs.

Four childhood cluster patterns of behavioural RFs labelled ‘most healthy’, ‘high PA’, ‘most unhealthy’, and ‘breakfast skippers’ were identified. The unhealthier childhood clusters predicted a significantly higher adult MetS score (‘most unhealthy’: $\beta=0.10$, 95%CI=0.01, 0.19) and adult waist circumference (‘most unhealthy’: $\beta=2.29$, 95%CI=0.90, 6.67; ‘breakfast skippers’: $\beta=2.15$, 95%CI=0.30, 4.00). These associations were independent of adult behavioural RFs and socio-economic position.

These findings emphasise the impact of multiple childhood behavioural RFs on important adult health outcomes and may be useful for the development of early intervention strategies, where identification of children at higher risk of poorer adult cardio-metabolic health is vital.

Keywords

Cluster analysis, youth, cardio-metabolic risk, young adulthood, prevention, metabolic syndrome

Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide (Wang et al., 2016). Modifiable lifestyle behaviours such as smoking, alcohol use, physical inactivity and dietary behaviour contribute significantly toward the development of CVD (Ford et al., 2012; Lim et al., 2013; Loef and Walach, 2012; MacMahon et al., 1990; Martin-Diener et al., 2014; Verschuren et al., 1995), and although CVD primarily emerges in adulthood, there is a strong body of evidence to suggest that CVD precursors and behaviour patterns are established during childhood and adolescence (Craigie et al., 2011; Gordon-Larsen et al., 2004; Kelder et al., 1994; Lake et al., 2006; Mikkilä et al., 2005; Nelson et al., 2008).

CVD behavioural risk factors are prevalent in children and adolescents. Many Australian children and adolescents do not achieve the recommended 60-minutes of moderate to vigorous physical activity per day (Australian Bureau of Statistics, 2013; Hallal et al., 2012; Hardy et al., 2013), do not meet the dietary guidelines for vegetable intake, and are regularly consuming discretionary foods that are nutrient poor and high in sugar and/or fat (Australian Bureau of Statistics, 2015; Department of Health and Ageing et al., 2007; Hardy et al., 2013). While most young people consume an adequate amount of fruit, this declines with age (Australian Bureau of Statistics, 2015; Department of Health and Ageing et al., 2007; Hardy et al., 2013), and only a small proportion of children and young adolescents are current smokers and engage in risky consumption of alcohol (Australian Institute of Health and Welfare, 2011, 2012). It is also important to explore psychological health in addition to other major CVD behavioural risk factors as psychological factors have been shown to be independent risk factors for CVD (Bunker et al., 2003; Stewart et al., 2005), and because they are common. In 2007, approximately 9% of young people had high or very high levels of psychological distress and one in four experienced at least one mental disorder (Australian Institute of Health and Welfare, 2011). The high prevalence of these CVD behavioural risk factors in childhood and adolescence is a major concern because they often track into adulthood (Craigie et al., 2011; Kelder et al., 1994; Lake et al., 2006; Mikkilä et al., 2005; Northstone and Emmett, 2008; Telama et al., 2005), highlighting the need for early intervention and to target health promotion strategies towards children and adolescents. Emerging evidence suggests that health-related behaviours co-occur or cluster together in children and adolescents (Leech et al., 2014). This means that behavioural risk factors are not randomly distributed across the population but occur in combination with other behavioural risk

factors (Berrigan et al., 2003; French et al., 2008; Poortinga, 2007). Much of what is known about child and adolescent clusters of health-related behaviours comes from cross-sectional studies. While understanding how and which health-related behaviours cluster together in childhood and adolescence is useful for describing behaviour patterns, it provides little information about the long term health impacts of different behavioural cluster profiles on adult health such as cardio-metabolic risk.

Cardio-metabolic risk represents the overall risk of developing CVD and type 2 diabetes. These conditions are due to a number of common cardio-metabolic risk factors such as hypertension, elevated blood glucose and high triglycerides (Singh et al., 2013), which are commonly associated with behavioural risk factors such as physical inactivity, poor diet and smoking (Department of Health, 2009; Folsom et al., 2011; Spring et al., 2012). Several large cohort studies have shown that cardio-metabolic and behavioural risk factors, and, in particular, clusters of these risk factors (in adulthood) are associated with a high risk of developing CVD and CVD mortality (Baer et al., 2011; Jousilahti et al., 1995; Khaw et al., 2008; Van Dam et al., 2008; Wilson et al., 1999). One study also showed that among young adults an unhealthy lifestyle (based upon behavioural risk factors) was clearly associated with a worse cardiovascular risk profile as indicated by blood pressure and lipid profile) (Gall et al., 2009). Although the literature suggests that many of the behavioural risk factors associated with CVD originate during childhood and adolescence (Craigie et al., 2011; Gordon-Larsen et al., 2004; Kelder et al., 1994; Lake et al., 2006; Mikkilä et al., 2005; Nelson et al., 2008) and have been shown to cluster in childhood and adolescence (Leech et al., 2014), there have been no reports of studies examining whether clusters of CVD behavioural risk factors in childhood and adolescence are associated with cardio-metabolic risk factors in adulthood (independent of adult behaviours).

The aims of this study were 1) to identify clustering patterns of CVD behavioural risk factors in children and adolescents, and 2) to examine the longitudinal relationship between cluster patterns of childhood and adolescent CVD behavioural risk factors and adult cardio-metabolic risk factors.

Methods

Participants

The Childhood Determinants of Adult Health (CDAH) study is a follow-up of the 1985 Australian Schools Health and Fitness Survey (ASHFS), a nationally representative study of 8498 children aged 7-15 years from 109 primary and secondary schools. For the purposes of this study, participants in 1985 are termed ‘children’ although adolescents were included in this group. The sampling method has been described elsewhere (Gall et al., 2009; Pyke, 1985).

During 2001-2002, 6840 participants (80%) of the original cohort were traced from current and historical electoral rolls, electronic telephone directories and school networks (Gall et al., 2009). Of those individuals found, 5170 agreed to participate (61% of the baseline sample) and completed a brief postal or telephone questionnaire. During 2004-2006 (CDAH-1), when the participants were aged 26-36 years, 1589 participants (19% of the baseline sample) completed questionnaires only, whilst a further 2410 participants (28% of the baseline sample) also attended one of 34 study clinics for physical measurements (by trained data collectors) that were held in major cities and regional centres around Australia.

