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ORIGINAL ARTICLE

Proximal correlates of metabolic phenotypes during 'at-risk' and 'case' stages of the metabolic disease continuum

MT Haren[1,2,3], G Misan[4], JF Grant[5], JD Buckley[6], PRC Howe[7], AW Taylor[8], J Newbury[9] and RA McDermott[10]

OBJECTIVE: To examine the social and behavioural correlates of metabolic phenotypes during 'at-risk' and 'case' stages of the metabolic disease continuum.
DESIGN: Cross-sectional study of a random population sample.
PARTICIPANTS: A total of 718 community-dwelling adults (57% female), aged 18–92 years from a regional South Australian city.
MEASUREMENTS: Total body fat and lean mass and abdominal fat mass were assessed by dual energy x-ray absorptiometry. Fasting venous blood was collected in the morning for assessment of glycated haemoglobin, plasma glucose, serum triglycerides, cholesterol lipoproteins and insulin. Seated blood pressure (BP) was measured. Physical activity and smoking, alcohol and diet (96-item food frequency), sleep duration and frequency of sleep disordered breathing (SDB) symptoms, and family history of cardiometabolic disease, education, lifetime occupation and household income were assessed by questionnaire. Current medications were determined by clinical inventory.
RESULTS: 36.5% were pharmacologically managed for a metabolic risk factor or had known diabetes ('cases'), otherwise were classified as the 'at-risk' population. In both 'at-risk' and 'cases', four major metabolic phenotypes were identified using principal components analysis that explained over 77% of the metabolic variance between people: fat mass/insulinemia (FMI); BP; lipidaemia/lean mass (LLM) and glycaemia (GLY). The BP phenotype was uncorrelated with other phenotypes in 'cases', whereas all phenotypes were inter-correlated in the 'at-risk'. Over and above other socioeconomic and behavioural factors, medications were the dominant correlates of all phenotypes in 'cases' and SDB symptom frequency was most strongly associated with FMI, LLM and GLY phenotypes in the 'at-risk'.
CONCLUSION: Previous research has shown FMI, LLM and GLY phenotypes to be most strongly predictive of diabetes development. Reducing SDB symptom frequency and optimising the duration of sleep may be important concomitant interventions to standard diabetes risk reduction interventions. Prospective studies are required to examine this hypothesis.

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Keywords: metabolic trait expression; abdominal obesity; sleep disordered breathing symptoms; principal components analysis

INTRODUCTION

A considerable proportion of obese individuals do not co-express metabolic risk (metabolically healthy obese) and a considerable proportion of normal weight individuals express multiple metabolic risk factors (metabolically unhealthy lean).[1] In both obese and lean individuals, the main predictors of metabolic ill-health in the U.S. NHANES were older age and lower participation in leisure-time physical activity.[1]

The co-expression of metabolic traits vary both in nature (the traits that co-express) and in magnitude (the level to which they express) across individuals and populations,[2–5] and likely result from interactions between genetic and environmental factors, which have not been fully characterised.[4,6] Understanding the specificity of socio-economic and behavioural determinants of metabolic trait co-expression at different stages of the metabolic disease continuum may aid in tailoring diabetes prevention and management programs to individuals and communities with particular metabolic trait or risk profiles.

Current understandings of the social and behavioural determinants of metabolic status have come from studies, which use either individually measured risk factors or metabolic syndrome classifications as outcomes.[7–9] The former approach may be limited by the inability to account for the co-expression of metabolic traits in individuals and the clinical dichotomy of the latter excludes examination of either the nature or the magnitude of trait co-expression.

Standardised definitions for metabolic phenotypes (such as metabolically healthy obese and metabolically unhealthy lean) do not exist, which limits the comparability of findings across studies, and if they did, they would have the same limitations as

[1]Division of Health Sciences, Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, Australia; [2]Spencer Gulf Rural Health School (SGRHS), University of South Australia and The University of Adelaide, Whyalla Norrie, South Australia, Australia; [3]Centre for Rural Health and Community Development (CRHaCD), University of South Australia, Whyalla Norrie, South Australia, Australia; [4]Centre for Rural Health and Community Development (CRHaCD), University of South Australia, Whyalla Norrie, South Australia, Australia; [5]Population Research and Outcomes Studies, Discipline of Medicine, The University of Adelaide, Adelaide, South Australia, Australia; [6]Nutrition Physiology Research Centre, University of South Australia, Adelaide, South Australia, Australia; [7]Nutrition Physiology Research Centre, University of South Australia, Adelaide, South Australia, Australia; [8]Population Research and Outcomes Studies, Discipline of Medicine, The University of Adelaide, Adelaide, South Australia, Australia; [9]Spencer Gulf Rural Health School (SGRHS), University of South Australia and The University of Adelaide, Whyalla Norrie, South Australia, Australia and [10]Sansom Institute for Health Research, University of South Australia, Adelaide, South Australia, Australia. Correspondence: Dr MT Haren, Division of Health Sciences, Sansom Institute for Health Research (CEA-01), University of South Australia, City East Campus, North Terrace (P4-24), GPO Box 2471, Adelaide, South Australia 5001, Australia.
E-mail: Matt.Haren@unisa.edu.au
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definitions for metabolic syndrome. Since 1994 a substantial literature has emerged from factor or principal components analysis (PCA)[10] that has identified four canonical (accepted) latent (underlying/unmeasured) metabolic factors (phenotypes) in the pathophysiology of diabetes: body/fat mass/insulinemia (FMI) glycaemia (GLY), lipidaemia and blood pressure (BP).[11-13] Despite these phenotypes being studied as determinants of diabetes,[12] to our knowledge no studies have extensively examined the social and behavioural determinants of phenotype expression.

The objective of this study was to examine the specificity of social and behavioural correlates of latent metabolic phenotypes during 'at-risk' and 'case' stages of the metabolic disease continuum. The study aimed to confirm the presence of the canonical latent factors and to examine their social and behavioural correlates in 'at-risk' and 'case' sub-populations.

PARTICIPANTS AND METHODS

Research context

The Whyalla Intergenerational Study of Health (WISH) is a population-based cohort recruited between February 2008 and July 2009, within the city of Whyalla, an industrial outer regional city that is located on the eastern Eyre Peninsula of South Australia.[14] The city had a population of over 22 000 in 2006.

When compared with South Australia and Australia overall, Whyalla has a workforce enriched with blue-collar workers, and the demand for such occupations may explain the higher proportion of adults who had not completed year 12 of high school (or equivalent). The proportion of UK/Irish born and people of Australian Aboriginal or Torres Strait Islander origin appear higher than in South Australia and Australia overall.[14]

Previous investigations of the health of this population have revealed obesity,[15] asthma,[15,16] chronic lung disease,[15,16] chronic liver disease and lung cancer[16] to be higher in Whyalla than in South Australia overall, or demographically and geographically comparative communities. A previous ecological study suggested that behavioural risk factors were unable to explain the apparent poorer respiratory and hepatic health outcomes in this population.[16]

Sampling and Recruitment

Whyalla households ($n = 2500$) were randomly selected from the residential housing database of the State Planning Authority. The strength of this sampling frame was the completeness, however, approach and recruitment was a complex multi-stage process because of limited contact information in the databases (residential address only). This novel sampling frame was used instead of telephone listings (Electronic White Pages) owing to a high proportion of households without landline telephone connections in the city. Invitations to participate were mailed to 'The Householder' co-ordinated with a community-wide media campaign informed by a Community Advisory Group. Householders were invited to register online or by telephone, providing their telephone number and basic demographic information. One hundred seventy-eight (7%) households responded to this approach. The second stage successfully matched 1183 household addresses in the sample to names and telephone numbers in the Electronic White Pages. Third, remaining unmatched households were approached by door knocking, a minimum of two attempts to contact were made and calling cards were left.

