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Inverse associations between muscle mass, strength, and the metabolic syndrome

Evan Atlantis[a,*], Sean A. Martin[b], Matthew T. Haren[b,c], Anne W. Taylor[b], Gary A. Wittert[b]
Members of the Florey Adelaide Male Ageing Study

[a]*Faculty of Health Sciences, The University of Sydney, Sydney 2141, Australia*
[b]*Discipline of Medicine, University of Adelaide, Adelaide 5005, Australia*
[c]*Spencer Gulf Rural Health School, Centre for Rural Health and Community Development, University of South Australia, Whyalla Norrie 5608, Australia*

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Abstract

The metabolic syndrome (MetS) is a clustering of individual cardiovascular disease risk factors, which doubles the risk of early mortality. The authors' aimed to determine the prevalence and population attributable risk (PAR%) of the MetS among men according to demographic, physical, and lifestyle risk factors. A cross-sectional study was conducted in 1195 men in the Florey Adelaide Male Ageing Study, a regionally representative cohort of Australian men aged 35 to 81 years conducted in 2002-2005 (response rate, 45.1%). Prevalent MetS was determined according to the Adult Treatment Panel III (ATPIII) and International Diabetes Federation (IDF) classifications; and an extensive list of demographic, physical (including muscle strength, body composition by dual-energy x-ray absorptiometry, sex hormones), and lifestyle factors was accounted for. Prevalence estimates were 37.7% and 41.8% for ATPIII and IDF classifications. Odds ratios for present MetS were determined using multiple-adjusted logistic regression. Odds for present ATPIII MetS decreased (in order of importance) for lower insulin and increased for lower muscle mass, lower strength, and 3+ medical conditions. Odds for present IDF MetS decreased for lower insulin and increased for lower muscle mass, strength, and sex hormone–binding globulin levels; older age; and being married. Significant PAR% due to lowest insulin, muscle mass, and strength quarters were −44%, 27%, and 17% for the ATPIII Met, and −48%, 31%, and 20% for the IDF MetS. A substantial proportion of MetS cases would have been theoretically prevented if prior exposure to low muscle mass and strength were eradicated (PAR% ranged from 14% to 24%). Findings indicate that insulin resistance is a central abnormality in the MetS and that muscle mass and strength are strong protective factors independent of insulin resistance and abdominal fat accumulation. If confirmed prospectively, increases in muscle mass and strength needed to prevent a substantial proportion of MetS cases would be achievable with a short-term strength training intervention.

1. Introduction

The *metabolic syndrome* (MetS) is variably defined as a clustering of obesity, insulin resistance, dyslipidemia, and hypertension [1,2]. In essence, the MetS classifies individuals into 2 subgroups according to the presence or absence of a minimum number of individual well-established risk factors for important clinical end points, such as type 2 diabetes mellitus and cardiovascular disease [3]. Dichotomizing multiple risk factors is somewhat arbitrary, but convenient for population-based studies for determining one level of exposure that substantially increases the risk of important end points. Clinical justification for its use as a prognostic tool has gained support by a growing body of high-quality prospective cohort studies [4,5].

Epidemiologic studies in different populations have reported several demographic, physical, and lifestyle factors to be associated with the MetS. The prevalence of the MetS increases with age among men and women in developed

All protocols and procedures were approved by the Royal Adelaide Hospital Research Ethics Committee and, where appropriate, the Aboriginal Health Research Ethics Committee of South Australia.

The authors have no conflicts of interest to disclose.

* Corresponding author. Faculty of Health Sciences, The University of Sydney, New South Wales 2141, Australia. Tel.: +612 93519277; fax: +612 93519204.
E-mail address: e.atlantis@usyd.edu.au (E. Atlantis).