Participants were eligible for inclusion in the current study if: 1) they were aged 9-15 years at baseline (1985); 2) had complete data on the study factors (childhood CVD behavioural risk factors); 3) had complete data on the outcome measures (adult cardio-metabolic risk factors); 4) had complete covariate data (age, sex, baseline body mass index, baseline waist circumference, healthy lifestyle score at follow-up (CDAH-1), and parental and individual education). Participants aged 7-8 years (at baseline) were not eligible for inclusion in the current study as they did not complete the questionnaire on the study factors, because it was deemed that they were too young to complete it reliably. After the exclusion of those with incomplete data, 1265 participants (15% of the baseline sample) were included in the analyses (Figure 1).

At baseline, the Directors of Education in each state and territory granted ethical approval, and consent was obtained from children and parents. At follow-up, ethical clearance was obtained from the Southern Tasmanian Health and Medical Ethics Committee and participants provided informed consent.

Study factors (baseline – 1985)

Children aged 9-15 years (n=6559) completed a self-report questionnaire (ASHFS) on demographics and behavioural risk factors in small groups of four, under supervision from a study staff member.

Smoking

Smoking was assessed by the question “How long have you been smoking regularly?” in which children could respond with ‘I don’t smoke’ (classified as non-smoker), or ‘just started’, ‘1 month up to 6 months’, ‘7 months up to 1 year’, ‘1 year up to 2 years’, ‘2 years up to 4 years’ or ‘more than 4 years’ (classified as smoker).

Alcohol consumption

For alcohol consumption children were asked “how often do you usually drink alcohol?” Responses included ‘I don’t drink alcohol’ (classified as never drink), ‘Less than once a week’ (classified as less than once/week), or ‘on 1 or 2 days a week’, ‘on 3 or 4 days a week’, ‘on 5 or 6 days a week’, ‘everyday’ (classified as once a week or more).

Physical activity

Participants were asked about all exercise and sport they had participated in during the last week. The students were asked how often (how many times last week?), how long (how many hours and minutes were spent each session?), and how much effort (did you huff and puff?) they spent travelling to and from school using a bicycle, travelling to and from school by walking, doing school physical education, doing school sport and doing other activities (students could list up to four activities). For each of these questions, minutes per week spent in these activities were calculated, and each total was summed to provide an estimate of total minutes of past week physical activity. As intensity of physical activity is highly subjective and likely to vary according to a range of factors including weight status, gender, age and cardiorespiratory fitness levels, reported intensity was not factored into the estimates of physical activity.

Breakfast consumption

Dietary behaviour was assessed using breakfast consumption as regular breakfast skipping has been reported to be associated with consuming a poorer diet in both children and adults

(Ruxton and Kirk, 1997). The questionnaire asked the children “Do you usually eat something before school?” which they could respond with ‘yes’ or ‘no’.

Psychological wellbeing

A single item asking “During the past few weeks, how often have you felt depressed or unhappy?” from Bradburn’s Negative Affect Scale (McDowell and Praught, 1982), was used as a marker for psychological well-being. Responses were dichotomised as ‘often’ versus ‘sometimes/never’ which is consistent with previous literature (McKercher et al., 2014; McKercher et al., 2012). This Negative Affect Scale has been found to be a reliable and valid indicator of psychological distress (McDowell, 2010).

Outcome measures (follow-up – 2004-06)

Waist circumference

Waist circumference (cm) was measured by trained data collectors at the study clinics 3 times over light clothing at the narrowest point between the lower coastal boarder and the iliac crest, at the end of normal expiration. The mean of the 3 measurements was calculated and used.

Clinical measures

Blood pressure (BP, mmHg) was measured three times using an Omron HEM-907 Digital Automatic Blood Pressure Monitor (Omron Corporation, Kyoto, Japan). The mean value was used in the analysis. Raised blood pressure was defined as the use of blood pressure-lowering medication, or systolic blood pressures ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg (James et al., 2014). A 30ml blood sample was collected from the antecubital vein after an overnight fast by a trained venipuncturist. At the end of each clinic, samples were sent to the laboratory (Medvet, Adelaide, South Australia) in insulated containers with cold packs via overnight courier. Triglycerides (mmol/l), high-density lipoprotein (HDL) cholesterol (mmol/L) and fasting glucose (mmol/L) were analysed enzymatically on an Olympus AU5400 Mira plus autoanalyzer (Olympus Optical, Tokyo, Japan).

Continuous metabolic syndrome score

A continuous metabolic syndrome score was created using the validated methods described by Wijndaele et al. (2006) and Schmidt et al. (2009). A continuous score was used to eliminate the need to dichotomise continuous outcomes and because cardio-metabolic risk

increases progressively with increasing numbers of risk factors. Calculation of the continuous score involved two steps. First, principal component (PC) analysis with varimax rotation was applied separately by sex to the normalised metabolic syndrome risk factors (waist circumference, triglycerides, HDL cholesterol, blood pressure and fasting plasma glucose) (Alberti et al., 2009) to derive the PCs accounting for large proportions (eigenvalues ≥ 1.0) of the metabolic syndrome variance. Similar to previous studies using this method (Wijndaele et al., 2006), 2 principal components were identified. In men, PC1 and PC2 explained 34% and 26% of variance, respectively, and in women PC1 and PC2 explained 31% and 25% of variance, respectively. Second, these principal components were then summed and weighted according to the relative proportion of variance explained, to compute the continuous metabolic syndrome score. A higher continuous metabolic syndrome score indicates an increased cardio-metabolic risk.

Covariates

Individual-level socioeconomic position (SEP) at baseline and follow-up

Parental education was used as an indicator of childhood (baseline) SEP, retrospectively reported by participants at follow-up (adulthood). For each parent separately, participants reported the highest level of education completed by their father/mother for most of the time until they were 12 years of age, similar to measures used in other epidemiological studies (Krieger et al., 1998; Lidfeldt et al., 2007; Lynch et al., 1994; Power et al., 2005; Smith et al., 1998). At follow-up (adulthood), individual education was used as an indicator of adult SEP, with participants self-reporting their own highest level of education. Both the parental (paternal and maternal) education at baseline and own individual education at follow-up variables were categorised into three categories: high (bachelor degrees or higher); medium (certificate/diploma, trade/apprenticeship or year 12 or equivalent); and low (all schooling up to the completion of Year 11).