Once telephone numbers were obtained, Computer Assisted Telephone Interviewing technology was used to recruit the adult ($\geqslant$18 years) in each household who last had their birthday ('index adult'), and to collect demographic, health and risk factor data and schedule clinical assessments. Interviews were conducted by trained interviewers under established protocols.[17] Participants provided written informed consent at the time of clinical assessment. Protocols and procedures were approved by the Human Research Ethics Committee of The University of South Australia and the Aboriginal Health Research Ethics Committee of South Australia.

Definitions of 'at-risk' and 'case' stratification

'At-risk' was defined as the absence of both known diabetes and pharmacological management with diabetes or cardiovascular system agents (Anatomical Therapeutic Classification codes A10, C01-C03 and C07-C10). 'Case' was defined as diagnosed diabetes or management with the aforementioned therapeutic classes.

Major outcome measures

Body composition was assessed using DXA (Lunar Prodigy, GE Medical Systems, Madison, WI, USA) with the manufacturer's software (enCORE 2003 version 7.52). Scans were performed according to the manufacturer's protocols with participants' supine. Total fat and lean masses (g) were determined automatically from the manufacturer's software. Total abdominal and intra-abdominal fat masses were determined by defining two regions of interest in the abdomen by drawing quadrilateral boxes with the base touching the top of the iliac crest, the upper margins touching the most inferior aspect of the ribs and the lateral borders extending to the edge of the abdominal soft tissue for total abdominal fat, and the inner border of the rib cage for intra-abdominal fat.

Fasting, morning venous blood samples were collected ($\sim$40 ml) and assayed by a National Association of Testing Authorities accredited laboratory. Fasting plasma glucose concentration was measured using a Chemistry analyser system (Olympus AU5400, Olympus Optical C Ltd, Japan) with inter-assay CVs of 2.41% at 3.41 mmol l^{-1} and 2.21% at 19.72 mmol l^{-1}. HbA1c was assayed by cation-exchange high pressure liquid chromatography using instrumentation, kits and reagents from Bio-Rad laboratories (Hercules, CA, USA) with inter-assay CVs of 2.4% at A1c of 5.7 and 2.2% at A1c of 10.0. Fasting serum triglycerides and cholesterol lipoproteins were determined enzymatically using a Roche Hitachi 911 chemistry analyser (Roche, Boehringer, Germany) with inter-assay CV's of: 2.63% at 2.44 mmol l^{-1} and 3.16% at 1.0 mmol l^{-1} of triglyceride; 2.05% at 5.83 mmol l^{-1} and 2.83% at 2.55 mmol l^{-1} of total cholesterol; 3.29% at 2.04 mmol l^{-1} and 3.2% at 0.9 mmol l^{-1} of high-density lipoprotein (HDL) cholesterol. Fasting serum insulin concentration was measured in serum collected, separated and frozen at $-80\,^{\circ}C$ within 2 h of collection. Radioimmunoassay was performed on an Abbott Architect immunoassay analyser (Abbott Park, IL, USA) with inter-assay CVs of 7.81% at 8.44 mU l^{-1}, 5.87% at 57.44 mU l^{-1} and 8.53% at 97.90 mU l^{-1}. Systolic and diastolic BP were measured using an automatic sphygmomanometer (Welch Allyn Spot Vital Signs 420 Series, Skaneateles Falls, NY, USA). Two measurements were taken after the participant had been seated and rested for 5 and 10 min. A third measurement was taken if readings differed by more than 10%. The mean of the two readings or the median of three readings was calculated for both pressures. Height was determined to within 1 mm using a wall stadiometer (Surgical and Medical Products No. 26SM, Mentone Education Supplies, Melbourne, Australia), body mass was measured to the nearest 100 g with an electronic scale (Tanita BF-681, Tanita, Arlington Heights, IL, USA) and waist circumference was measured twice to the nearest 0.5 mm using a steel girth tape (Lufkin W606PM) and the mean value obtained. A third measurement was taken if the two varied by greater than 1%, and the median was used.[18] Body mass index (BMI) was calculated as weight (kg)/height (m^2).

For comparison with national prevalence data, abdominal obesity was classified as waist circumference $\geqslant$102 cm for males and $\geqslant$88 cm for females and general obesity was classified as

BMI $\geqslant 30\,kg\,m^{-2}$.[19] Elevated systolic and diastolic BP were defined as $\geqslant 140$ and $\geqslant 90$ mm Hg, respectively.[20] Elevated fasting triglyceride concentrations were defined as $\geqslant 2.0\,mmol\,l^{-1}$ and low HDL cholesterol was defined as $\leqslant 1.0\,mmol\,l^{-1}$.[20] Impaired fasting glucose was defined as a fasting plasma glucose concentration $> 5.5\,mmol\,l^{-1}$(ref.21) and diabetes was indicated by a fasting plasma glucose concentration $> 7\,mmol\,l^{-1}$.[20] Undiagnosed diabetes was defined as having a fasting plasma glucose concentration $> 7\,mmol\,l^{-1}$ without having reported a previous diagnosis of diabetes.

Metabolic phenotype expression scores

Intra-abdominal, abdominal and total fat masses, total lean mass, fasting serum concentrations of triglycerides, HDL and insulin, fasting plasma concentration of glucose, HbA1c, seated systolic and diastolic BP were subject to PCA for dimension reduction to the latent factors. This analysis assigned a score to each participant representing how strongly they expressed each latent phenotype.

