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Cardio-metabolic Risk Variables in Pre-Adolescent Children: A Factor Analysis

Running Title: Cardio-metabolic pattern analysis in Children

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ABSTRACT

Background: Atherosclerosis begins during pre-adolescence and is occurring at an accelerated rate. This acceleration has been linked to poor lifestyle behaviors and subsequent cardio-metabolic complications. Although the clustering of cardio-metabolic risk factors has been recognized for over two decades, previous studies in children have predominantly examined the relationships between atherosclerosis and individual cardio-metabolic risk factors, or have grouped together pre-adolescent and adolescent children. Further, no known studies have included glycosylated haemoglobin (HbA1c), or central hemodynamic measures such as central systolic blood pressure (cSBP) and augmentation index (AIx). **Methods and Results:** Principal component analysis was performed on a cross-sectional sample of 392 children (9.5 y, 50% F) from three representative sample sites across New Zealand. Four factors explained 60% of the variance in the measured variables. In order of variance explained, the factors were: blood pressure (cSBP, peripheral systolic and diastolic blood pressure), adiposity (waist circumference, body mass index, HbA1c), lipids (total cholesterol, low-density lipoproteins, high-density lipoproteins) and vascular (AIx, heart rate, fasting blood glucose [FBG]). **Conclusions:** In accordance with previous findings in adults and adolescents, one common factor is unlikely to define cardio-metabolic health in pre-adolescent children. Each of the factors, except vascular, which was predominantly explained by AIx, are in agreement with previous findings in adolescents. An additional novel finding was that HbA1c and FBG loaded on to different factors, supporting previous work suggesting that FBG indicates short-term glycemic control whereas HbA1c reflects chronic glycemic control. **Clinical Trial Registration:** ID: ACTRN12614000433606, URL: www.anzctr.org.au/Trial/Registration/TrialReview.aspx?id=366098

KEY WORDS: cardiovascular; principal components analysis; obesity; glycated hemoglobin; pulse wave analysis

CLINICAL PERSPECTIVE

What is new?

- This study investigated the clustering of 13 cardiometabolic variables in pre-adolescent children.
- Several novel cardiometabolic variables were included: glycosylated haemoglobin, central blood pressure, and augmentation index.
- Findings are generally in accordance with those for adolescent and adults.
- However, the inclusion of augmentation index resulted in a novel factor.
- Additionally, glycosylated haemoglobin and fasting blood glucose loaded on to different factors.

What are the clinical implications?

- One common factor is unlikely to define cardio-metabolic health in pre-adolescent children.
- Augmentation index is a novel risk factor.
- Glycosylated haemoglobin and fasting blood glucose provide different information.
- The identified factors may enable the early identification of at-risk populations, and help in the design of longitudinal studies.

INTRODUCTION

The clinical manifestations of cardiovascular disease (CVD) typically appear during middle-age, but the underlying atherosclerotic process has a long asymptomatic phase of development that often starts during early childhood, and it seems likely that this process is occurring at an increasingly younger age.[1-3] Accelerated progression of atherosclerosis is linked to poor lifestyle behaviours, which in turn also contribute to cardio-metabolic risk factors, including obesity.[3-5] The clustering of cardio-metabolic risk factors has been recognized for over two decades[6] but past studies in children mainly explore associations between atherosclerosis and individual cardio-metabolic risk factors, rather than overall cardio-metabolic risk.[1, 2] Relatively few studies report details of the clustering of components of cardio-metabolic components in children.[7-14] Further, the majority of these studies group together pre-adolescents and adolescents together.[7-10] In addition, we were unable to identify studies of this kind that have included glycosylated haemoglobin (HbA1c), central hemodynamic measures such as central systolic blood pressure (cSBP), or a measurement of arterial wave reflection such as the augmentation index (AIx).

Studies which explore clustering of cardio-metabolic risk factors in children or adolescents have included fasting blood glucose (FBG),[10-12] which is a standard component for defining metabolic syndrome in adults and in children aged ten years and older.[15] However, FBG indicates short-term glycaemic control,[16] whereas HbA1c reflects chronic glycaemic control.[17] Findings in adults suggest that HbA1c and FBG have different patterns of association with cardiovascular risk profiles.[18] For example, HbA1c is more strongly associated with increased risk of cardiovascular events than FBG.[19, 20] We could identify no studies that explored whether Hb1Ac and FBG are differentially associated with cardiovascular risk profiles in children.

