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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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1 ABSTRACT

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

20

21 **KEY WORDS:** cardiovascular; principal components analysis; obesity; glyated hemoglobin; pulse wave analysis

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23

24

1 **CLINICAL PERSPECTIVE**

2 What is new?

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

9

10 What are the clinical implications?

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

16

1 INTRODUCTION

2 The clinical manifestations of cardiovascular disease (CVD) typically appear during middle-age, but the underlying
3 atherosclerotic process has a long asymptomatic phase of development that often starts during early childhood,
4 and it seems likely that this process is occurring at an increasingly younger age.¹⁻³ Accelerated progression of
5 atherosclerosis is linked to poor lifestyle behaviours, which in turn also contribute to cardio-metabolic risk factors,
6 including obesity.³⁻⁵ The clustering of cardio-metabolic risk factors has been recognized for over two decades⁶ but
7 past studies in children mainly explore associations between atherosclerosis and individual cardio-metabolic risk
8 factors, rather than overall cardio-metabolic risk.^{1,2} Relatively few studies report details of the clustering of
9 components of cardio-metabolic components in children.⁷⁻¹⁴ Further, the majority of these studies group together
10 pre-adolescents and adolescents together.⁷⁻¹⁰ In addition, we were unable to identify studies of this kind that have
11 included glycosylated haemoglobin (HbA1c), central hemodynamic measures such as central systolic blood
12 pressure (cSBP), or a measurement of arterial wave reflection such as the augmentation index (AIx).

13
14 Studies which explore clustering of cardio-metabolic risk factors in children or adolescents have included fasting
15 blood glucose (FBG),¹⁰⁻¹² which is a standard component for defining metabolic syndrome in adults and in children
16 aged ten years and older.¹⁵ However, FBG indicates short-term glycaemic control,¹⁶ whereas HbA1c reflects chronic
17 glycaemic control.¹⁷ Findings in adults suggest that HbA1c and FBG have different patterns of association with
18 cardiovascular risk profiles.¹⁸ For example, HbA1c is more strongly associated with increased risk of cardiovascular
19 events than FBG.^{19,20} We could identify no studies that explored whether Hb1Ac and FBG are differentially
20 associated with cardiovascular risk profiles in children.

21
22 Although past research in this area has included peripheral blood pressure when examining cardio-metabolic risk
23 clustering in children¹⁰⁻¹² this may not accurately reflect the effects of peak arterial blood pressure on centrally
24 located organs.²¹ The prognostic value of cSBP has been recognized by expert consensus,^{22,23} and a meta-analysis
25 ²⁴ reports that cSBP is more strongly associated with the risk of future cardiovascular events than peripheral blood
26 pressure. Furthermore, the degree of central pressure augmentation, AIx, also predicts future cardiovascular

1 events and all-cause mortality in models that also adjust for peripheral or central blood pressure.^{25, 26} The advent
2 of oscillometric pulse wave analysis (PWA) devices permit measures of cSBP and Alx relatively simply, accurately²⁷,
3 and precisely.²⁸

4
5 The aims of the study reported here are to explore: (1) underlying factors associated with individual cardio-
6 metabolic risk factors in pre-adolescents using principal components analysis; (2) the unique value of Hb1Ac, cSBP
7 and Alx in these factors; and finally (3) the associations between being overweight or obese in pre-adolescent
8 children in relation to these underlying factors. Considering the atherosclerotic process often begins during
9 childhood, and cardio-metabolic risk factors tend to cluster, findings from this study may enable the early
10 identification of at-risk populations, and may help in the design of longitudinal studies of trajectories of
11 cardiometabolic risk

12

13 **METHODS**

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

16

17 PARTICIPANTS AND STUDY DESIGN

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

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

4
5 The data, and analyses, described in this paper were part of a larger cross-sectional study of the associations
6 between measurements of cardiac and metabolic variables and measurements related to physical performance,
7 the Pre-Adolescent Cardio-Metabolic Associations and Correlates, 'PACMAC', and details of the larger study have
8 been previously published.³⁰ All measurements described in this paper were assessed in the child participants'
9 schools between 0900 and 1200 hours and children were asked to have been fasting for at least three hours and to
10 have refrained from exercise for 24 hours before assessment.