Independent variables

Similarly, the consumption frequencies for ninety-six food and beverage items collected using an updated version (version 3.1) of the Australian Cancer Council of Victoria's Dietary Questionnaire[22] were entered into a PCA for dimension reduction to latent dietary patterns, which assigned a score to each participant representing how strongly their diet reflected each of the identified patterns. From the same questionnaire, alcohol consumption was computed in grams. Smoking status was defined as never-, past- and current-smoker. Total time spent in leisure-time physical activities (LTPA) was determined by questionnaire. Intensity weights (3.5 for walking, 5.0 for moderate and 7.5 for vigorous intensity exercise) were used to compute metabolic equivalent hours (MET-h), where <1600 MET-h/week was defined as sedentary or low; and >1600 MET-h/week as moderate to high physical activity.[23] Average hours spent sleeping each day was self reported. Owing to evidence that both short and long sleep durations are associated with increased risk of diabetes,[24] sleep duration was categorised as short (<7 h per day) or long ($\geqslant 9$ h per day) sleep and examined relative to normal sleep duration (7 – <9 h per day). A sleep disordered breathing (SDB) symptom score (range 0–12) was computed as the sum of symptom frequency from zero (never) to four (>4 times per week) for three symptoms: snorting or gasping; loud snoring; and breathing cessation, choking or struggling for breath during sleep. Family history (parents and grandparents) of diabetes, high BP, stroke and heart disease were obtained by self-report. Pictograms[25] were used to estimate maternal and paternal somatotypes at age 40 years. Fifteen year retrospective somatotyping of parents, by offspring, using these pictograms, correlated highly with previously measured height and weight.[26] Educational attainment was categorised as Bachelor degree or higher, high school or vocational certificate, or did not complete high school. Lifetime primary occupation was coded according the Australian and New Zealand Classification of Occupations and reduced to 'Manager/professional', 'White collar worker' and 'Blue collar worker'. Gross annual household income was collected in approximate $20 000 increments and reduced to three categories of $40 000 increments for analysis.

Standard population data

Baseline data from the Australian Obesity Diabetes and Lifestyle (AusDiab) Study, a stratified sample of adults 25 years and over from 42 randomly selected Census Collector Districts in Australia in 1999–2000 ($n = 11\,247$, pseudo-response rate 55%),[27] were used to estimate standardised prevalence ratios (SPR) for cardiometabolic risk factors in the study population.

Australian and South Australian behavioural risk factor data from the 2007–08 Australian National Health Survey[28] were used to estimate SPRs for behavioural risk factors in the study population.

Statistical analysis

Data analysis was performed using STATA 10.1 for Windows (StataCorp., College Station, TX, USA). For population prevalence estimates, data were weighted to the age and sex distribution of the Estimated Residential Population of Whyalla in 2007(ref. 29) and the likelihood of being recruited into the study, as per the equation: weight = hhld_adult × (bnh/lnh) × (ln/bn); where hhld_adult is the number of people aged 18 and over (adults) residing in the household; bnh is the adult population size of Whyalla by sex and age-group; bn is the total adult population of Whyalla; lnh is the adult sample size of WISH by sex and age-group; and ln is the total adult sample size of the WISH cohort. For SPRs, the stratum-specific prevalence estimates from the national standard population data (AusDiab and Australian National Health Survey) were used to calculate the expected number of cases in the study population (WISH). Expected cases were summed across strata, and compared with the number of observed cases, the SPR was calculated as the ratio of observed to expected cases.

PCA with oblique rotation (oblimin) was used to define the principal latent metabolic phenotypes and the principal latent dietary patterns in the population. Components were maintained for further analysis based on Eigen values >1 (see Supplementary Information, Figure 1) and limited to four for interpretability. To minimise the likelihood of over-specifying the number of components, potentially outlying and influential observations were examined using scatter-plots and bi-plots of the first and last two components as suggested by Jolliffe.[30] Components scores were standardised for further analysis.

Hierarchical, multivariate (multiple outcomes) regression was used to model the associations of age, sex, education, lifetime primary occupational class, household income, family history of cardiometabolic disease, dietary pattern scores, alcohol consumption, past and current smoking, moderate-high LTPA, sleep duration and SRB symptoms with latent phenotypes.

RESULTS

Participants

The participant flow and response rates are summarised in Figure 1. Overall, 32.2% of eligible adults participated in the clinical study. Married people were over-represented by ~20% and divorced/separated people and those who had never married were under-represented by ~10%. The sample was 10% over-represented by adults who owned their residences or rented privately and 10% under-represented by those renting from the State Housing administration. There was an ~5% over-representation of adults born in the UK and Ireland and a 1.5% under-representation of Aboriginal or Torres Strait Islanders (data not shown).

Table 1 describes the metabolic, behavioural and socio-economic characteristics of the 'At-risk' and 'Case' sub-populations by sex. The prevalence of both abdominal obesity (48.4% (95% CI 44.1−52.7%)) and low HDL cholesterol (17.7% (95% CI 14.2−21.8%)) was higher than national estimates (SPR for abdominal obesity 1.6 (95% CI 1.4−1.8), SPR for low HDL cholesterol 1.3 (95% CI 1.1−1.6)). All other metabolic risk markers were equivalent to the national prevalence. Hypertension prevalence was 31.3% (95% CI 27.7−35.1%); 8.7% (95% CI 6.7−11.4%) were untreated and 55.8% (95% CI 47.6−63.7%) were adequately controlled below 140/90 mmHg. The prevalence of hypertriglyceridaemia was 22.1% (95% CI 18.8−25.9%). After excluding diabetes that was only associated with pregnancy (13 cases), the prevalence of self-reported doctor-diagnosed diabetes was 7.5% (95% CI 5.8−9.8%). Four percent (4.3%) of the population had biochemical evidence

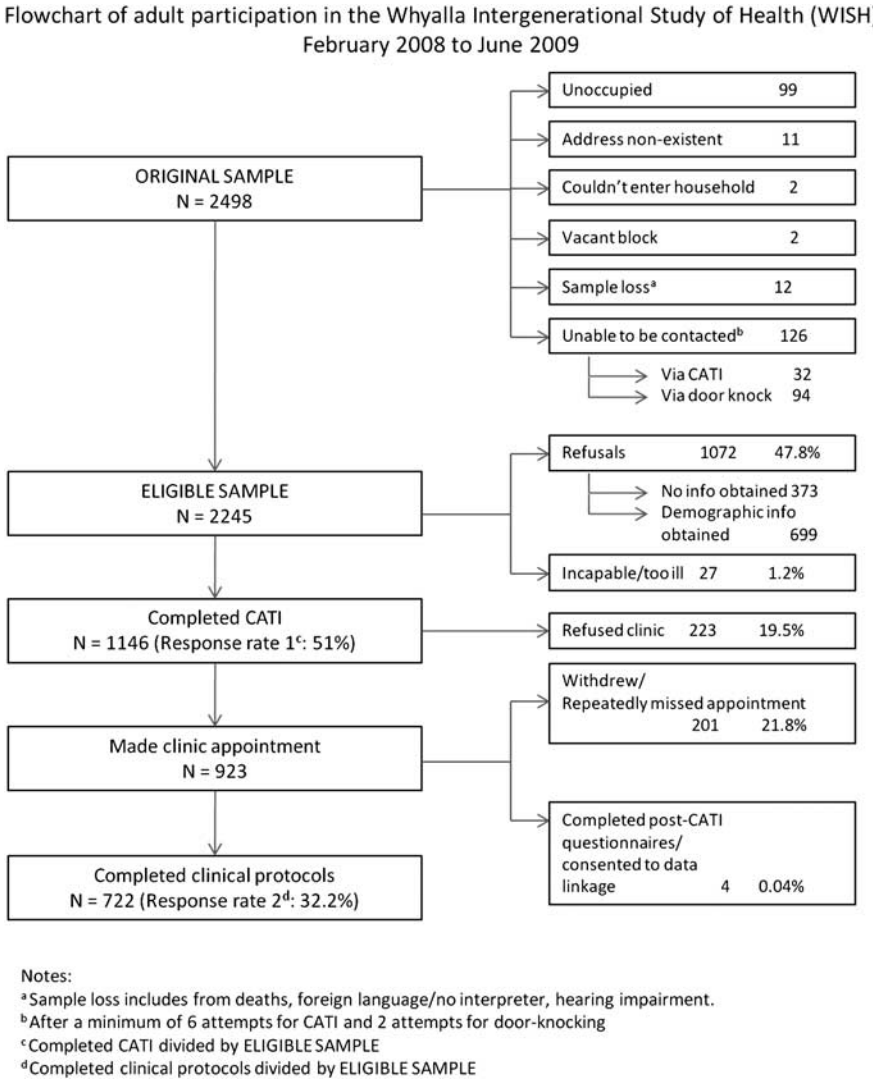

Figure 1. Participation flowchart. Reprinted with permission of SA Health from Haren *et al*.[14]