Although past research in this area has included peripheral blood pressure when examining cardio-metabolic risk clustering in children[10-12] this may not accurately reflect the effects of peak arterial blood pressure on centrally located organs.[21] The prognostic value of cSBP has been recognized by expert consensus,[22, 23] and a meta-analysis [24] reports that cSBP is more strongly associated with the risk of future cardiovascular events than peripheral blood pressure. Furthermore, the degree of central pressure augmentation, AIx, also predicts future cardiovascular

events and all-cause mortality in models that also adjust for peripheral or central blood pressure.[25, 26] The advent of oscillometric pulse wave analysis (PWA) devices permit measures of cSBP and AIx relatively simply, accurately[27], and precisely.[28]

The aims of the study reported here are to explore: (1) underlying factors associated with individual cardio-metabolic risk factors in pre-adolescents using principal components analysis; (2) the unique value of Hb1Ac, cSBP and AIx in these factors; and finally (3) the associations between being overweight or obese in pre-adolescent children in relation to these underlying factors. Considering the atherosclerotic process often begins during childhood, and cardio-metabolic risk factors tend to cluster, findings from this study may enable the early identification of at-risk populations, and may help in the design of longitudinal studies of trajectories of cardiometabolic risk

METHODS

This non-experimental observational study was carried out in accordance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.[29]

PARTICIPANTS AND STUDY DESIGN

Children aged between 8 and 10 years of age were recruited from schools in three major cities in New Zealand (NZ): Wellington, Christchurch and Dunedin. In New Zealand nearly all schools are publicly funded and currently classified by the predominant socioeconomic status of attending students in a decile classification system. Funding for schools is partly determined by this system so that schools with pupils from deprived areas, Decile 1, attract more funding than those from those from wealthy areas, Decile 10. In order to recruit children from a variety of socioeconomic backgrounds, schools within the three cities were stratified by high (6-10) or low (1-5) Decile. Schools were randomly sampled from within these strata to approach for participation. Within schools all children in the appropriate age range were eligible for participation, except those prescribed any cardiovascular medications, or with an orthopedic injury in the past three months. Parental or guardian consent and child assent

were obtained before participation, in accordance with the requirements of the New Zealand Health and Disability Ethics Committee (14/CEN/83). The trial was prospectively registered with the Australia and New Zealand Clinical Trial Registry (ACTRN12614000433606).

The data, and analyses, described in this paper were part of a larger cross-sectional study of the associations between measurements of cardiac and metabolic variables and measurements related to physical performance, the Pre-Adolescent Cardio-Metabolic Associations and Correlates, 'PACMAC', and details of the larger study have been previously published.[30] All measurements described in this paper were assessed in the child participants' schools between 0900 and 1200 hours and children were asked to have been fasting for at least three hours and to have refrained from exercise for 24 hours before assessment.

ANTHROPOMETRIC AND BODY COMPOSITION

Body weight was assessed to the nearest 0.05 kg using an electric scale (A&D Instruments, Adelaide, Australia) and children were assessed in light clothing without shoes or other footwear, and height to the nearest 0.1 cm with a stadiometer, with children in bare feet (Surgical and Medical Products, Seven Hills, Australia). Waist circumference was measured using non-elastic tape (Seca, Germany), during mid-expiration at the midpoint between the lower costal margin and the level of the anterior superior iliac crest. Hip circumference was measured around the widest portion of the buttocks. Age and sex specific body mass index (BMI) z-scores were calculated using the 2007 WHO method,[31] and children were classified as overweight or obese if the BMI z-score was greater than one standard deviation above the age and sex specific mean. This is equivalent to a BMI of 25 kg/m^2 at age 19 years.[31]

PULSE WAVE ANALYSIS

Peripheral systolic blood pressure (SBP), peripheral diastolic blood pressure (DBP), SBP, and AIx were recorded using the BP+ device (Uscom, Sydney, Australia). The BP+ device incorporates an oscillometric blood pressure module, which complies with the Association for the Advancement of Medical Instrumentation (AAMI