11

12 ANTHROPOMETRIC AND BODY COMPOSITION

13 Body weight was assessed to the nearest 0.05 kg using an electric scale (A&D Instruments, Adelaide, Australia) and
14 children were assessed in light clothing without shoes or other footwear, and height to the nearest 0.1 cm with a
15 stadiometer, with children in bare feet (Surgical and Medical Products, Seven Hills, Australia). Waist circumference
16 was measured using non-elastic tape (Seca, Germany), during mid-expiration at the midpoint between the lower
17 costal margin and the level of the anterior superior iliac crest. Hip circumference was measured around the widest
18 portion of the buttocks. Age and sex specific body mass index (BMI) z-scores were calculated using the 2007 WHO
19 method,³¹ and children were classified as overweight or obese if the BMI z-score was greater than one standard
20 deviation above the age and sex specific mean. This is equivalent to a BMI of 25 kg/m² at age 19 years.³¹

21

22 PULSE WAVE ANALYSIS

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

1 SP10) requirements and receives an A/A rating from the British Hypertension Society evaluation protocol.³²
2 Following 20 minutes of undisturbed supine rest, oscillometric pressure waveforms were recorded by a single
3 operator on the left upper arm, following standard manufacturer guidelines.³³ Each measurement cycle was
4 approximately 40 seconds, consisting of a brachial blood pressure recording and then a 10 second supra-systolic
5 recording. A corresponding aortic pressure waveform was generated using a validated transfer function, from
6 which cSBP was estimated.³⁴ Alx was calculated from the suprasystolic waveform using the formula: $Alx = (P_3 - P_0)$
7 $/ (P_1 - P_0)$, where P_0 denotes the pressure at the onset of the pulse, P_1 the peak pressure of the incident wave, and
8 P_3 the peak pressure of the reflective wave. This index describes the relative height of the reflected pressure wave
9 when compared to the incident waveform. Only recordings with a high signal quality were accepted (signal to noise
10 ratio of greater than 3dB), and two high signal quality measurements were taken within a five-minute interval. A
11 third recording was taken, and the closest two recordings were averaged, if blood pressures differed by greater
12 than 5 mmHg or the Alx by greater than 4%.³⁵

13

14 CARDIAC AND METABOLIC MARKERS

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

18

19 STATISTICAL ANALYSIS

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

24

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

1
2 Cardio-metabolic factors were derived from a principal components analysis of the variables: SBP, DBP, cSBP, waist
3 circumference, BMI, triglyceride concentration, HbA1c, total cholesterol, LDL-cholesterol, HDL-cholesterol, Alx, and
4 heart rate. The number of factors was determined by the minimum eigenvalue principle of a principal components
5 analysis (PCA) of the correlation matrix. The number of factors was determined by the number of eigenvalues
6 greater than one, the implication being that if an eigenvalue is less than one the derived dimension captures less
7 variability in the data than any single variable. The principal components were then subject to orthogonal 'varimax'
8 rotation and the factor loadings, the correlation between the derived factors and the underlying variables, were
9 used to interpret each factor. We used a loading of greater than 0.40 to interpret the factor pattern. In the event
10 (and as described in the results section) we identified four factors representing blood pressure, adiposity, lipids,
11 and a vascular factor. From this factor structure we then derived a cardio-metabolic risk factor by summing the
12 individual factors scores for each individual for the four factors as a summary risk score.

13
14 To determine whether overweight-obese status was associated with heightened risk for poor cardio-metabolic
15 health, the individual factor scores and the summary risk score were then used as response variables in separate
16 hierarchical linear models. Overweight-obesity status was specified as dummy coded variable (normal-weight = 0,
17 overweight-obese = 1), using the 2007 WHO criteria,³¹ as discussed above. In these models we also adjusted for
18 age, sex, ethnicity and socioeconomic status (as indicated by the decile of the school the participants attended).
19 Although the derived individual factors and the summed risk score represent cardio-metabolic indicators there is
20 no natural interpretation of the differences in these factor scores in relation to the body weight indicator variable.
21 Therefore, standardized effect sizes were estimated by dividing the pooled variance by the mean difference
22 between groups, i.e., the beta for overweight-obesity. We used cut-points suggested by Cohen³⁸ of: 0.20, 0.50 and
23 0.80 to represent small, medium and large associations, respectively.

24

25 **RESULTS**

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

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

12
13 The associations between weight status, overweight-obese (N=113) compared to not (N=279), with the individual
14 factor scores and the cumulative risk score are shown in Table 4. Standardized effect sizes are also reported to
15 illustrate the strength of association, as discussed in the methods. There is a medium and statistically significant
16 association between the cumulative risk score and overweight-obesity status. Inspection of the individual factors
17 reveals that, as might be anticipated, the strongest association was between the adiposity factor and overweight-
18 obesity status. However, there was also a small but statistically significant association between the overweight-
19 obesity status and the vascular factor. There was no important association with the lipid or blood pressure factors.