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populations [6], and is highest among urban- compared with rural-dwelling populations [7] and among low socioeconomic subgroups [8]. Physical factors associated with the MetS prevalence or incidence include high body mass index [9], large visceral fat depots [10], low plasma sex hormone–binding globulin (SHBG) levels [11], and low cardiorespiratory fitness and muscle strength [12,13]. Lifestyle factors associated with the MetS prevalence or incidence include low physical activity [9], as well as current and previous smoking [14]. Further well-designed observational research is needed because the existing body of evidence is insufficient. In addition, the main set of factors associated with the MetS is unknown because previous research has accounted for only a select few risk factors simultaneously. Given the predictive value of the MetS, particularly in the context of worldwide rising rates of obesity and aging populations, clear identification and prioritization of potentially preventable risk factors are of importance. This is particularly so in men who have substantially higher rates of and mortality from preventable diseases such as those associated with the MetS [15]. The aim of this report was to determine the prevalence and population attributable risk (PAR%) of the MetS according to demographic, physical, and lifestyle risk factors in a regionally representative population-based sample of Australian men.

2. Methods

2.1. Study sample and design

The information source for this report was the baseline data collected from the Florey Adelaide Male Ageing Study (FAMAS), a regionally representative cohort study of 1195 men aged 35 to 80 years at recruitment and living in the northwest regions of Adelaide, Australia. A sample size of 1200 was initially targeted for chronic diseases, which allowed for a minimum detectable relative risk of disease greater than 1 of 1.52 and less than 1 of 0.61 between groups of participants with and without risk factor exposure in univariate analyses, using the following assumptions: (1) sample power of 80%, (2) 2-tailed test, (3) 5% chance of type 1 error, (4) estimated risk factor prevalence of 30% (conservative estimate for behavioral risk factors such as physical inactivity), and (5) estimated disease prevalence in the reference group of 15% (conservative estimate for prevalence of at least 1 main chronic noncommunicable disease). Details of the FAMAS design, procedures, and participants have been published elsewhere [16]. A response rate of 45.1% was computed as the number of participants who attended clinical assessments divided by the total number of randomly sampled households with eligible participants (1195/2650). Nonresponders were more likely to live alone, be current smokers, have a higher prevalence of self-reported diabetes and stroke, and have a lower prevalence of hypercholesterolemia. In addition, comparisons with the Census 2001 data showed that participants matched the population for most key demographics, although younger groups and never-married men were underrepresented and older participants were overrepresented [16]. All protocols and procedures were approved by the Royal Adelaide Hospital Research Ethics Committee and, where appropriate, the Aboriginal Health Research Ethics Committee of South Australia.

2.2. Demographic and lifestyle variables

Demographic and lifestyle data were mostly obtained by self-administered questionnaires. Socioeconomic status was assessed by self-reported total household income and by the relative advantage/disadvantage index from the Socio-Economic Indexes for Areas, a classification by the Australian Bureau of Statistics based on the 2001 Census of Population and Housing. Low values indicate community-dwelling areas of disadvantage, with a relatively low proportion of people with high incomes or a skilled workforce, as well as a relatively high proportion of people with low incomes and of unskilled people in the workforce. Smoking status was determined using question items from the Australian National Health Survey. Leisure-time physical activity during the past 2 weeks was determined using question items from the National Physical Activity Survey 1999. Total time spent in leisure-time physical activities was multiplied by intensity weights (3.5 for walking, 5.0 for moderate-intensity exercise, and 7.5 for vigorous-intensity exercise) to compute metabolic equivalent hours (MET-h). The MET is a proxy estimate of total energy expenditure during exercise expressed as multiples of standard resting energy expenditure (equivalent to 1 MET unit). The semiquantitative food frequency questionnaire developed by the Cancer Council of Victoria was used to estimate usual energy-providing macronutrient intakes. The food frequency questionnaire has 74 items with 10 frequency response options and contains 3 photographs of scaled portions for 4 foods. Questionnaires were processed by the Cancer Council of Victoria's Nutrition Assessment Office to compute macronutrient intakes.

2.3. Erectile dysfunction and lower urinary tract symptoms

The Global Impotence Rating (GIR) scale and lower urinary tract symptoms on the International Prostate Symptom Scale (IPSS), also known as the *American Urological Symptom Index for Benign Prostatic Hyperplasia*, were factors accounted for. The GIR measures symptoms associated with erectile dysfunction (highest scores = most severe), and the IPSS measures symptoms associated with prostatic enlargement (highest scores = most severe).