SP10) requirements and receives an A/A rating from the British Hypertension Society evaluation protocol.[32] Following 20 minutes of undisturbed supine rest, oscillometric pressure waveforms were recorded by a single operator on the left upper arm, following standard manufacturer guidelines.[33] Each measurement cycle was approximately 40 seconds, consisting of a brachial blood pressure recording and then a 10 second supra-systolic recording. A corresponding aortic pressure waveform was generated using a validated transfer function, from which cSBP was estimated.[34] AIx was calculated from the suprasystolic waveform using the formula: $AIx = (P_3 – P_0) / (P_1 – P_0)$, where P_0 denotes the pressure at the onset of the pulse, P_1 the peak pressure of the incident wave, and P_3 the peak pressure of the reflective wave. This index describes the relative height of the reflected pressure wave when compared to the incident waveform. Only recordings with a high signal quality were accepted (sign to noise ratio of greater than 3dB), and two high signal quality measurements were taken within a five-minute interval. A third recording was taken, and the closest two recordings were averaged, if blood pressures differed by greater than 5 mmHg or the AIx by greater than 4%.[35]

CARDIAC AND METABOLIC MARKERS

Standard finger prick procedures were used to extract capillary blood for measurement of fasting total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TAG), and serum glucose (CardioChek PA, PTS Diagnostics, IN, USA)[36] and HbA1C (A1CNow+, PTS Diagnostics, IN, USA).[37]

STATISTICAL ANALYSIS

Statistical analyses were performed using Statistical Package for Social Sciences version 22 (SPSS, Inc., Chicago, Illinois) and HLM6 (Scientific Software International, Inc., Lincolnwood, Illinois). The corresponding author had full access to the data in the study and was responsible for the integrity of the data set and the data analysis. Only children with full data sets were included in the analyses.

Participant data are summarised by counts and proportions and mean and standard deviation for all participants and by sex.

Cardio-metabolic factors were derived from a principal components analysis of the variables: SBP, DBP, cSBP, waist circumference, BMI, triglyceride concentration, HbA1c, total cholesterol, LDL-cholesterol, HDL-cholesterol, AIx, and heart rate. The number of factors was determined by the minimum eigenvalue principle of a principal components analysis (PCA) of the correlation matrix. The number of factors was determined by the number of eigenvalues greater than one, the implication being that if an eigenvalue is less than one the derived dimension captures less variability in the data than any single variable. The principal components were then subject to orthogonal 'varimax' rotation and the factor loadings, the correlation between the derived factors and the underlying variables, were used to interpret each factor. We used a loading of greater than 0.40 to interpret the factor pattern. In the event (and as described in the results section) we identified four factors representing blood pressure, adiposity, lipids, and a vascular factor. From this factor structure we then derived a cardio-metabolic risk factor by summing the individual factors scores for each individual for the four factors as a summary risk score.

To determine whether overweight-obese status was associated with heightened risk for poor cardio-metabolic health, the individual factor scores and the summary risk score were then used as response variables in separate hierarchical linear models. Overweight-obesity status was specified as dummy coded variable (normal-weight = 0, overweight-obese = 1), using the 2007 WHO criteria,[31] as discussed above. In these models we also adjusted for age, sex, ethnicity and socioeconomic status (as indicated by the decile of the school the participants attended). Although the derived individual factors and the summed risk score represent cardio-metabolic indicators there is no natural interpretation of the differences in these factor scores in relation to the body weight indicator variable. Therefore, standardized effect sizes were estimated by dividing the pooled variance by the mean difference between groups, i.e., the beta for overweight-obesity. We used cut-points suggested by Cohen[38] of: 0.20, 0.50 and 0.80 to represent small, medium and large associations, respectively.

RESULTS

Study participants are described in Table 1. All children had complete data sets, and were included in the analyses.

Correlations among all variables are shown in Table 2, and the factor analysis is summarized in Table 3 and Figure 1. Using the minimum eigenvalue principle, of greater than one, four dimensions were retained in the factor analysis. The table shows the correlation of each variable with the four factors and these factors are labelled: a blood pressure factor, adiposity, lipids, and vascular factor. Collectively, the four factors explained 60% of the variance in the measured variables. The cSBP loaded positively on to the blood pressure factor, but no other factor. The HbA1c loaded positively on to the adiposity factor, whereas fasting blood glucose loaded positively on to the vascular factor. This is consistent with these two assessments of glycaemia (glucose for acute and HbA1c for chronic glycaemia) may be related to two different latent constructs, a vascular factor for glucose and adiposity for HbA1c. However, for the variables: triglycerides, HbA1c, and glucose; only a relatively small proportion of their variance, less than 40%, is explained by a four factor model.