of diabetes (fasting plasma glucose $\geqslant 7\,\text{mmol}\,l^{-1}$) at clinical assessment. Based on self-reported diagnoses and biochemical evidence, the estimated prevalence of likely undiagnosed diabetes was 1.5% resulting in an estimated population prevalence for total diabetes of 9.1% (95% CI 7.1−11.6%). This equated to one undiagnosed diabetic for every 5 diagnosed cases in Whyalla. The estimated population prevalence of impaired fasting glucose was 6.4% (95% CI 4.5−9.2%). The prevalence of moderate-high LTPA (35.0% (95% CI 30.8−39.2%)) was significantly higher than the national prevalence (SPR 1.3 (95% CI 1.1−1.5)). Current smoking (23.0% (95% CI 19.6−26.7%)), past smoking (28.6% (95% CI 25.1−32.4%)) and never smoking (48.4% (95% CI 44.1−52.8%)) were similar to national and state estimates.

Latent metabolic phenotypes and dietary factors

Four latent metabolic phenotypes were confirmed in both 'at-risk' and 'case' groups: FMI; BP; lipidaemia/lean mass (LLM) and GLY (Table 2). Moderate correlations existed between all latent phenotypes except for BP in 'cases', which was uncorrelated with the other phenotypes. Four latent dietary patterns were identified that are described as: Mediterranean; Fruit; Anglo; and Junk (See Supplementary data file).

Socio-economic, familial and behavioural correlates

The covariate-adjusted models of phenotype expression in 'at-risk' and 'case' sub-populations are shown in Tables 3 and 4, respectively (see Supplementary data file for the sequential models). In the 'at-risk' strata, high school and/or vocational education and a unit increase in SDB symptom score were associated with a 0.51 and 0.11 s.d. increase in FMI expression, respectively. Blue-collar occupation and a unit increase in the maternal endomorphic-ectomorphic scale were associated with a 0.38 s.d. and 0.13 s.d. decrease. In 'cases', a 1-year age increase and long sleep was associated with a 0.03 s.d. and 0.56 s.d. decrease, and taking diuretics with a 0.62 s.d. increase in FMI expression.

In the 'at-risk', female gender and current smoking were associated with a 0.84 s.d. and 0.35 s.d. decrease in BP expression, respectively. A 1-year age increase was associated with a 0.02 s.d. increase. In 'cases', a one unit increase in 'fruit' diet pattern score was associated with a 0.08 s.d. increase, and taking diuretics with a 0.60 s.d. decrease in BP expression.

In the 'at-risk', female gender, household income up to $40 000 p.a. and a 100 g per month increase in alcohol consumption (10 Australian standard drinks) were associated with a 1.17 s.d., 0.28 s.d. and 0.01 s.d. decrease in LLM expression, respectively. Current

Table 1. Metabolic, behavioural and socio-economic characteristics of the 'at-risk' and 'cases', by sex