Body mass index (BMI) and waist circumference at baseline

Baseline BMI (in kg/m^2) was calculated from measured height (cm) and weight (kg) and baseline waist circumference was measured by trained technicians to the nearest 0.1 centimetre.

Healthy lifestyle score at follow-up

The healthy lifestyle score is an evidence-based simple assessment of adult health related lifestyle behaviours. The healthy lifestyle score aligns with evidence-based recommendations from peak bodies, such as the National Heart Foundation of Australia and has been described in detail elsewhere (Gall et al., 2010). Briefly, the healthy lifestyle score is based on 10 healthy characteristics or behaviours: BMI < 25, eating ≥ 7 servings/day of vegetables and fruit, eating fish or seafood ≥ 2 times/week, eating red meat < 5 times/week, regular use of skim milk, not adding salt to food, using margarine as a spread on savoury items, not smoking tobacco during the previous year, ≥ 3 hours/week of moderate or vigorous physical activity, and drinking ≤ 20 grams of alcohol/day. The score was calculated by assigning a point for each healthy characteristic/behaviour and applied to the 2004-06 dataset. These were then summed, giving a total score ranging from 0 (no healthy characteristics/behaviours) to 10 (all healthy characteristics/behaviours). The lifestyle score has been shown to predict mortality in elderly men (Spencer et al., 2005) and is inversely associated with metabolic risk factors in young adults (Gall et al., 2009).

Data analysis

Descriptive statistics were used to describe the socio-demographic characteristics of the sample at baseline and follow-up. TwoStep cluster analysis (IBM SPSS Statistics Version 22) was used to group participants based on their co-occurring patterns of childhood CVD behavioural risk factors. This method was chosen as it offers some key advantages over other methods for cluster analysis, in that no assumptions about the number of clusters must be made prior to analysis and it automatically determines the “optimal” number of clusters (Han et al., 2011). TwoStep cluster analysis is also appropriate for clustering both continuous and categorical variables and is designed to efficiently handle large datasets (Han et al., 2011). Regardless of the clustering method used researchers are still required to interpret the final cluster solutions to ensure ‘meaningfulness’ and that the clusters make sense in light of the aims of the analysis. As is convention, the labelling (naming) of each cluster reflects the predominant variable/s. Cluster names were developed by consensus between three authors (KP, KF and VC).

Eight childhood CVD behavioural risk factors (smoking, alcohol consumption, breakfast consumption, psychological wellbeing and four physical activity variables - school sport, physical education, active commuting and leisure-related physical activity) were used as cluster analysis inputs and the objective was to identify the optimal number of clusters as

well as maximise the similarity within the clusters and the variability between clusters as measured by the maximum average silhouette width, lowest Schwarz's Bayesian Information Criterion (BIC) and highest ratio of distance measures. To explore whether the cluster patterns differed by age and/or sex, multiple iterations of the cluster analysis were carried out for boys and girls, and for younger (9-12 years) and older (13-15 years) age groups, separately. The decision to combine or separate the final cluster solutions by age and/or sex was by consensus between two authors (KP and KF).

Linear regression (for continuous outcome variables) and log-binomial regression (for categorical outcome variables) were used to examine the associations between cluster patterns of childhood behavioural risk factors and adult metabolic syndrome score, as well as the following components of the score: waist circumference, blood pressure, and fasting blood glucose and lipids. For continuous variables, beta coefficients and 95% confidence intervals were reported and for categorical variables relative risks and 95% confidence intervals were reported. To show the effect (if any) of SEP factors and adult behavioural risk factors on the associations, the regression estimates were adjusted for sex, age, baseline BMI and baseline waist circumference (model 1), additionally adjusted for the healthy lifestyle score in adulthood (model 2), and additionally adjusted for parental and own highest level of education (model 3). These covariates were chosen according to *a priori* knowledge of association with the study factors and outcome variables, and because adjustment for these covariates changed the estimated coefficients by more than 10% in univariable analyses.

Sensitivity analyses were conducted to explore the impact of loss to follow-up on our longitudinal results using three methods. First, participants and non-participants were compared using data collected in 1985. Second, the sample was compared to the general population of 25-34-year-old Australians using Census data and Australian National Health Survey data. Third, inverse probability weights using variables from the full 1985 sample were calculated and applied to examine the differences in the magnitude of effect between weighted and unweighted results. Additionally, sensitivity analyses (using TwoStep cluster analysis) were conducted to examine whether the cluster patterns of childhood behavioural risk factors differed between the full 1985 sample (of 9-15 year olds) and the sub-sample used in the current study.

Results

Characteristics of the participants at baseline (1985) and follow-up (2004-06) are presented in Table 1.

Table 1. Characteristics of the participants at baseline (1985) and follow-up (2004-06)

Characteristics	1985 Baseline	2004-06 Follow-up
	Total (n=1265)	Total (n=1265)
Age (years), M (SD)	11.9 (2.0)	32.4 (2.1)
Sex, % (n)		
Male	48.8 (617)	48.8 (617)
Female	51.2 (648)	51.2 (648)
Paternal education ^a , % (n)		
High	22.9 (290)	-
Medium	40.2 (509)	-
Low	36.8 (466)	-
Maternal education ^a , % (n)		
High	16.2 (205)	-
Medium	18.8 (238)	-
Low	65.0 (822)	-
Own highest level of education, % (n)		
High	-	44.4 (562)
Medium	-	43.9 (555)
Low	-	11.7 (148)
BMI (kg/m ²), M (SD)	18.5 (2.7)	25.5 (4.9)
Weight Status ^b , % (n)		
Normal weight	92.1 (1165)	49.6 (628)
Overweight	6.9 (87)	36.1 (456)
Obese	1.0 (13)	14.3 (181)
Metabolic syndrome score ^c , M (SD)	-	0.02 (0.72)
Waist circumference (cm), M (SD)	65.0 (7.8)	83.9 (12.3)
Systolic blood pressure (mm/Hg), M (SD)	-	117.9 (12.5)
Diastolic blood pressure (mm/Hg), M (SD)	-	72.8 (9.1)
HDL Cholesterol (mmol/L), M (SD)	-	1.4 (0.3)
Triglycerides (mmol/L), M (SD)	-	1.1 (0.8)
Fasting glucose (mmol/L), M (SD)	-	5.0 (0.5)