20
21 Table 5 presents example linear combinations for each factor, using one overweight and one normal-weight
22 female child, both of which are 10 years old.

23

24 **DISCUSSION**

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

1 cholesterol and vascular factors, of which the majority of the variance was explained by blood pressure. Each of
2 these factors, except vascular, which was predominantly explained by A1c, are consistent with similar studies
3 conducted in children¹¹⁻¹⁴ An additional novel finding was that HbA1c and FBG loaded on to different factors,
4 supporting previous work suggesting that FBG indicates short-term glycaemic control,¹⁶ whereas HbA1c reflects
5 chronic glycaemic control.¹⁷ Lastly, we found that overweight-obese children were more likely to have higher
6 (worse) risk scores for the adiposity, vascular and cumulative risk scores.

7

8 STRENGTHS AND LIMITATIONS OF THIS STUDY

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

21

22 COMPARISON WITH OTHER STUDIES

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

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

5
6 The Alx represents central arterial wave reflection, which depends primarily on aortic stiffness.⁴⁰ In young healthy
7 subjects, the reflected wave arrives back at the ascending aorta during diastole, enhancing diastolic coronary
8 perfusion. However, as the arterial system stiffens the pulse waves travel faster and gets reflected sooner, thereby
9 arriving back at the ascending aorta during systole and augmenting central systolic blood pressure, and increasing
10 afterload. The findings from this study indicate the Alx and blood pressure, including cSBP, represent different
11 constructs, and that Alx may be an important cardiovascular measurement in children. In adults, a meta-analysis²⁴
12 of 11 longitudinal studies (n = 5,648, mean follow-up 45 m) reports that a 10% increase in Alx increases the risk of
13 future cardiovascular events and all-cause mortality by 32% and 38%, respectively. In children, a limited number of
14 studies have employed this methodology,⁴¹⁻⁴⁵ and findings from this study support the need to generate reference
15 values relevant to children.

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

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

3
4 In the current sample 29% (n=113) were overweight-obese. This is consistent with NZ national estimates of
5 prevalence of 33%. The children were more likely to have higher (worse) risk scores for the adiposity (large effect),
6 vascular (small effect) and cumulative risk scores (medium effect). These differences are striking because these
7 children are pre-adolescent and otherwise healthy. This suggests that adiposity and vascular targets may be
8 important for screening overweight-obese children, and refining their risk of future cardiovascular events.

9 10 IMPLICATIONS

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

15 16 CONCLUSIONS

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

1 longitudinal studies of trajectories of cardiometabolic risk.

2

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7 **CONFLICT(S) OF INTEREST/DISCLOSURE(S)**