The associations between weight status, overweight-obese (N=113) compared to not (N=279), with the individual factor scores and the cumulative risk score are shown in Table 4. Standardized effect sizes are also reported to illustrate the strength of association, as discussed in the methods. There is a medium and statistically significant association between the cumulative risk score and overweight-obesity status. Inspection of the individual factors reveals that, as might be anticipated, the strongest association was between the adiposity factor and overweight-obesity status. However, there was also a small but statistically significant association between the overweight-obesity status and the vascular factor. There was no important association with the lipid or blood pressure factors.

Table 5 presents example linear combinations for each factor, using one overweight and one normal-weight female child, both of which are 10 years old.

DISCUSSION

This results of the analysis of cardio-metabolic risk in this study suggests that one common factor does not fully explain cardio-metabolic health pre-adolescent children. Four factors were identified, blood pressure, adiposity,

cholesterol and vascular factors, of which the majority of the variance was explained by blood pressure. Each of these factors, except vascular, which was predominantly explained by AIx, are consistent with similar studies conducted in children[11-14] An additional novel finding was that HbA1c and FBG loaded on to different factors, supporting previous work suggesting that FBG indicates short-term glycaemic control,[16] whereas HbA1c reflects chronic glycaemic control.[17] Lastly, we found that overweight-obese children were more likely to have higher (worse) risk scores for the adiposity, vascular and cumulative risk scores.

STRENGTHS AND LIMITATIONS OF THIS STUDY

While our findings are internally robust, this study had several potential limitations. First, the majority of the participants were New Zealand European (Caucasian), and whether this factor structure would generalize to other population subgroups is unclear. Nonetheless, the proportion of Maori (9% vs. national: 14%) and Pacific (6% vs. national: 7%) participants are close to nationally representative.[39] Past reports from factor analysis studies with child participants have not identified important differences in factor patterns based on demographic characteristics.[13, 14] Second, our sample was recruited from three major cities, and did not recruit from rural areas, which may limit the generalizability of our findings. However, the three cities were geographically varied, and wide sample zones were utilized within these regions. Third, body composition was evaluated using typical epidemiological measures, including BMI and waist circumference. Subsequent investigation is warranted utilizing assessments which can distinguish fat- and fat-free mass, such as dual-energy X-ray absorptiometry or bio-impedance analysis. Finally, this was a cross-sectional study, and further longitudinal studies are needed to determine whether the identified factors present different pathological processes.

COMPARISON WITH OTHER STUDIES

Our findings are consistent with similar studies conducted in children,[11-14] each of which identified a blood pressure factor, three of which identified a lipids/cholesterol factor,[11, 12, 14] and two which identified adiposity.[11, 12] For the two studies that did not identify adiposity as a factor, only one adiposity variable (BMI) was specified, which did load on to two factors in one study,[11] and one factor only in the other study.[13] For the current analysis,

two body composition variables were specific, BMI and waist circumference, and only loaded on to one factor, using a cut point of 0.4. An important difference between the current analysis and past studies, is that cSBP, AIx, and Hb1Ac were included in the analysis. While cSBP loaded on to the blood pressure factor, the interpretation is not different from previous studies. However, AIx and HbA1c loadings do affect the interpretation of findings.

The AIx represents central arterial wave reflection, which depends primarily on aortic stiffness.[40] In young healthy subjects, the reflected wave arrives back at the ascending aorta during diastole, enhancing diastolic coronary perfusion. However, as the arterial system stiffens the pulse waves travel faster and gets reflected sooner, thereby arriving back at the ascending aorta during systole and augmenting central systolic blood pressure, and increasing afterload. The findings from this study indicate the AIx and blood pressure, including cSBP, represent different constructs, and that AIx may be an important cardiovascular measurement in children. In adults, a meta-analysis[24] of 11 longitudinal studies (n = 5,648, mean follow-up 45 m) reports that a 10% increase in AIx increases the risk of future cardiovascular events and all-cause mortality by 32% and 38%, respectively. In children, a limited number of studies have employed this methodology,[41-45] and findings from this study support the need to generate reference values relevant to children.