Abbreviations: M, mean; SD, standard deviation

^a Paternal and maternal education were reported retrospectively by the participants in adulthood (2004-06 follow-up)

^b For baseline data, normal weight, overweight and obese categories are based on international standard age-specific and sex-specific BMI cut-points (Cole et al., 2000)

^c A higher metabolic syndrome score indicates an increased cardio-metabolic risk

Loss to follow-up

Using baseline (1985) characteristics, those with follow-up data were more often female (54% participants versus 45% non-participants), from regional/rural areas (41% participants versus 34% non-participants) and were less commonly overweight (9% participants versus 11% non-participants) in 1985 than those without follow up data. In the restricted sample of participants included in the current analyses (n=1265), those who had complete data at follow-up (CDAH-1) more commonly lived in major cities (76% versus 64%), were more likely to be university educated (44% versus 39%), more likely to be employed as managers/professionals (71% versus 63%) and more likely to be overweight (36% versus 31%) but slightly less likely to be obese (14% versus 16%) than those who did not have complete follow up data at CDAH-1. Further information on the characteristics of the study participants included in the current analysis (n=1265) compared to the original 1985 cohort can be found in Supplementary Table S3.

At follow-up, the sample of the current study compared favourably with the Australian population aged 24-35 years in terms of the proportion of never smokers (study sample, 58%; Australian population, 52%), married (study sample, 70%; Australian population, 62%), overweight or obese (study sample, 49%; Australian population, 47%), and low-risk alcohol consumption (study sample, 88%; Australian population, 87%) (Australian Bureau of Statistics, 2004-2005). The sample of the current study had a higher proportion of people who were university educated (study sample, 45%; Australian population, 22%) and employed as managers/professionals (study sample, 56%; Australian population, 39%) than the general population of the same age (Australian Bureau of Statistics, 2006).

Cluster analysis

Based on the point at which Schwarz's BIC was at its lowest and the ratio of distance measure was at its highest, a four-cluster solution was identified. The average silhouette width of the four-cluster solution was 0.5, which represents good cohesion and separation between clusters. The decision to combine boys and girls as well as younger and older age groups in the final cluster solution was made, as sex-specific and age-specific solutions did not reveal clusters that were unique to males or females or to younger or older age groups. In addition, separating the clusters by age and/or sex did not improve the cohesion or separation between clusters.

As is convention, the clusters were named based on the variable/s that appeared to dominate each cluster (Table 2). Of those included in the final sample, 46% were assigned to cluster 1 (labelled ‘most healthy’), 8% to cluster 2 (labelled ‘high physical activity’), 33% to cluster 3 (labelled ‘most unhealthy’) and 13% to cluster 4 (labelled ‘breakfast skippers’). The descriptive data of the four cluster profiles are shown in Table 2. Differences in BMI, waist circumference and the health lifestyle score between the four cluster profiles are provided in Supplementary Table 4.

Table 2. Cluster patterns of child CVD behavioural risk factors formed by TwoStep cluster analysis^a

Child CVD behavioural risk factors	Clusters			
	Most healthy (n=580)	High PA (n=103)	Most unhealthy (n=417)	Breakfast skippers (n=169)
Breakfast consumption, % (n)				
No	0.0 (0)	7.8 (8)	0.0 (0)	100.0 (169)
Yes	100.0 (580)	92.2 (95)	100.0 (417)	0.0 (0)
Smoking status, % (n)				
Non-smoker	100.0 (580)	97.1 (100)	77.9 (325)	83.4 (141)
Smoker	0.0 (0)	2.9 (3)	22.1 (92)	16.6 (28)
Alcohol consumption, % (n)				
Never drink	100.0 (580)	81.6 (84)	18.9 (79)	67.5 (114)
Less than once a week	0.0 (0)	13.6 (14)	63.6 (265)	23.6 (40)
Once a week or more	0.0 (0)	4.8 (5)	17.5 (73)	8.9 (15)
Depressed or unhappy, % (n)				
Sometimes or never	100.0 (580)	97.1 (100)	79.4 (331)	92.3 (156)
Often	0.0 (0)	2.9 (3)	20.6 (86)	7.7 (13)
PA (mins/week), Median (IQR)				
School sport	45 (0, 90)	120 (0, 360)	40 (0, 90)	30 (0, 90)
Physical education	50 (0, 90)	60 (0, 150)	60 (0, 100)	60 (0, 100)
Active commuting	20 (0, 60)	50 (0, 210)	15 (0, 75)	25 (0, 75)
Leisure-related	110 (0, 250)	380 (120, 1305)	120 (45, 300)	120 (20, 300)

Abbreviations: PA, physical activity; IQR, inter-quartile ranges

^aThe variables that best characterise each cluster have been bolded to ease interpretation

Sensitivity analysis to examine whether the cluster patterns of childhood CVD behavioural risk factors differed between the full 1985 sample (of 9-15-year-olds) and the restricted sub-sample used in the current study showed similar results (see Supplementary Table S1).

Associations between cluster patterns of childhood CVD behavioural risk factors and adult metabolic syndrome score

The longitudinal associations between cluster patterns of childhood CVD behavioural risk factors and adult metabolic syndrome score are presented in Table 3. Compared to the ‘most healthy’ cluster, all other clusters had a higher metabolic syndrome score in adulthood, although the effects were small. These associations were statistically significant for the ‘most unhealthy’ cluster and the ‘breakfast skippers’ cluster but not for the ‘high physical activity’ cluster. Adjustment for adult healthy lifestyle score did not affect these associations (model 2). Additional adjustments for parental and own highest level of education (model 3) slightly attenuated the results and the association between the ‘breakfast skippers’ cluster and adult metabolic syndrome score was no longer significant.