	At-risk		*Cases*	
	Men	*Women*	*Men*	*Women*
Mean (s.d.) range of *n*	*170–201*	*221–255*	*81–107*	*119–155*
Age (years)	45.26 (13.62)	42.11 (14.04)	62.15 (12.18)	59.24 (14.94)
Waist circumference (cm)	96.61 (13.54)	88.99 (13.99)	107.34 (13.59)	97.44 (16.34)
Body mass index (kg m^{-2})	27.57 (5.35)	27.88 (6.04)	30.62 (5.59)	31.44 (7.92)
Fasting serum triglyceride (mmol l^{-1})	1.67 (1.03)	1.26 (0.63)	1.88 (1.12)	1.56 (0.83)
Fasting serum HDL (mmol l^{-1})	1.29 (0.3)	1.55 (0.41)	1.23 (0.26)	1.49 (0.39)
Fasting serum insulin (mU l^{-1})	10.1 (8.41)	8.66 (6.31)	14.43 (10.75)	12.32 (10.03)
Fasting plasma glucose (mmol l^{-1})	5.34 (0.68)	4.89 (0.48)	6.22 (1.95)	5.39 (1.04)
Fasting glycated haemoglobin (%)	5.47 (0.49)	5.32 (0.44)	6.07 (1.09)	5.73 (0.67)
Systolic BP (mm Hg)	125.29 (13.97)	115.65 (12.4)	135.67 (17.91)	130.75 (18.42)
Diastolic BP (mm Hg)	78.98 (8.59)	74.42 (7.36)	80.61 (8.98)	78.09 (9.3)
Intra-abdominal fat mass (g)	1907.24 (1152.2)	1681.7 (825.37)	2708.57 (1095.23)	2057.25 (950.84)
Abdominal fat mass (g)	2384.73 (1512.57)	2474.49 (1300.23)	3276.12 (1451.72)	2945.34 (1490.96)
Total body fat mass (g)	24 053.86 (12009)	30 909.23 (11 918.13)	31 058.41 (11 613.22)	36 071.47 (134 66.33)
Total body lean mass (g)	56 895.56 (8085.45)	40 167.74 (5356.88)	57 874.64 (9158.44)	41 269.17 (8074.74)
FMI metabolic factor[a], standard units	−0.08 (1.11)	0.07 (0.9)	0.19 (1)	−0.14 (0.98)
BP metabolic factor[a], standard units	0.49 (0.96)	−0.39 (0.85)	0.22 (0.96)	−0.15 (1)
LLM metabolic factor[a], standard units	0.67 (0.85)	−0.53 (0.77)	0.53 (0.89)	−0.37 (0.90)
GLY metabolic factor[a], standard units	0.32 (1.11)	−0.25 (0.82)	0.34 (1.24)	−0.24 (0.70)
Mediterranean diet factor, standard units	0.01 (0.98)	0.13 (0.98)	−0.28 (0.96)	−0.02 (1.06)
Fruit and yoghurt diet factor, standard units	−0.36 (0.99)	0.11 (0.94)	−0.16 (0.85)	0.42 (1.02)
Anglo (meat and three vegetables) diet factor, standard units	−0.15 (0.94)	−0.12 (0.96)	0.17 (1)	0.28 (1.08)
Junk diet factor, standard units	0.43 (1.03)	-0.05 (0.96)	−0.08 (0.85)	−0.43 (0.91)
Alcohol (g per month)	524.94 (1472.64)	447.12 (1946.26)	276.67 (420)	169.73 (681.73)
Sleep duration (h per day)	7.16 (1.17)	7.37 (1.35)	7.33 (1.69)	7.15 (1.33)
Normal sleep duration (7–9 h per day), n(%)	115.00 (57.21)	148.00 (58.04)	49.00 (45.79)	74.00 (47.13)
Short sleep duration (<7 h per day), n(%)	60.00 (29.85)	65.00 (25.49)	34.00 (31.78)	49.00 (31.21)
Long sleep duration (⩾9 h per day), n(%)	16.00 (7.96)	30.00 (11.76)	16.00 (14.95)	14.00 (8.92)
SDB, symptom frequency score (0–12)	1.24 (2.17)	0.9 (2.01)	1.69 (2.95)	1.03 (2.07)
Somatotype at 40 (mother), 9-point scale	5.29 (1.46)	5.15 (1.54)	5.17 (1.34)	4.88 (1.53)
Somatotype at 40 (father), 9-point scale	5.34 (1.46)	5.3 (1.71)	5.66 (1.55)	5.59 (1.61)
No. (%)				
Highest education level				
Bachelor degree+	31 (15.42)	51 (20)	10 (9.35)	11 (7.01)
Completed HS/vocational qualification	118 (58.71)	115 (45.1)	60 (56.07)	53 (33.76)
Did not complete HS	51 (25.37)	86 (33.73)	37 (34.58)	88 (56.05)
Missing	1 (0.5)	3 (1.18)	0 (0)	5 (3.18)
Lifetime primary occupational class				
Managers and professionals	46 (22.89)	73 (28.63)	18 (16.82)	32 (20.38)
White collar employees	18 (8.96)	95 (37.25)	14 (13.08)	58 (36.94)
Blue collar employees	134 (66.67)	65 (25.49)	74 (69.16)	46 (29.3)
Missing	3 (1.49)	22 (8.63)	1 (0.93)	21 (13.38)
Household income				
>$80 000 p.a.	65 (32.34)	73 (28.63)	20 (18.69)	17 (10.83)
$40 001 to $80 000 p.a.	84 (41.79)	96 (37.65)	25 (23.36)	30 (19.11)
Up to $40 000 p.a.	52 (25.87)	86 (33.73)	62 (57.94)	105 (66.88)
Missing			0 (0)	5 (3.18)
Family history (positive)				
Diabetes	54 (26.87)	103 (40.39)	30 (28.04)	50 (31.85)
Heart disease	87 (43.28)	127 (49.8)	64 (59.81)	81 (51.59)
Stroke	61 (30.35)	73 (28.63)	32 (29.91)	45 (28.66)
High blood pressure	91 (45.27)	133 (52.16)	41 (38.32)	72 (45.86)
Missing			*2 (1.87)*	*6 (3.82)*
Current smoker	63 (31.34)	71 (27.84)	14 (13.08)	25 (15.92)
Past smoker	55 (27.36)	73 (28.63)	59 (55.14)	59 (37.58)
Moderate to high LTPA	85 (42.29)	92 (36.08)	45 (42.06)	34 (21.66)
Self-reported diagnosed diabetes	0 (0)	0 (0)	37 (34.58)	35.00 (22.29)
Missing			3 (2.8)	11 (7.01)
Undiagnosed diabetes, FPG⩾7 mmol l^{-1}	5 (2.49)	5 (1.96)	2.00 (1.87)	1.00 (0.64)
Missing			16.00 (14.95)	9.00 (5.73)

Table 1 (*Continued*)

	At-risk		*Cases*	
	Men	*Women*	*Men*	*Women*
Medications				
Diabetes (ATC A10)	0 (0)	0 (0)	27 (25.23)	17 (10.83)
Cardiac therapy (ATC C01)	0 (0)	0 (0)	10 (9.35)	6 (3.82)
Antihypertensives (ATC C02)	0 (0)	0 (0)	9 (8.41)	5 (3.18)
Diuretics (ATC C03)	0 (0)	0 (0)	17 (15.89)	20 (12.74)
Beta blocking agents (ATC C07)	0 (0)	0 (0)	22 (20.56)	18 (11.46)
Calcium channel blockers (ATC C08)	0 (0)	0 (0)	19 (17.76)	23 (14.65)
Renin–angiotensin system (ATC C09)	0 (0)	0 (0)	64 (59.81)	78 (49.68)
Lipid modifying agents (ATC C10)	0 (0)	0 (0)	56 (52.34)	77 (49.04)
Total	201 (100)	255 (100)	107 (100)	157 (100)

Abbreviations: ATC, anatomical therapeutic classification, BP, blood pressure; FMI, fat mass/insulinemia; FPG, fasting plasma glucose; GLY, glycaemia; HDL, high-density lipoprotein; LLM, lipidaemia/lean mass; LTPA, leisure-time physical activities; p.a., per annum; SDB, sleep disordered breathing. [a]Derived separately for 'at-risk' and 'case' sub-populations.

Table 2. Component loadings for original metabolic variables with oblique rotation of components in the 'at-risk' and 'case' sub-populations

Component number	*At-risk*				*Cases*			
	1	*2*	*3*	*4*	*1*	*2*	*3*	*4*
	FMI	*BP*	*LLM*	*GLY*	*FMI*	*GLY*	*LLM*	*BP*
Fasting serum triglyceride	0.03	0.04	**0.47**	0.08	−0.07	−0.07	**0.70**	0.07
Fasting serum HDL	0.02	0.11	**−0.70**	0.03	−0.03	−0.06	**−0.61**	0.14
Fasting serum insulin	**0.34**	−0.02	0.16	0.13	**0.22**	**0.23**	0.17	0.06
Fasting serum glucose	0.00	0.09	0.03	**0.65**	−0.01	**0.67**	0.01	0.01
Fasting HbA1c	−0.01	−0.07	−0.03	**0.74**	−0.01	**0.68**	−0.03	−0.01
Systolic BP	−0.04	**0.70**	−0.03	0.03	−0.04	0.09	−0.06	**0.70**
Diastolic BP	0.04	**0.66**	0.00	−0.04	0.04	−0.09	0.05	**0.69**
Intra-abdominal fat mass	**0.50**	0.07	0.08	0.02	**0.52**	0.06	0.03	0.04
Abdominal fat mass	**0.55**	0.01	0.01	0.00	**0.55**	0.00	−0.04	−0.01
Total body fat mass	**0.57**	−0.06	−0.10	−0.05	**0.54**	−0.11	−0.09	−0.05
Total body lean mass	0.00	**0.21**	**0.51**	−0.02	**0.29**	0.09	**0.31**	0.10
Percentage of variance	29.2	17.8	16.0	14.0	30.4	18.9	15.0	14.9
Correlation coefficients								
Component 1	1.000				1.000			
Component 2	0.268	1.000			0.268	1.000		
Component 3	0.313	0.232	1.000		0.275	0.228	1.000	
Component 4	0.196	0.229	0.298	1.000	−0.019	−0.037	0.067	1.000

Abbreviations: BP, blood pressure; FMI, fat mass/insulinemia; GLY, glycaemia; HbA1c, haemoglobin A1 c; HDL, high-density lipoprotein; LLM, lipidaemia/lean mass. Loadings further than |0.30| from zero were considered a major contributor to the component and are shown in bold. Oblique rotation was applied to components, allowing correlation between the components. The percentage of variance is that of the original 11 variables, which is accounted for by each component.

smoking and a unit increase in SDB symptom score were associated with a 0.31 s.d. and 0.05 s.d. increases, respectively. In 'cases', female gender and a 1-year age increase were associated with a 1.34 s.d. and 0.02 s.d. decrease in LLM expression, respectively. Lipid-lowering medications were not associated with LLM expression.