2.4. Muscle strength

Bilateral handgrip peak force was measured during maximal isometric contraction using a grip dynamometer (Smedley, Chicago, IL). Participants were instructed to complete 3 handgrip contraction trials bilaterally, alternating

hands between trials. Participants were verbally motivated by the assessor to exert maximal force during each contraction trial. The peak (highest) force (F) value in kilograms obtained during any of the triplicate dominant and nondominant handgrip trials was used in analyses. Peak handgrip strength correlated better with lean mass (LM) of the arms than with whole-body LM ($r = 0.6$ vs $r = 0.5$, both at $P < .001$); and thus, a standardized relative strength variable was computed as F divided by LM per arm (kilogram F per kilogram LM per arm).

2.5. Blood pressure

Resting systolic and diastolic blood pressures were measured by auscultation using a stethoscope and mercury sphygmomanometer (Accoson, London, England) after 10 minutes of seated rest. Systolic pressure was recorded at the level of detection of the first beats (phase I Korotkoff), and diastolic pressure was recorded at the level of disappearance of the beats (phase V Korotkoff). Two measurements were obtained, and the mean values in millimeters of mercury were used in analyses. Differences between duplicate measurements were no more than 5 mm Hg for more than 1000 participants for systolic blood pressure and for more than 1100 participants for diastolic blood pressure. The coefficients of variation (CVs) for duplicate systolic and diastolic blood pressure measurements were both less than 9% for 99% of the sample.

2.6. Waist circumference

Anthropometry was performed using standard protocols in the morning, before breaking an overnight fast, with participants barefoot and in light clothing. Waist circumference was measured in triplicate using a fiberglass tape measure (Gulik II; Country Technology, Gay Mills, WI) taken at the level of the narrowest point (or midway) between the lower costal border and the top of the iliac crest and read in the midaxillary line, and the mean of the 3 measurements in centimeters was used in analyses. The CVs for triplicate waist circumference measurements are less than 1.6% for 99% of the sample.

2.7. Body composition

Whole and regional body composition was measured by dual-energy x-ray absorptiometry performed either on a fan-beam (Prodigy DF + 14759, Encore software version 9.15) or pencil-beam (DPX+, Lunar software version 4.7e) densitometer (both machines from GE Lunar, Madison, WI). Fat mass (FM), LM (excludes bone mass), and bone mineral content (BMC) in kilograms were defined for whole body using default settings. For assessment of soft tissue composition in the abdominal region, the top of lumbar vertebrae L2 to the bottom of L4 and extending outward to a vertical line touching the inner edges of the rib cage was adopted as the customized anatomical setting. Percentage whole-body LM was computed as [LM/(FM + LM + BMC)] * 100, whereas percentage abdominal FM was computed as [abdominal FM/(abdominal FM + abdominal LM)] * 100.

A cross-calibration analysis had previously demonstrated no significant differences between densitometers [17]. In our laboratory, means for body composition measures (FM, LM, BMC, and bone mineral density) obtained using both densitometers in a subsample of FAMAS participants (n = 18; age range, 44-70 years; body mass range, 56-121 kg) were found to be highly correlated (all $r > 0.95$); and small systematic differences were detected (weaker correlations, but all $r > 0.82$) for LM, BMC, and FM% for older (<55 years vs 55+ years) and heavier men (<87 kg vs 87+ kg).