Among the five component indicators of the metabolic syndrome score, waist circumference was the only indicator significantly associated with the cluster patterns of childhood CVD behavioural risk factors (Table 4). Compared to the participants in the ‘most healthy’ cluster, participants in the ‘most unhealthy’ cluster and the ‘breakfast skippers’ cluster had a significantly larger waist circumference. The associations were slightly attenuated after adjustment for adult healthy lifestyle score, parental and own highest level of education, but remained significant.

Sensitivity analyses

The longitudinal associations between the cluster patterns of childhood CVD behavioural risk factors, adult metabolic syndrome score and waist circumference were very similar between the sensitivity analyses (inverse probability weighting) and the complete case analyses (see Supplementary Table S2). In some cases, the associations were slightly stronger in the sensitivity analyses compared to the complete case analyses, suggesting that loss to follow-up was not a major source of bias and the magnitude of effects may have been underestimated.

Table 3. Adjusted beta coefficients and 95% confidence intervals for associations between the cluster patterns of child (aged 9-15 years) CVD behavioural risk factors and adult (aged 26-36 years) metabolic syndrome score

Risk factors		Clusters			
		Most Healthy (n=580)	High PA (n=103)	Most Unhealthy (n=417)	Breakfast Skippers (n=169)
Metabolic syndrome score ^a , β (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	0.11 (-0.04, 0.26)	0.12 (0.03, 0.21)	0.13 (0.01, 0.26)
2	M1+adult HLS	Reference	0.11 (-0.04, 0.26)	0.12 (0.02, 0.21)	0.13 (0.01, 0.25)
3	M2+education	Reference	0.09 (-0.06, 0.24)	0.10 (0.01, 0.19)	0.11 (-0.01, 0.24)

Abbreviations: BMI, Body Mass Index; WC, waist circumference; CI, confidence interval; HLS, healthy lifestyle score

Model 1: Adjusted for sex, age, baseline BMI and baseline waist circumference

Model 2: Model 1 + adult healthy lifestyle score

Model 3: Model 2 + parental and own highest level of education

^aA higher metabolic syndrome score indicates an increased cardio-metabolic risk

Table 4. Adjusted beta coefficients and 95% confidence intervals or relative risks and 95% confidence intervals between the cluster patterns of child (aged 9-15 years) behavioural risk factors and the adult (aged 26-36 years) metabolic syndrome score components

Components of the metabolic syndrome score		Clusters			
		Most Healthy (n=580)	High PA (n=102)	Most Unhealthy (n=219)	Breakfast Skippers (n=169)
Waist Circumference, β (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	1.04 (-1.23, 3.32)	2.56 (1.17, 3.96)	2.53 (0.66, 4.39)
2	M1+adult HLS	Reference	1.03 (-1.25, 3.31)	2.54 (1.15, 3.93)	2.50 (0.63, 4.36)
3	M2+education	Reference	0.66 (-1.60, 2.92)	2.23 (0.84, 3.61)	2.16 (0.30, 4.01)
Triglycerides, β (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	0.01 (-0.17, 0.18)	0.04 (-0.07, 0.14)	0.11 (-0.03, 0.25)
2	M1+adult HLS	Reference	0.01 (-0.17, 0.18)	0.03 (-0.08, 0.14)	0.10 (-0.04, 0.24)
3	M2+education	Reference	-0.01 (-0.18, 0.17)	0.02 (-0.09, 0.13)	0.10 (-0.05, 0.24)
HDL Cholesterol, β (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	-0.01 (-0.08, 0.05)	-0.02 (-0.06, 0.02)	-0.02 (-0.07, 0.04)
2	M1+adult HLS	Reference	-0.01 (-0.08, 0.05)	-0.02 (-0.06, 0.02)	-0.02 (-0.07, 0.04)
3	M2+education	Reference	-0.01 (-0.07, 0.06)	-0.02 (-0.06, 0.02)	-0.01 (-0.06, 0.04)
Glucose, β (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	0.02 (-0.07, 0.11)	0.01 (-0.05, 0.07)	-0.01 (-0.09, 0.06)
2	M1+adult HLS	Reference	0.02 (-0.07, 0.11)	0.01 (-0.05, 0.06)	-0.01 (-0.09, 0.06)
3	M2+education	Reference	0.02 (-0.07, 0.11)	0.01 (-0.05, 0.07)	-0.01 (-0.09, 0.07)
Elevated blood pressure, RR (95% CI)					
Model	Adjustment				
1	Sex, age, baseline BMI, baseline WC	Reference	1.05 (0.71, 1.55)	1.00 (0.77, 1.29)	1.21 (0.88, 1.68)
2	M1+adult HLS	Reference	1.06 (0.72, 1.58)	0.99 (0.76, 1.27)	1.18 (0.85, 1.64)
3	M2+education	Reference	1.05 (0.71, 1.55)	0.96 (0.75, 1.24)	1.16 (0.84, 1.60)

Abbreviations: BMI, Body Mass Index; WC, waist circumference; CI, confidence interval; HLS, healthy lifestyle score

Model 1: Adjusted for sex, age, baseline BMI and baseline waist circumference

Model 2: Model 1 + adult healthy lifestyle score

Model 3: Model 2 + parental and own highest level of education

Discussion

To our knowledge, this is the first study to examine the prospective associations of child CVD behavioural risk factor cluster patterns on adult cardio-metabolic risk factors. The study identified four distinct CVD behavioural risk factor cluster patterns among children and found that the unhealthier clusters in childhood ('most unhealthy' and 'breakfast skippers') were significantly associated with a higher metabolic syndrome score and a larger waist circumference in adulthood. While these associations were slightly attenuated after adjustment for adult CVD behavioural risk factors, parental education and own highest level of education, they remained significant. These findings emphasise the impact of multiple childhood CVD behavioural risk factors on adult health outcomes, irrespective of adult behaviours. As such, early behavioural and lifestyle interventions for high-risk children and adolescents may be beneficial to decrease overall cardiovascular risk and prevent the progression of CVD in adulthood.