In the 'at-risk', female gender and blue-collar occupation were associated with a 0.51 s.d. and 0.28 s.d. decrease in GLY expression, respectively. A 1-year age increase, a 1 unit increase in SDB symptom score and short sleep duration were associated with a 0.03 s.d., 0.05 s.d. and 0.38 s.d. increase, respectively. In 'cases', being female was associated with a 0.40 s.d. decrease and family history of diabetes, moderate-high LTPA, short sleep and taking medication for diabetes were associated with a 0.37 s.d., 0.41 s.d., 0.34 s.d. and 1.06 s.d. increase in GLY expression, respectively.

DISCUSSION

Metabolic health profile of the population

Almost one in two adults in the study population had abdominal obesity, which, when standardised to 10-year old Australian national estimates, represented 1.6 cases to every case nationally. Despite the excess of abdominal obesity, which may be expected given the age of the reference data, the prevalence of diabetes, hypertriglyceridaemia and hypertension were equivalent to estimates from the same national data. This suggests that metabolic risk in Whyalla was either well controlled or had not emerged from the observed abdominal obesity. Whyalla had higher prevalence of controlled and lower prevalence of untreated hypertension suggesting that the incongruence between abdominal obesity and hypertension may be due to improvements in detection and management over the past decade, as has been demonstrated internationally.[31] Improved pharmacological man-

Table 3. Social, family history and behavioural associates of latent metabolic phenotype scores in the 'at-risk' sub-population

	FMI		*BP*		*LLM*		*GLY*	
	Coefficient	*95% CI*	*Coefficient*	*95% CI*	*Coefficient*	*95% CI*	*Coefficient*	*95% CI*
At-risk								
Female	0.108	−0.149, 0.364	−0.835***	−1.075, −0.596	−1.169***	−1.389, −0.948	−0.514***	−0.771, −0.257
Age (years)	−0.001	−0.011, 0.009	0.020***	0.010, 0.029	−0.009*	−0.017, 0.000	0.027***	0.017, 0.037
Education								
Bachelor degree or higher	Referent		Referent		Referent		Referent	
HS-vocational qualification	0.507***	0.166, 0.848	0.254	−0.065, 0.573	0.203	−0.091, 0.497	0.045	−0.296, 0.387
Less than HS certificate	0.286	−0.144, 0.715	0.287	−0.114, 0.689	0.018	−0.352, 0.388	0.098	−0.332, 0.529
Lifetime 1° occupational class								
Manager/professional	Referent		Referent		Referent		Referent	
White collar	−0.227	−0.567, 0.114	0.040	−0.278, 0.358	−0.049	−0.343, 0.244	−0.117	−0.458, 0.223
Blue collar	−0.382**	−0.697, −0.066	−0.081	−0.377, 0.214	−0.148	−0.420, 0.124	−0.282*	−0.598, 0.035
Household income, gross p.a.								
Greater than $80 000	Referent		Referent		Referent		Referent	
$40 001 to $80 000	0.036	−0.210, 0.282	−0.029	−0.259, 0.202	0.047	−0.166, 0.259	−0.081	−0.327, 0.166
Up to $40 000	−0.090	−0.410, 0.229	0.012	−0.287, 0.311	−0.295**	−0.570, −0.019	−0.154	−0.474, 0.166
Somatotype at 40 (mother)	−0.128***	−0.203, −0.053	0.012	−0.058, 0.082	−0.008	−0.073, 0.056	−0.024	−0.098, 0.051
Somatotype at 40 (father)	−0.010	−0.080, 0.059	0.016	−0.049, 0.082	0.017	−0.043, 0.077	0.026	−0.045, 0.096
Family history, diabetes	0.222*	−0.014, 0.458	0.163	−0.057, 0.384	0.048	−0.155, 0.252	0.038	−0.198, 0.274
Family history, CHD	0.062	−0.155, 0.278	−0.095	−0.297, 0.107	0.052	−0.134, 0.239	−0.064	−0.281, 0.153
Family history, stroke	0.072	−0.157, 0.300	0.062	−0.152, 0.276	−0.047	−0.245, 0.150	0.068	−0.161, 0.297
Family history, hypertension	−0.024	−0.244, 0.196	−0.060	−0.266, 0.146	−0.080	−0.270, 0.109	0.182	−0.038, 0.402
Diet, Mediterranean	−0.013	−0.159, 0.133	0.069	−0.067, 0.206	−0.080	−0.206, 0.046	0.076	−0.071, 0.222
Diet, fruit and yoghurt	−0.108	−0.251, 0.034	−0.032	−0.166, 0.101	−0.043	−0.166, 0.080	−0.098	−0.241, 0.045
Diet, Anglo (meat and three vegetables)	0.108	−0.032, 0.248	−0.081	−0.212, 0.050	0.088	−0.033, 0.209	−0.083	−0.224, 0.057
Diet, junk	0.009	−0.106, 0.123	0.030	−0.077, 0.137	0.003	−0.096, 0.102	0.015	−0.099, 0.130
Alcohol (g per month)	−0.000	−0.000, 0.000	0.000	−0.000, 0.000	−0.000***	−0.000, −0.000	−0.000	−0.000, 0.000
Smoking, current	−0.266**	−0.528, −0.003	−0.351***	−0.596, −0.105	0.308***	0.082, 0.535	0.175	−0.088, 0.438
Smoking, past	0.121	−0.116, 0.358	0.080	−0.142, 0.301	0.193*	−0.011, 0.398	−0.160	−0.398, 0.077
LTPA, mod-high	−0.209*	−0.427, 0.010	0.001	−0.203, 0.206	0.089	−0.100, 0.277	0.077	−0.142, 0.296
Sleep duration								
Normal sleep	Referent		Referent		Referent		Referent	
Short sleep	0.163	−0.069, 0.395	0.188*	−0.029, 0.405	−0.136	−0.336, 0.064	0.380***	0.148, 0.612
Long sleep	0.092	−0.295, 0.478	0.176	−0.186, 0.538	0.192	−0.141, 0.526	0.131	−0.257, 0.519
SDB, symptom score	0.112***	0.061, 0.163	0.020	−0.028, 0.068	0.047**	0.003, 0.091	0.052**	0.001, 0.104
R-squared (observed)	0.248 (313)		*0.312 (313)*		0.453 (313)		0.277 (313)	

Abbreviations: BP, blood pressure; CHD, coronary heart disease; CI, confidence intervals; FMI, fat mass/insulinemia; GLY, glycaemia; LLM, lipidaemia/lean mass; LTPA, leisure-time physical activities; p.a., per annum; SDB, sleep disordered breathing. Data presented are regression coefficients and 95% CI. Data were modelled using multivariate regression, which adjusts for the correlation structure of the four PCA-derived phenotypes (outcome variables). ***$P<0.001$, **$P<0.01$, *$P<0.1$.

agement may also explain the incongruent hyperlipidemia prevalence, however, it is unlikely to explain the incongruent impaired fasting glucose and diabetes prevalence as the use of insulin sensitising or beta-cell preserving agents for diabetes prevention is not yet widespread despite emerging positive evidence.[32-34] The prevalence of moderate-high LTPA was higher than the contemporary national prevalence, which may confer metabolic risk reduction independent of fat loss.[35,36] Understanding the determinants of this (and other) particular community metabolic profiles has implications for the design of diabetes prevention programs.