The finding that HbA1c loaded on the adiposity factor, while FBG loaded on to the vascular factor is consistent with research identifying that the these two variables reflect different underlying physiological constructs, with FBG reflecting short-term glycaemic control,[16] and HbA1c reflecting chronic glycaemic control.[17] The American Heart Association has recommended an ideal HbA1c of <5.55 mmol/L (100 mg/dL) for paediatric patients,[46] which was exceed by 16% (n=61) of the children in the current sample. However, there is evidence to suggest that hyper-insulinism is the first metabolic abnormality seen in obese paediatric patients, and impaired fasting glucose occurs at a much later stage in the progression toward type 2 diabetes mellitus.[47, 48] Further, in adults, HbA1c and FBG are also differentially associated with cardiovascular risk profiles,[18] with HbA1c being more strongly associated with increased risk of cardiovascular events than FBG.[19, 20] While the findings from the current study cannot corroborate

the previous findings in adults, both the adiposity (HbA1c) and vascular (FBG) factors were different for Overweight-Obese children compared to normal weight children.

In the current sample 29% (n=113) were overweight-obese. This is consistent with NZ national estimates of prevalence of 33%. The children were more likely to have higher (worse) risk scores for the adiposity (large effect), vascular (small effect) and cumulative risk scores (medium effect). These differences are striking because these children are pre-adolescent and otherwise healthy. This suggests that adiposity and vascular targets may be important for screening overweight-obese children, and refining their risk of future cardiovascular events.

IMPLICATIONS

This analysis indicates that the clustering of cardiometabolic risks variables can be used to derive summary factors and a cumulative risk score in pediatric populations. These factors and cumulative risk score may enable the early identification of at-risk populations, and may help in the design of longitudinal studies of trajectories of cardiometabolic risk.

CONCLUSIONS

The purpose of this study was to explore: (1) underlying factors that explain cardio-metabolic risk factors in pre-adolescents using principle components analysis; (2) the unique value of Hb1Ac, cSBP and AIx in these factors; and finally (3) the associations between being overweight or obese in pre-adolescent children in relation to these underlying factors. Four factors were identified, blood pressure, adiposity, cholesterol and vascular factors. Each of the factors, except vascular, which was predominantly explained by AIx, is consistent with similar studies conducted in children. An additional novel finding was that HbA1c and FBG loaded on to different factors, supporting previous work suggesting that FBG indicates short-term glycemic control whereas HbA1c reflects chronic glycemic control. Lastly, we found that overweight-obese children were more likely to have higher (worse) risk scores for the adiposity, vascular and cumulative risk scores. These findings suggest the identified factors and cumulative risk score may enable the early identification of at-risk populations, and help in the design of

longitudinal studies of trajectories of cardiometabolic risk.

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None.

AFFILIATIONS

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FIGURES

Figure1: Component plots with factor diagrams from principle component analysis with varimax rotation

AIx, augmentation index, DBP, diastolic blood pressure; HDL, high-density lipoprotein, HR, heart rate; HbA1c, glycosylated haemoglobin; LDL, low-density lipoprotein; whoBMI, body mass index (BMI) Z scores, calculated using the 2007 World Health Organization (WHO) method

TABLES

Table 1: Participant data description

Table 2: Correlation matrix of all variables

Abbreviations: cSBP, central systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoproteins; LDL, low-density lipoproteins; SBP, systolic blood pressure; TG, triglycerides

Table 3: Cardio-metabolic factor correlations and communalities

Table 4: Hierarchical linear model associations between overweight-obesity status and individual and cumulative cardio-metabolic risk derived from factor analysis

Effect sizes were estimated by dividing the pooled variance by the mean difference between groups