The association between the childhood behavioural cluster patterns and adult metabolic syndrome score (in the current study) was largely explained by waist circumference (one component of the score). There were no associations between the unhealthier clusters in childhood and other cardio-metabolic risk factors in adulthood, such as blood pressure, triglycerides, HDL cholesterol and fasting plasma glucose (the other four components of the metabolic syndrome score). One explanation for this, is that metabolic syndrome is thought to be mainly a consequence of abdominal obesity, with central fatness being a well-recognised trigger of the syndrome, which is strongly associated with insulin resistance/hyperinsulinemia, dyslipidemia, and hypertension (Ferreira et al., 2005; Schmidt et al., 2011; Srinivasan et al., 2002). A study by Ferreira et al. (2005) that investigated potential determinants (including fatness, cardiopulmonary fitness and lifestyle variables) of metabolic syndrome from adolescence to adulthood also found that of all the determinants explored, an increase in total and central fatness from adolescence to adulthood was critical in the development of metabolic syndrome. As such, interventions and prevention strategies should target weight control (including the associated modifiable lifestyle risk factors), particularly in childhood, to prevent the development of metabolic syndrome and its complications, such as cardiovascular disease and type 2 diabetes.

The longitudinal associations between the unhealthier clusters ('most unhealthy' and 'breakfast skippers') in childhood and a higher waist circumference and metabolic syndrome score in adulthood were independent of adult behavioural risk factors. This suggests that there is long-lasting impact of childhood behavioural risk factors on adult health outcomes. There is a considerable amount of evidence to suggest that dietary, physical activity, smoking and alcohol consumption habits are formed in childhood and adolescence and often track into adulthood (Craigie et al., 2011; Gordon-Larsen et al., 2004; Kelder et al., 1994; Lake et al., 2006; Mikkilä et al., 2005; Nelson et al., 2008). Earlier work has also shown that the uptake of heavy alcohol consumption, substance use and smoking primarily occurs in adolescence and those who engage in these behaviours in adolescence are more likely to continue them into adulthood (Tucker et al., 2005). In contrast, if adolescents do not engage in these behaviours at this stage of their lives they are less likely to engage in them beyond adolescence (Tucker et al., 2005). Furthermore, the results of the current study show that collecting healthy behaviours as a child is also important for adult cardio-metabolic risk factors, and better than one unhealthy behaviour such as "skipping breakfast".

This study has limitations that should be taken into account when interpreting the results. The large loss to follow-up and the proportion of participants excluded from the analyses because of missing data may limit the generalizability of the current study; however, the sample was similar to the general population for several key health behaviours and the inverse probability weighting analyses demonstrated that the magnitude of effects may have been underestimated in some instances, by having a cohort that comprised adults of higher socioeconomic position. It is also important to note that measurement error (self-reported physical activity, diet included in the healthy lifestyle score) may explain why adult CVD behavioural risk factors did not account for the associations that were found between the cluster patterns of childhood CVD behavioural risk factors and adult cardio-metabolic risk factors, although reliable and valid measures were used.

The key strength of this study is that it is the first study to comprehensively examine the prospective associations of child CVD behavioural risk factor cluster patterns on adult cardio-metabolic risk factors. Previous clustering studies tend to be descriptive and cross-sectional in nature, meaning little is known about the long-term relationship of clustering patterns on adult health outcomes. Other strengths include the large national sample of both males and females, the outcome measures taken by trained staff using standardised protocols

(minimising possibility of measurement error), and measures of a wide range of socio-demographic and other lifestyle factors that were included in our models to reduce possible confounding.

Conclusion

This is the first study internationally to show that unhealthier cluster patterns of CVD behavioural risk factors in childhood were significantly associated with a higher adult metabolic syndrome score and a larger adult waist circumference. These associations were independent of adult CVD behavioural risk factors, parental and own highest level of education, indicating that risk behaviours in childhood and adolescence may play a critical role in the development of adult cardio metabolic disease. These findings may be useful for the development of early intervention strategies, where identification of children at higher risk of poorer adult cardio-metabolic health is vital. They may also be useful for informing the development of holistic, tailored interventions that target multiple relevant behaviours (rather than single behaviours) in childhood. Doing so may decrease overall cardiovascular risk and prevent the progression of cardio-vascular disease in adulthood.

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Competing interests

The authors declare that they have no competing interests.

References

Alberti, K., Eckel, R.H., Grundy, S.M., Zimmet, P.Z., Cleeman, J.I., Donato, K.A., Fruchart, J.-C., James, W.P.T., Loria, C.M., et al., 2009. Harmonizing the metabolic syndrome: a joint interim statement of the international diabetes federation task force on epidemiology and prevention; national heart, lung, and blood institute; American heart association; world heart federation; international atherosclerosis society; and international association for the study of obesity. *Circulation* 120:1640-45.

Australian Bureau of Statistics, 2004-2005. National health survey: summary of results. Australian Bureau of Statistics, Canberra.

Australian Bureau of Statistics, 2006. Census of population and Housing table. Australia Bureau of Statistics, Canberra.

Australian Bureau of Statistics, 2013. Australian health survey: Physical activity, 2011–12. Australian Bureau of Statistics, Canberra.

Australian Bureau of Statistics, 2015. National health survey: First results, 2014-15. Children's risk factors. Australian Bureau of Statistics, Canberra.

Australian Institute of Health and Welfare, 2011. Young Australians: Their health and wellbeing 2011. Australian Institute of Health and Welfare, Canberra.

Australian Institute of Health and Welfare, 2012. A picture of Australia's children 2012. Australian Institute of Health and Welfare, Canberra.

Baer, H.J., Glynn, R.J., Hu, F.B., Hankinson, S.E., Willett, W.C., Colditz, G.A., Stampfer, M., Rosner, B., 2011. Risk factors for mortality in the nurses' health study: a competing risks analysis. *Am. J. Epidemiol.* 173:319-29.

Berrigan, D., Dodd, K., Troiano, R.P., Krebs-Smith, S.M., Barbash, R.B., 2003. Patterns of health behavior in US adults. *Prev. Med.* 36:615-23.

Bunker, S.J., Colquhoun, D.M., Esler, M.D., Hickie, I.B., Hunt, D., Jelinek, V.M., Oldenburg, B.F., Peach, H.G., Ruth, D., et al., 2003. "Stress" and coronary heart disease: psychosocial risk factors. *Med. J. Aust.* 178:272-6.