2.8. Assays

Blood samples were drawn between 8:00 AM and 11:00 AM after a 12-hour overnight fast. Plasma total testosterone levels were determined by chemiluminescent immunoassay using the Immulite (Siemens Medical Solutions, Tarrytown, NY) auto analyzer. The CV for this assay is 9.3% at 10.7-nmol/L concentration. This was measured on an Immulite analyzer with a CV of 10.6% in the 2005 cycle of the Australian national pathology quality assurance program. Plasma bioavailable testosterone levels (includes non–SHBG-bound free and albumin-bound fractions of plasma total testosterone levels) were determined by the ammonium sulphate precipitation method [18]. Interassay CVs at different concentrations for assessment of bioavailable testosterone in our laboratory are 14.17% at 0.18 nmol/L, 3.32% at 1.38 nmol/L, 6.15% at 4.99 nmol/L, and 3.02% at 8.13 nmol/L. Plasma SHBG levels were determined by diluting serum to 1:21 by adding SHBG sample diluent and then assayed using the Immulite (Siemens Medical Solutions) autoanalyzer, a solid-phase, 2-site chemiluminescent immunoassay. The CV for this assay is 4.0% at 32.3-nmol/L concentration. Determination of serum lipids was performed enzymatically using a Hitachi 911 chemistry analyzer (Boehringer, Ingelheim, Germany). The interassay CVs for the measurement of serum lipids are as follows: triglyceride, 3%; total cholesterol, 2.3%; high-density lipoprotein (HDL) cholesterol, 6.7%; and low-density lipoprotein (LDL) cholesterol, 3.7%. Glucose was determined using an automated chemistry analyzer system (Olympus AU5400; Olympus Optical, Tokyo, Japan). The interassay CVs for this assay are 2.5% at 3.5 mmol/L and 3.0% at 19.6 mmol/L. Insulin was measured on an Abbott (Abbott Park, IL) Architect immunoassay analyzer. The interassay CVs for this assay are 5.5% at 9.5 mIU/L, 4.3% at 72 mU/L, and 6.5% at 135 mIU/L.

2.9. Medical records/conditions

After specific consent from participants, data for use of national Medicare and Pharmaceutical Benefits Schemes were obtained from Medicare Australia and linked with self-reports of health conditions, health service, and medication use. Medical conditions were assessed by the following

Table 1
Demographic, physical, and lifestyle factors according to present or absent MetS

Factors	ATPIII MetS		IDF MetS	
	Present n = 445[a] (37.7%)	Absent n = 737[a]	Present n = 498[a] (41.8%)	Absent n = 691[a]
Demographic				
Age (y)	55 (12)*	52 (12)	55 (12)[a]	51 (12)
Married (% yes)	80.7	80.5	81.1	80.0
Household income (% ≤$20 000 AUD)	22.4	23.8	24.3	16.2
SEIFA index	935 (61)	947 (63)	935 (62)	947 (62)
Born in Australia (% yes)	69.7	67.6	68.6	68.2
Known family history (genetic proxy)				
Diabetes (% yes)	8.5	8.7	7.2	9.7
High blood pressure (% yes)	4.0	3.9	3.8	4.3
Obesity (% yes)	3.8	3.4	4.4	2.9
Physical				
Medical conditions (% 4+)	25.1*	11.2	22.1*	12.7
Whole-body LM (%)	66.6 (5.3)*	71.0 (6.1)	66.4 (4.7)*	71.4 (6.3)
Abdominal FM (%)	37.7 (6.8)*	31.3 (8.3)	38.0 (6.2)*	30.7 (8.3)
Peak handgrip strength (kg F/[kg LM arm])	13.4 (2.0)*	14.3 (2.0)	13.3 (1.9)*	14.4 (2.1)
Insulin (mIU/L)[b]	12.4 (1.8)*	7.0 (1.8)	12.1 (1.8)*	6.8 (1.8)
LDL cholesterol (mmol/L)	3.3 (1.0)*	3.6 (0.9)	3.4 (0.9)	3.5 (0.9)
Total testosterone (nmol/L)	12.2 (4.9)*	15.3 (5.6)	12.1 (4.8)*	15.5 (5.6)
Bioavailable testosterone (nmol/L)	4.7 (1.8)*	5.5 (2.0)	4.7 (1.8)*	5.6 (2.0)
SHBG (nmol/L)	30.8 (14.0)*	37.1 (17.1)	31.2 (15.5)*	37.2 (16.5)
GIR	1.0 (1.1)*	0.7 (0.9)	0.9 (1.1)*	0.7 (0.9)
IPSS	5.0 (5.4)	4.5 (4.9)	4.9 (5.3)	4.6 (5.0)
IPSS obstructive symptoms	2.1 (3.4)	1.8 (3.2)	1.9 (3.3)	1.9 (3.2)
IPSS irritative symptoms	2.9 (2.7)	2.7 (2.4)	3.0 (2.6)	2.7 (2.4)
Lifestyle				
Smokers (% yes)	18.2	21.8	19.7	21.0
MET-h/wk total	13.0 (25.0)	16.7 (29.2)	13.2 (26.4)	16.8 (28.5)
MET-h/wk, any time spent in VPA (% yes)	14.2	19.6	14.9	19.4
Dietary energy intake (kJ/d)	9481 (3064)	9645 (3187)	9527 (3107)	9635 (3160)
Dietary energy density (kJ/[g d])	20.4 (1.0)	20.3 (0.9)	20.3 (1.0)	20.3 (1.0)
Protein (%)	23.4 (4.1)	22.7 (3.6)	23.2 (3.9)	22.8 (3.8)
Saturated fat (%)	8.0 (2.0)	7.8 (2.0)	8.0 (1.9)	7.9 (2.1)
Polyunsaturated fat (%)	3.2 (1.1)	3.0 (1.0)	3.2 (1.1)	3.1 (1.0)
Monounsaturated fat (%)	7.2 (1.5)*	6.9 (1.4)	7.1 (1.4)	7.0 (1.5)
Sugars (%)	21.6 (5.9)	22.5 (5.8)	21.9 (5.9)	22.4 (5.8)
Starches (%)	29.3 (5.1)	29.8 (5.0)	29.4 (5.1)	29.8 (5.0)
Fiber (%)	5.2 (1.4)	5.2 (1.4)	5.2 (1.4)	5.2 (1.4)
Alcohol (g/d)	19.1 (22.7)	20.7 (21.5)	19.0 (22.4)	20.9 (21.5)
Glycemic index	54.8 (4.1)	54.3 (4.4)	54.8 (4.1)	54.3 (4.4)
Glycemic load	122.0 (44.5)	126.5 (47.6)	123.7 (45.2)	125.9 (47.3)