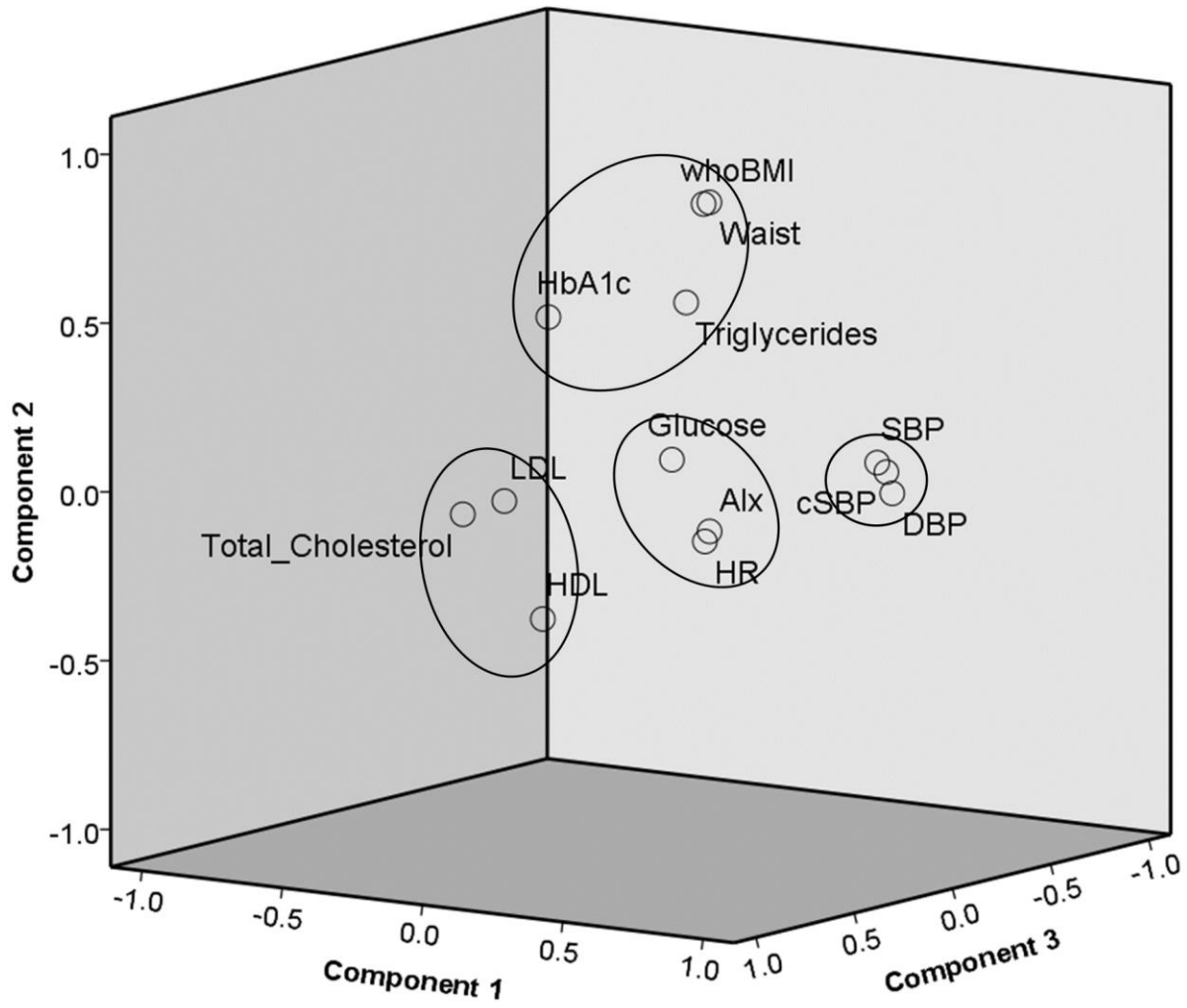
Adjusted model: age, sex, ethnicity and socioeconomic status

Abbreviations: Est., beta; SE, standard error; ES, standardized effect size

Table 5: Example linear combinations for each factor using one overweight-obese and one normal-weight female child, aged 10 years.

Note: Factor loadings shown in Table 2

1 Figure 1: Component plots with factor diagrams from principle component analysis with varimax rotation



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3 AIx, augmentation index, DBP, diastolic blood pressure; HDL, high-density lipoprotein, HR, heart rate; HbA1c,

4 glycosylated haemoglobin; LDL, low-density lipoprotein; whoBMI, body mass index (BMI) Z scores, calculated using

5 the 2007 World Health Organization (WHO) method

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1 Table 1: Participant data description