Cole, T.J., Bellizzi, M.C., Flegal, K.M., Dietz, W.H., 2000. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 320:1240.

Craigie, A.M., Lake, A.A., Kelly, S.A., Adamson, A.J., Mathers, J.C., 2011. Tracking of obesity-related behaviours from childhood to adulthood: a systematic review. *Maturitas* 70:266-84.

Department of Health, 2009. Chronic disease action plan for South Australia. Department of Health, South Australia.

Department of Health and Ageing, Department of Agriculture Fisheries and Forestry, Australian Food and Grocery Council, 2007. Australian national children's nutrition and physical activity survey: Main findings. Commonwealth of Australia, Canberra.

Ferreira, I., Twisk, J.W., van Mechelen, W., Kemper, H.C., Stehouwer, C.D., 2005. Development of fatness, fitness, and lifestyle from adolescence to the age of 36 years: determinants of the metabolic syndrome in young adults: the Amsterdam growth and health longitudinal study. *Arch. Intern. Med.* 165:42-48.

Folsom, A.R., Yatsuya, H., Nettleton, J.A., Lutsey, P.L., Cushman, M., Rosamond, W.D., 2011. Community prevalence of ideal cardiovascular health, by the American Heart Association definition, and relationship with cardiovascular disease incidence. *J. Am. Coll. Cardiol.* 57:1690-96.

Ford, E.S., Bergmann, M.M., Boeing, H., Li, C., Capewell, S., 2012. Healthy lifestyle behaviors and all-cause mortality among adults in the United States. *Prev. Med.* 55:23-27.

French, S., Rosenberg, M., Knuiman, M., 2008. The clustering of health risk behaviours in a Western Australian adult population. *Health Promotion Journal of Australia* 19:203-09.

Gall, S.L., Abbott-Chapman, J., Patton, G.C., Dwyer, T., Venn, A., 2010. Intergenerational educational mobility is associated with cardiovascular disease risk behaviours in a cohort of young Australian adults: The Childhood Determinants of Adult Health (CDAH) Study. *BMC Public Health* 10:1.

Gall, S.L., Jamrozik, K., Blizzard, L., Dwyer, T., Venn, A., 2009. Healthy lifestyles and cardiovascular risk profiles in young Australian adults: the Childhood Determinants of Adult Health Study. *European Journal of Cardiovascular Prevention & Rehabilitation* 16:684-89.

Gall, S.L., Jose, K., Smith, K., Dwyer, T., Venn, A., 2009. The Childhood Determinants of Adult Health Study: a profile of a cohort study to examine the childhood influences on adult cardiovascular health. *Australasian Epidemiologist* 16:35.

Gordon-Larsen, P., Nelson, M.C., Popkin, B.M., 2004. Longitudinal physical activity and sedentary behavior trends: adolescence to adulthood. *Am. J. Prev. Med.* 27:277-83.

Hallal, P.C., Andersen, L.B., Bull, F.C., Guthold, R., Haskell, W., Ekelund, U., 2012. Global physical activity levels: surveillance progress, pitfalls, and prospects. *The lancet* 380:247-57.

Han, J., Pei, J., Kamber, M., 2011. *Data mining: concepts and techniques*. Elsevier.

Hardy, L., King, L., Espinel, P., Cosgrove, C., Bauman, A., 2013. *NSW Schools Physical Activity and Nutrition Survey (SPANS) 2010: Full Report*. NSW Ministry of Health, NSW.

James, P.A., Oparil, S., Carter, B.L., Cushman, W.C., Dennison-Himmelfarb, C., Handler, J., Lackland, D.T., LeFevre, M.L., MacKenzie, T.D., et al., 2014. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 311:507-20.

Jousilahti, P., Tuomilehto, J., Vartiainen, E., Korhonen, H.J., Pitkaniemi, J., Nissinen, A., Puska, P., 1995. Importance of risk factor clustering in coronary heart disease mortality and incidence in eastern Finland. *J. Cardiovasc. Risk* 2:63-70.

Kelder, S.H., Perry, C.L., Klepp, K.-I., Lytle, L.L., 1994. Longitudinal tracking of adolescent smoking, physical activity, and food choice behaviors. *Am. J. Public Health* 84:1121-26.

Khaw, K.-T., Wareham, N., Bingham, S., Welch, A., Luben, R., Day, N., 2008. Combined impact of health behaviours and mortality in men and women: the EPIC-Norfolk prospective population study. *PLoS Med* 5:e12.

Krieger, N., Okamoto, A., Selby, J.V., 1998. Adult female twins' recall of childhood social class and father's education: a validation study for public health research. *Am. J. Epidemiol.* 147:704-08.

Lake, A.A., Mathers, J.C., Rugg-Gunn, A.J., Adamson, A.J., 2006. Longitudinal change in food habits between adolescence (11–12 years) and adulthood (32–33 years): the ASH30 Study. *Journal of Public Health* 28:10-16.

Leech, R.M., McNaughton, S.A., Timperio, A., 2014. The clustering of diet, physical activity and sedentary behavior in children and adolescents: a review. *International Journal of Behavioral Nutrition and Physical Activity* 11:1.

Lidfeldt, J., Li, T.Y., Hu, F.B., Manson, J.E., Kawachi, I., 2007. A prospective study of childhood and adult socioeconomic status and incidence of type 2 diabetes in women. *Am. J. Epidemiol.* 165:882-89.

Lim, S.S., Vos, T., Flaxman, A.D., Danaei, G., Shibuya, K., Adair-Rohani, H., AlMazroa, M.A., Amann, M., Anderson, H.R., et al., 2013. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. *The lancet* 380:2224-60.

Loef, M., Walach, H., 2012. The combined effects of healthy lifestyle behaviors on all cause mortality: a systematic review and meta-analysis. *Prev. Med.* 55:163-70.

Lynch, J.W., Kaplan, G.A., Cohen, R.D., Wilson, T.W., Smith, N., Kauhanen, J., Salonen, J.T., 1994. Childhood and adult socioeconomic status as predictors of mortality in Finland. *The Lancet* 343:524-27.