Values are means (standard deviations) unless stated otherwise and were age standardized to the Australian male population distribution according to the 2001 Census of Population and Housing. Macronutrient intakes in grams per day were computed as percentage of energy-providing food macronutrients. GIR measures symptoms associated with erectile dysfunction (highest scores = most severe). IPSS measures symptoms associated with prostatic enlargement (highest scores = most severe). AUD indicates Australian dollars; SEIFA, advantage/disadvantage index from the Socio-Economic Indexes for Areas (highest reflects most advantaged/least disadvantaged); VPA, vigorous intensity physical activity.

[a] Sample size may vary because of missing data for some variables.

[b] Log-transformed values were analyzed to account for extreme right skewness and are geometric means (geometric standard deviations) after back-transformation.

* Significant between-group differences at P less than .001 are for independent-samples t test (for equal or unequal variances as appropriate) for continuous variables or for χ^2 test for categorical variables.

question item: "Have you ever been told by a doctor that you have any of the following conditions?" The list of conditions included most of the chronic diseases applicable to men of this age group. Family history of known diabetes, high blood pressure, and obesity (specific to the MetS) were assessed by the following question item: "Do, or did, any of your relatives (blood/first-degree relations only) have [condition]?"

2.10. Metabolic syndrome classifications

Criteria proposed by both the National Cholesterol Education Program Adult Treatment Panel III (ATPIII) [2] and the International Diabetes Federation (IDF) [1] were used to classify participants with the MetS. Participants were classified as having the ATPIII MetS by the presence of any