	All	Female	Male
Categorical variables	**N/392 (%)**	**N/197 (%)**	**N/195 (%)**
Ethnicity			
New Zealand European	279 (71)	135 (69)	144 (74)
Māori	37 (9)	21 (11)	16 (8)
Pacific	22 (6)	12 (6)	10 (5)
Not Recorded	54 (14)	29 (15)	25 (13)
School Year			
4	82 (21)	45 (23)	37 (19)
5	114 (29)	55 (28)	59 (30)
6	127 (32)	62 (31)	65 (33)
7	69 (18)	35 (18)	34 (17)
School Decile			
Low (≤5)	211 (54)	106 (54)	105 (54)
High (>5)	181 (46)	91 (46)	90 (46)
Obesity status			
Overweight	113 (29)	60 (30)	53 (27)
Non-Overweight	279 (71)	137 (70)	142 (73)
Continuous variables		**Mean (SD)**	
	All N=392	**Female N=197**	**Male N=195**
Body Mass Index (kg/m^2)	17.9 (3.25)	17.9 (3.1)	17.8 (3.4)
Age (years)	9.54 (1.1)	9.52 (1.16)	9.56 (1.04)
Waist Circumference (cm)	20.3 (9.39)	18.6 (9.1)	22 (9.37)
Systolic Blood Pressure (mmHg)	101 (7.91)	101 (8.21)	101 (7.61)
Diastolic Blood Pressure (mmHg)	61.7 (6.32)	62 (6.52)	61.4 (6.11)
Central Systolic Blood Pressure (mmHg)	93.2 (9.04)	93.2 (10.6)	93.3 (7.13)
Heart Rate (bpm)	74.8 (11.4)	77.5 (12.1)	72 (9.87)
Fasting Blood Glucose (mmol/L)	5.04 (0.38)	4.97 (0.37)	5.11 (0.38)
Glycated haemoglobin (%)	5.11 (0.31)	5.12 (0.32)	5.1 (0.31)
Total Cholesterol (mmol/L)	3.55 (0.6)	3.61 (0.56)	3.49 (0.62)
High-Density Lipoprotein Cholesterol (mmol/L)	1.47 (0.39)	1.42 (0.33)	1.52 (0.43)
Low-Density Lipoprotein Cholesterol (mmol/L)	1.85 (0.5)	1.91 (0.52)	1.79 (0.48)
Triglycerides (mmol/L)	0.88 (0.42)	0.91 (0.39)	0.84 (0.45)
Augmentation Index (%)	56 (15.9)	56.5 (16.7)	55.5 (15.2)

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3

Table 2: Correlation matrix of all variables

	BMI	Waist	SBP	DBP	HR	FBG	HbA1c	TC	HDL-C	LDL-C	TG	cSBP	AIx
BMI	1.000	.773	.262	.146	.024	.124	.101	-.098	-.218	-.072	.238	.168	-.201
Waist	-	1.000	.307	.240	-.011	.125	.151	-.071	-.208	-.019	.222	.205	-.201
SBP	-	-	1.000	.756	.259	.139	-.099	.052	.026	.051	.067	.736	.003
DBP	-	-	-	1.000	.243	.048	-.144	-.016	.015	.018	.072	.660	.116
HR	-	-	-	-	1.000	.116	-.075	.070	-.017	.017	.010	.127	-.210
FBG	-	-	-	-	-	1.000	-.011	-.082	-.051	-.026	-.036	-.031	-.085
HbA1c	-	-	-	-	-	-	1.000	.085	-.079	.001	.119	-.095	.056
TC	-	-	-	-	-	-	.085	1.000	.467	.501	.035	.005	-.021
HDL-C	-	-	-	-	-	-	-	-	1.000	.017	-.193	-.032	.023
TG	-	-	-	-	-	-	-	-	-	1.000	-.159	.002	.017
cSBP	-	-	-	-	-	-	-	-	-	-	1.000	.105	.023
cSBP	-	-	-	-	-	-	-	-	-	-	-	1.000	.115
AIx	-	-	-	-	-	-	-	-	-	-	-	-	1.000

Abbreviations: cSBP, central systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin; HDL, high-density lipoproteins; LDL, low-density lipoproteins; SBP, systolic blood pressure; TG, triglycerides

Table 3: Cardio-metabolic factor correlations and communalities

	Factor1 Blood Pressure	Factor2 Adiposity	Factor3 Lipids	Factor4 Vascular	Communality
Systolic Blood Pressure	**0.89**	0.14	0.07	0.16	0.85
Diastolic Blood Pressure	**0.89**	0.04	0.00	0.04	0.80
Central Systolic Blood Pressure	**0.87**	0.10	-0.01	-0.09	0.77
Waist Circumference	0.21	**0.82**	-0.05	0.25	0.79
Body Mass Index	0.15	**0.81**	-0.10	0.29	0.76
Triglycerides	0.08	**0.51**	-0.11	-0.22	0.32
Glycated haemoglobin	-0.23	**0.47**	0.14	-0.28	0.37
Total Cholesterol	0.01	0.02	**0.92**	-0.05	0.84
LDL-Cholesterol	0.01	0.03	**0.71**	0.01	0.50
HDL-Cholesterol	0.04	-0.34	**0.55**	-0.02	0.42
Augmentation Index	0.20	-0.16	-0.07	**-0.74**	0.61
Heart Rate	0.28	-0.16	0.07	**0.57**	0.43
Fasting Blood Glucose	0.03	0.04	-0.11	**0.50**	0.27
Eigenvalue	2.6	2.0	1.7	1.4	
% Variance Explained	20	15	13	11	
% Cumulative Variance	20	35	49	60	