8 None.

9 **AFFILIATIONS**

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- 3

1 FIGURES

2

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

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

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

6 the 2007 World Health Organization (WHO) method

7

8 TABLES

9 Table 1: Participant data description

10

11 Table 2: Correlation matrix of all variables

12 Abbreviations: cSBP, central systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin;

13 HDL, high-density lipoproteins; LDL, low-density lipoproteins; SBP, systolic blood pressure; TG, triglycerides

14

15 Table 3: Cardio-metabolic factor correlations and communalities

16

17 Table 4: Hierarchical linear model associations between overweight-obesity status and individual and cumulative

18 cardio-metabolic risk derived from factor analysis

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

20 Adjusted model: age, sex, ethnicity and socioeconomic status

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

22

23 Table 5: Example linear combinations for each factor using one overweight-obese and one normal-weight female

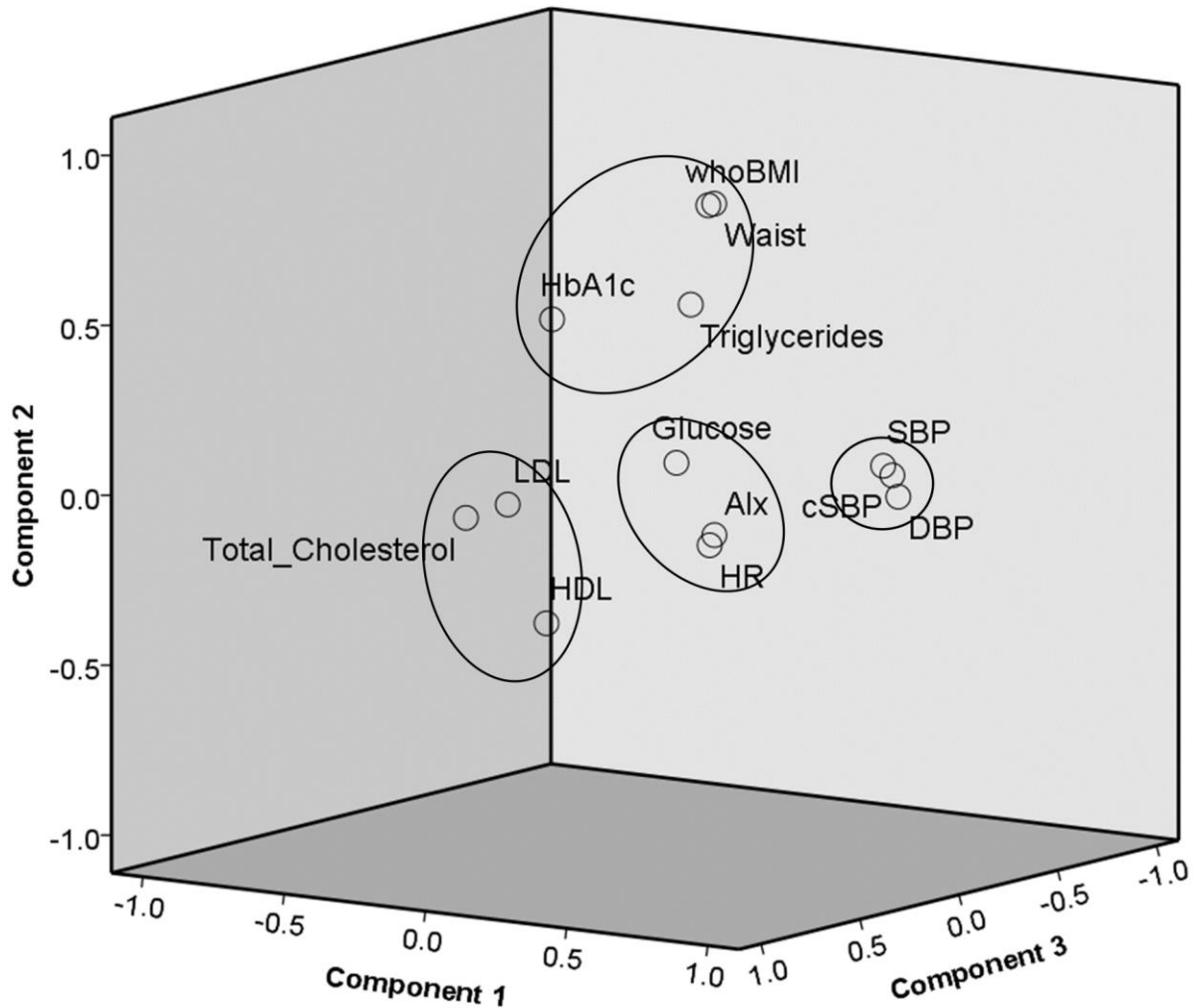
24 child, aged 10 years.

25 Note: Factor loadings shown in Table 2

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



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3 Alx, 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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7

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			
	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)

2

3

1 Table 2: Correlation matrix of all variables

	BMI	Waist	SBP	DBP	HR	FBG	HbA1c	TC	HDL-C	LDL-C	TG	cSBP	Alx
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
Alx	-	-	-	-	-	-	-	-	-	-	-	-	1.000

2

3 Abbreviations: cSBP, central systolic blood pressure; DBP, diastolic blood pressure; HbA1c, glycated hemoglobin;

4 HDL, high-density lipoproteins; LDL, low-density lipoproteins; SBP, systolic blood pressure; TG, triglycerides

5

1 Table 3: Cardio-metabolic factor correlations and communalities

	Factor1	Factor2	Factor3	Factor4	Communality
	Blood Pressure	Adiposity	Lipids	Vascular	
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	

2

3

4

1 Table 4: Hierarchical linear model associations between overweight-obesity status and individual and cumulative
 2 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

3 Adjusted model: age, sex, ethnicity and socioeconomic status

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

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

6

7

- 1 Table 5: Example linear combinations for each factor using one overweight-obese and one normal-weight female
 2 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

- 3 Note: Factor loadings shown in Table 2
 4