This study examined the dominant metabolic phenotypes, their coexpression patterns and their associations with socio-economic characteristics, health-related behaviours and family cardiometabolic health history in 'at-risk' and 'case' sub-populations. The dominance of the widely accepted underlying metabolic phenotypes, similar to those previously described in diabetics and non-diabetics[12] were confirmed in this population. GLY and FMI phenotypes have been shown to predict diabetes equivalently to NCEP defined metabolic syndrome; LLM is slightly inferior and BP has the lowest predictive value.[12] Consistent with this finding, the BP phenotype in 'cases' was uncorrelated with the other phenotypes, and in counter distinction with the GLY phenotype, explained less of the metabolic variance in the 'case' versus 'at-risk' sub-population.

Table 4. Social, family history and behavioural associates of latent metabolic phenotype scores in the 'case' sub-population

	FMI		*BP*		*LLM*		*GLY*	
	Coefficient	*95% CI*	*Coefficient*	*95% CI*	*Coefficient*	*95% CI*	*Coefficient*	*95% CI*
Female	−0.378*	−0.804, 0.048	−0.356	−0.797, 0.084	−1.341***	−1.781, −0.901	−0.397**	−0.752, −0.042
Age (years)	−0.029***	−0.049, −0.009	0.012	−0.009, 0.033	−0.024**	−0.045, −0.003	0.004	−0.012, 0.021
Education								
Bachelor degree or higher	Referent		Referent		Referent		Referent	
HS-vocational qualification	−0.111	−0.771, 0.550	−0.203	−0.886, 0.481	0.508	−0.174, 1.190	−0.050	−0.600, 0.501
Less than HS certificate	−0.039	−0.762, 0.684	−0.314	−1.062, 0.433	0.751**	0.005, 1.497	0.294	−0.308, 0.896
Lifetime 1° occupational class								
Manager/professional	Referent		Referent		Referent		Referent	
White collar	0.367	−0.110, 0.845	−0.190	−0.684, 0.303	−0.251	−0.744, 0.241	−0.073	−0.471, 0.324
Blue collar	0.340	−0.155, 0.836	0.188	−0.324, 0.700	−0.003	−0.514, 0.508	0.106	−0.306, 0.519
Household income, gross p.a.								
Greater than $80 000	Referent		Referent		Referent		Referent	
$40 001 to $80 000	0.194	−0.361, 0.749	−0.506*	−1.080, 0.068	−0.165	−0.738, 0.407	0.350	−0.112, 0.812
up to $40 000	0.365	−0.241, 0.971	−0.043	−0.670, 0.583	0.177	−0.448, 0.802	0.119	−0.386, 0.624
Somatotype at 40 (mother)	−0.061	−0.180, 0.058	−0.093	−0.216, 0.030	−0.008	−0.131, 0.114	−0.060	−0.158, 0.039
Somatotype at 40 (father)	−0.043	−0.156, 0.071	−0.022	−0.139, 0.096	0.028	−0.090, 0.145	0.011	−0.084, 0.106
Family history, diabetes	0.042	−0.327, 0.410	0.145	−0.236, 0.526	0.263	−0.117, 0.643	0.371**	0.065, 0.678
Family history, CHD	−0.097	−0.448, 0.253	−0.126	−0.489, 0.236	0.164	−0.198, 0.525	−0.001	−0.293, 0.291
Family history, stroke	0.111	−0.245, 0.466	0.148	−0.219, 0.516	0.101	−0.266, 0.468	0.042	−0.254, 0.338
Family history, hypertension	−0.302	−0.676, 0.073	−0.090	−0.478, 0.298	0.070	−0.317, 0.457	−0.068	−0.380, 0.244
Diet, Mediterranean	−0.026	−0.101, 0.049	−0.069*	−0.146, 0.008	0.002	−0.075, 0.079	−0.041	−0.104, 0.021
Diet, fruit and yoghurt	0.048	−0.027, 0.123	0.081**	0.003, 0.158	0.046	−0.031, 0.123	0.011	−0.051, 0.073
Diet, Anglo (meat and three vegetables)	0.040	−0.047, 0.127	−0.005	−0.095, 0.085	−0.059	−0.148, 0.031	0.012	−0.060, 0.084
Diet, junk	0.060	−0.030, 0.150	−0.001	−0.094, 0.092	−0.007	−0.100, 0.086	0.017	−0.058, 0.092
Alcohol (g per month)	−0.000	−0.000, 0.000	−0.000	−0.000, 0.000	−0.000	−0.000, 0.000	0.000	−0.000, 0.000
Smoking, current	−0.426	−0.981, 0.130	0.177	−0.398, 0.752	0.093	−0.480, 0.667	−0.169	−0.632, 0.294
Smoking, past	0.102	−0.268, 0.473	−0.016	−0.400, 0.367	−0.337*	−0.719, 0.045	0.084	−0.224, 0.393
LTPA, mod-high	−0.187	−0.572, 0.198	0.048	−0.350, 0.446	−0.326	−0.723, 0.072	0.407**	0.086, 0.728
Sleep duration								
Normal sleep	Referent		Referent		Referent		Referent	
Short sleep	−0.098	−0.476, 0.280	−0.020	−0.411, 0.372	0.310	−0.081, 0.700	0.341**	0.026, 0.656
Long sleep	−0.561**	−1.108, −0.015	−0.236	−0.801, 0.330	0.170	−0.395, 0.734	−0.050	−0.505, 0.406
SDB, symptom score	0.073**	0.002, 0.144	0.024	−0.049, 0.098	−0.011	−0.084, 0.063	−0.019	−0.078, 0.041
Medications								
Diabetes (ATC A10)	0.244	−0.192, 0.680	−0.401*	−0.852, 0.051	0.194	−0.257, 0.644	1.059***	0.696, 1.422
Cardiac (ATC C01)	−0.234	−0.995, 0.527	−0.675*	−1.462, 0.112	−0.410	−1.195, 0.375	−0.029	−0.663, 0.605
Antihypertensives (ATC C02)	0.117	−0.537, 0.771	−0.334	−1.010, 0.342	0.504	−0.171, 1.179	−0.163	−0.707, 0.382
Diuretic (ATC C03)	0.617**	0.071, 1.162	−0.593**	−1.157, −0.029	−0.175	−0.738, 0.387	0.026	−0.428, 0.481
Beta-blocking agents (ATC C07)	0.128	−0.359, 0.614	0.305	−0.198, 0.809	0.184	−0.318, 0.686	0.360*	−0.045, 0.765
Calcium-channel blockers (ATC C08)	−0.080	−0.552, 0.393	0.307	−0.182, 0.796	−0.303	−0.791, 0.185	−0.068	−0.462, 0.326
Renin-angiotensin system agents (ATC C09)	0.290*	−0.053, 0.632	0.179	−0.175, 0.533	0.023	−0.330, 0.377	−0.209	−0.494, 0.077
Lipid-modifying agents (ATC C10)	−0.155	−0.502, 0.193	−0.053	−0.412, 0.307	0.080	−0.279, 0.438	−0.192	−0.481, 0.098
R-squared (observed)	0.302 (152)		0.266 (152)		0.385 (152)		0.521 (152)	