MacMahon, S., Peto, R., Collins, R., Godwin, J., Cutler, J., Sorlie, P., Abbott, R., Neaton, J., Dyer, A., et al., 1990. Blood pressure, stroke, and coronary heart disease: part 1, prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. *The Lancet* 335:765-74.

Martin-Diener, E., Meyer, J., Braun, J., Tarnutzer, S., Faeh, D., Rohrmann, S., Martin, B.W., 2014. The combined effect on survival of four main behavioural risk factors for non-communicable diseases. *Prev. Med.* 65:148-52.

McDowell, I., 2010. Measures of self-perceived well-being. *J. Psychosom. Res.* 69:69-79.

McDowell, I., Praught, E., 1982. On the measurement of happiness: an examination of the Bradburn Scale in the Canada Health Survey. *Am. J. Epidemiol.* 116:949-58.

McKercher, C., Sanderson, K., Schmidt, M.D., Otahal, P., Patton, G.C., Dwyer, T., Venn, A.J., 2014. Physical activity patterns and risk of depression in young adulthood: a 20-year cohort study since childhood. *Soc. Psychiatry Psychiatr. Epidemiol.* 49:1823-34.

McKercher, C., Schmidt, M.D., Sanderson, K., Dwyer, T., Venn, A.J., 2012. Physical activity and depressed mood in primary and secondary school-children. *Mental Health and Physical Activity* 5:50-56.

Mikkilä, V., Räsänen, L., Raitakari, O., Pietinen, P., Viikari, J., 2005. Consistent dietary patterns identified from childhood to adulthood: the cardiovascular risk in Young Finns Study. *Br. J. Nutr.* 93:923-31.

Nelson, M.C., Story, M., Larson, N.I., Neumark-Sztainer, D., Lytle, L.A., 2008. Emerging adulthood and college-aged youth: an overlooked age for weight-related behavior change. *Obesity* 16:2205-11.

Northstone, K., Emmett, P.M., 2008. Are dietary patterns stable throughout early and mid-childhood? A birth cohort study. *Br. J. Nutr.* 100:1069-76.

Poortinga, W., 2007. The prevalence and clustering of four major lifestyle risk factors in an English adult population. *Prev. Med.* 44:124-8.

Power, C., Graham, H., Due, P., Hallqvist, J., Joung, I., Kuh, D., Lynch, J., 2005. The contribution of childhood and adult socioeconomic position to adult obesity and smoking behaviour: an international comparison. *Int. J. Epidemiol.* 34:335-44.

Pyke, J.E., 1985. Australian Health and Fitness Survey 1985. The Australian Council for Health, Physical Education and Recreation Adelaide, SA.

Ruxton, C.H., Kirk, T.R., 1997. Breakfast: a review of associations with measures of dietary intake, physiology and biochemistry. *Br. J. Nutr.* 78:199-213.

Schmidt, M., Dwyer, T., Magnussen, C., Venn, A., 2011. Predictive associations between alternative measures of childhood adiposity and adult cardio-metabolic health. *Int. J. Obes.* 35:38-45.

Schmidt, M.D., Cleland, V.J., Shaw, K., Dwyer, T., Venn, A.J., 2009. Cardiometabolic risk in younger and older adults across an index of ambulatory activity. *Am. J. Prev. Med.* 37:278-84.

Singh, G.M., Danaei, G., Farzadfar, F., Stevens, G.A., Woodward, M., Wormser, D., Kaptoge, S., Whitlock, G., Qiao, Q., et al., 2013. The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PloS one* 8:e65174.

Smith, G.D., Hart, C., Blane, D., Hole, D., 1998. Adverse socioeconomic conditions in childhood and cause specific adult mortality: prospective observational study. *BMJ* 316:1631-35.

- Spencer, C.A., Jamrozik, K., Norman, P.E., Lawrence-Brown, M., 2005. A simple lifestyle score predicts survival in healthy elderly men. *Prev. Med.* 40:712-17.
- Spring, B., Moller, A.C., Coons, M.J., 2012. Multiple health behaviours: overview and implications. *Journal of Public Health* 34:i3-i10.
- Srinivasan, S.R., Myers, L., Berenson, G.S., 2002. Predictability of childhood adiposity and Insulin for developing insulin resistance syndrome (syndrome X) in young adulthood the bogalusa heart study. *Diabetes* 51:204-09.
- Stewart, T., Yusim, A., Desan, P., 2005. Depression as a risk factor for cardiovascular disease. *Prim Psychiatry* 12:36-41.
- Telama, R., Yang, X., Viikari, J., Välimäki, I., Wanne, O., Raitakari, O., 2005. Physical activity from childhood to adulthood: a 21-year tracking study. *Am. J. Prev. Med.* 28:267-73.
- Tucker, J.S., Ellickson, P.L., Orlando, M., Martino, S.C., Klein, D.J., 2005. Substance use trajectories from early adolescence to emerging adulthood: A comparison of smoking, binge drinking, and marijuana use. *Journal of Drug Issues* 35:307-32.
- Van Dam, R.M., Li, T., Spiegelman, D., Franco, O.H., Hu, F.B., 2008. Combined impact of lifestyle factors on mortality: prospective cohort study in US women. *BMJ* 337:a1440.
- Verschuren, W.M., Jacobs, D.R., Bloemberg, B.P., Kromhout, D., Menotti, A., Aravanis, C., Blackburn, H., Buzina, R., Dontas, A.S., et al., 1995. Serum total cholesterol and long-term coronary heart disease mortality in different cultures: Twenty-five—year follow-up of the seven countries study. *JAMA* 274:131-36.
- Wang, H., Naghavi, M., Allen, C., Barber, R.M., Bhutta, Z.A., Carter, A., Casey, D.C., Charlson, F.J., Chen, A.Z., et al., 2016. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *The Lancet* 388:1459-544.

Wijndaele, K., Beunen, G., Duvigneaud, N., Matton, L., Duquet, W., Thomis, M., Lefevre, J., Philippaerts, R.M., 2006. A Continuous Metabolic Syndrome Risk Score Utility for epidemiological analyses. *Diabetes Care* 29:2329-29.

Wilson, P.W., Kannel, W.B., Silbershatz, H., D'Agostino, R.B., 1999. Clustering of metabolic factors and coronary heart disease. *Arch. Intern. Med.* 159:1104-09.