Table 4: Hierarchical linear model associations between overweight-obesity status and individual and cumulative cardio-metabolic risk derived from factor analysis

	Unadjusted				Adjusted			
	Est.	SE	p	ES	Est.	SE	p	ES
Adiposity								
Intercept	-0.480	0.075	<0.001		-0.473	0.079	<0.001	
Overweight-Obese	1.459	0.083	<0.001	1.368	1.423	0.085	<0.001	1.282
Blood Pressure								
Intercept	0.019	0.128	0.885		0.017	0.135	0.905	
Overweight-Obese	0.173	0.108	0.108	0.105	0.159	0.110	0.150	0.093
Lipids								
Intercept	0.014	0.112	0.906		-0.006	0.111	0.956	
Overweight-Obese	-0.061	0.111	0.582	-0.040	-0.035	0.114	0.759	-0.023
Vascular								
Intercept	-0.115	0.118	0.355		-0.093	0.119	0.454	
Overweight-Obese	0.424	0.107	<0.001	0.274	0.403	0.109	<0.001	0.256
Cumulative								
Intercept	-0.569	0.184	0.013		-0.566	0.198	0.019	
Overweight-Obese	2.008	0.194	<0.001	0.782	1.996	0.198	<0.001	0.738

Adjusted model: age, sex, ethnicity and socioeconomic status

Abbreviations: Est., beta; SE, standard error; ES, standardized effect size

Effect sizes were estimated by dividing the pooled variance by the mean difference between groups

Table 5: Example linear combinations for each factor using one overweight-obese and one normal-weight female child, aged 10 years.

	Overweight (BMI: +2SD)					Normal-weight (BMI: -2SD)				
	Z score	BP	Adip.	Chol.	Vasc.	Z score	BP	Adip.	Chol.	Vasc.
Systolic Blood Pressure	-0.99	-0.89	-0.14	-0.07	-0.16	0.46	0.41	0.06	0.03	0.07
Diastolic Blood Pressure	-1.22	-1.09	-0.05	0.00	-0.04	0.76	0.68	0.03	0.00	0.03
Central Systolic Blood Pressure	-0.85	-0.74	-0.08	0.01	0.08	0.59	0.51	0.06	-0.01	-0.05
Waist Circumference	0.90	0.19	0.74	-0.04	0.23	-1.20	-0.25	-0.99	0.06	-0.30
Body Mass Index	1.29	0.20	1.04	-0.13	0.37	-2.13	-0.33	-1.72	0.21	-0.61
Triglycerides	0.10	0.01	0.05	-0.01	-0.02	-0.42	-0.04	-0.21	0.05	0.09
Glycated haemoglobin	0.29	-0.07	0.14	0.04	-0.08	-0.35	0.08	-0.16	-0.05	0.10
Total Cholesterol	-0.56	0.00	-0.01	-0.51	0.03	-0.28	0.00	0.00	-0.25	0.01
LDL-Cholesterol	-0.48	0.00	-0.01	-0.34	-0.01	-0.30	0.00	-0.01	-0.21	0.00
HDL-Cholesterol	-0.73	-0.03	0.25	-0.40	0.01	-0.26	-0.01	0.09	-0.14	0.01
Augmentation Index	-1.06	-0.21	0.17	0.07	0.78	0.82	0.16	-0.13	-0.06	-0.60
Heart Rate	-0.02	-0.01	0.00	0.00	-0.01	-0.37	-0.11	0.06	-0.03	-0.21
Fasting Blood Glucose	-0.37	-0.01	-0.01	0.04	-0.19	-1.15	-0.04	-0.04	0.13	-0.58
Linear combinations by factor										
Blood Pressure		-2.66					1.07			
Adiposity			2.08					-2.97		
Lipids				-1.35					-0.27	
Vascular					0.99					-2.05

Note: Factor loadings shown in Table 2