Abbreviations: ATC, anatomical therapeutic classification, BP, blood pressure; CHD, coronary heart disease; CI, confidence interval; FMI, fat mass/insulinemia; GLY, glycaemia; LLM, lipidaemia/lean mass; LTPA, leisure-time physical activities; p.a., per annum; SDB, sleep disordered breathing. Data presented are regression coefficients and 95% CI. Data were modelled using multivariate regression, which adjusts for the correlation structure of the four PCA-derived phenotypes (outcome variables). ***$P<0.001$, **$P<0.01$, *$P<0.1$.

Correlates of metabolic phenotypes in 'cases': implications for management

These differences likely reflect the impact of pharmacological regulation of metabolic traits in 'cases' as opposed to physiological regulation in the 'at-risk'. The absence of associations between phenotype expression and medication may indicate successful treatment to target, that is, those taking medication have, on average, the same phenotype expression as those not taking medication. This was the case for lipid modifying agents, but not diuretics, which were strongly associated with lower BP and higher FMI expression, suggesting that they lower BP below the untreated average and increase fat mass and fasting insulin above the untreated average. Diuretics such as amiloride can raise fasting insulin[37] and may predict type 2 diabetes in people with impaired glucose tolerance.[38] In particular, thiazide diuretics increase hepatic fat content and c-reactive protein, both of which are associated with reduced insulin sensitivity.[39] Thus, while diuretics may lower BP, they can have adverse metabolic effects, in particular reducing insulin sensitivity. In contradistinction, diabetic medication was associated with higher GLY expression (and therefore, failure to achieve normoglycaemia). Lowering glucose concentrations to normal in diabetics, however, may not be the treatment goal as the benefits versus risks of aggressive management are still unclear.[40,41] Similarly, moderate-high LTPA was not associated with GLY expression in the 'at-risk', but was associated with higher expression in 'cases', suggesting that it fails to downregulating expression to normoglycaemia in 'cases'.

In both 'at-risk' and 'cases', moderate-high LTPA was inversely associated with FMI expression, consistent with studies, which have shown improvements in fat mass and insulin regulation across the metabolic disease continuum[42,43] through increasing cardiorespiratory fitness.[44] As moderate-high LTPA was associated with the lower FMI expression only, it does not explain the incongruence between abdominal obesity and metabolic risk in this population. Instead, the higher prevalence of self-reported moderate-high LTPA may reflect greater perceived exertion due to physical activities in the less metabolically fit.[45] This highlights the importance of physical activity for secondary prevention during progression along the metabolic disease continuum.

Interestingly, long sleep was associated with a more favourable FMI expression in 'cases', which is consistent with the mounting evidence that sleep curtailment promotes weight gain and the onset of obesity.[46] Current clinical trials in obese individuals aim to investigate the effect of extending sleep duration on obesity and cardiometabolic risk factor trajectories.[47] Consistent with studies showing and increased likelihood of having diabetes in short and long sleepers,[48,49] short sleep in this study was associated with less favourable GLY expression in both 'cases' and 'at-risk' subpopulations. This suggests a negative impact on glucose regulation throughout the metabolic disease continuum or alternatively, shortened sleep as a result of even sub-clinical derangements in glycaemic regulation. The association between sleep duration, obesity and glycaemic dysregulation is potentially mediated by an increase in appetite.[50] Intervening on diet and exercise in overweight people with Impaired Glucose Tolerance improve body weight and insulin sensitivity to similar degrees in both short and long sleepers, but appeared to produce greater reductions in the incidence of type 2 diabetes in long sleepers.[51]

Correlates of metabolic phenotypes in the 'at-risk': implications for prevention

Of all the socio-economic, family history and behavioural variables examined, the frequency of SDB symptoms was the only variable associated with multiple phenotypes, after adjustment for sleep duration and other covariates. More frequent symptoms were associated with greater expression of FMI, LLM and GLY phenotypes, suggesting that these modifiable symptoms may be partly responsible for phenotype co-expression, leading to greater risk of diabetes. Consistent with this interpretation, the BP phenotype, which holds the lowest predictive value for future diabetes,[12] was not associated with SDB in 'at-risk' adults. Associations of clinically defined SDB with glucose intolerance and insulin resistance have been previously reported.[52] Although there are fewer than 20 prospective studies in this field, current evidence suggests that SDB may be a prevalent cause of diabetes[53,54] and poor glycaemic control in diabetics, which can be ameliorated by continuous positive airway pressure therapy.[55] Both SDB symptoms and risk of diabetes are modifiable by weight loss in very fat people.[56] The causal role of SDB in dyslipidaemia is less clear.[57]

In addition, mid-level education, family history of diabetes and maternal adiposity were major correlates of FMI expression in the 'at-risk'. Higher adherence to the 'fruit' and 'Anglo' diet patterns were associated with lower GLY expression, however, this was not independent of family history, other behaviours or SDB. These findings are contrary to those of other studies linking Mediterranean diet to reduced risk of metabolic syndrome.[58] This may be owing to differences in what this dietary pattern represents locally versus in the international literature on 'Mediterranean diet'. Higher alcohol consumption and not being a current smoker were associated with lower LLM expression, consistent with the beneficial effect of alcohol consumption on increasing HDL cholesterol[59] and negative effects on muscle mass and function.[60]

The strengths of this study include the metabolic characterisation of participants, particularly the use of DXA to quantify fat and lean masses. Limitations include the characterisation of behaviour by self-report. This study provides insight into the specificity of proximal social and behavioural factors as correlates of metabolic phenotypes underlying diabetes development. The findings have implications for tailoring diabetes prevention programs in communities and specific interventions in individuals with different phenotype expression. Reducing the frequency of SDB symptoms may be effective in reducing the expression of the three latent phenotypes that most strongly predict diabetes development. Moreover, management of optimal sleep duration may have added benefits for the glycaemic regulation across the full continuum of metabolic health. These hypotheses require prospective examination due to the possibility of reverse causality despite the stratification used in this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information is available at the Nutrition and Diabetes website (http://www.nature.com/nutd)