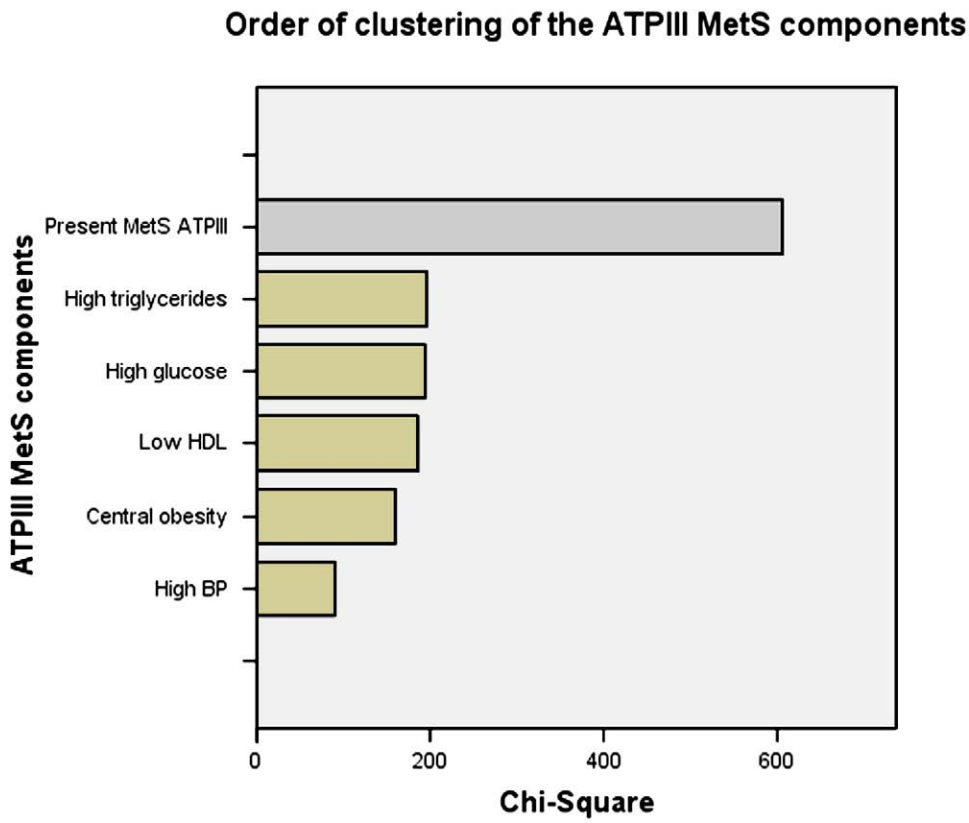

Fig. 1. Hierarchical order of clustering of the ATPIII MetS components.

3 of the following 5 conditions: (1) High triglycerides of at least 1.7 mmol/L (≥150.6 mg/dL) or specific treatment of this lipid abnormality. Specific treatment was determined by self-report medications (hypolipidemic agents) or by medical records (lipid-modifying agents). (2) Low HDL cholesterol of less than 1.03 mmol/L (<39.83 mg/dL) or specific treatment of this lipid abnormality. Specific treatment was determined by self-report medications (hypolipidemic agents) or by medical records (lipid-modifying agents). (3) High systolic (≥130 mm Hg) or diastolic (≥85 mm Hg) blood pressure or treatment of previously diagnosed hypertension. Specific treatment was determined by self-report medications (antihypertensive agents) or by medical records (diuretics, calcium channel blockers, agents acting on renin-angiotensin system, and antihypertensive agents). (4) High fasting plasma glucose of at least 5.6 mmol/L (≥100.9 mg/dL) or previously diagnosed type 2 diabetes mellitus or specific treatment of this blood glucose abnormality. Previous diagnosis of type 2 diabetes mellitus was determined by self-report. Specific treatment was determined by self-report medications (hypoglycemic agents) or by medical records (agents used for diabetes). (5) High waist circumference (≥102 cm) was used to define central obesity. Participants were classified as having the IDF MetS by the presence of central obesity, determined using sex- and ethnic-specific (by country of birth) waist circumference cutoffs (≥94 cm for Europids [97.2%]; ≥90 cm for Asians [2.8%]), plus any 2 of the remaining 4 abovementioned ATPIII conditions.

2.11. Statistical analysis

Statistical analyses were performed using SPSS 15.0 (SPSS, Chicago, IL). The sample was age standardized to the Australian male population distribution according to the 2001 Census of Population and Housing to account for sampling errors. Significant differences (at $P < .001$ level) between subgroups classified with and without the MetS for demographic, physical, and lifestyle factors were determined using χ^2 analysis for categorical and independent-samples t test for continuous data. Prevalence odds ratios (ORs) (99.5% confidence intervals [CIs]) for present MetS were determined using multiple-adjusted binary logistic regression analyses. Quartiles were used to create quarter (Q) comparison groups, using Q4 as the reference. The set of risk factors that best explained the odds for MetS classification was chosen using a stepwise selection process, starting with a full model (backward elimination: entered if $P < .05$; removed if $P > .01$) including all factors listed in Table 1. TwoStep Cluster Analysis (SPSS) was used to determine the distribution of individual components within each MetS classification. Population attributable risk with associated CIs (99.5% CI) was computed based on the Bonferroni

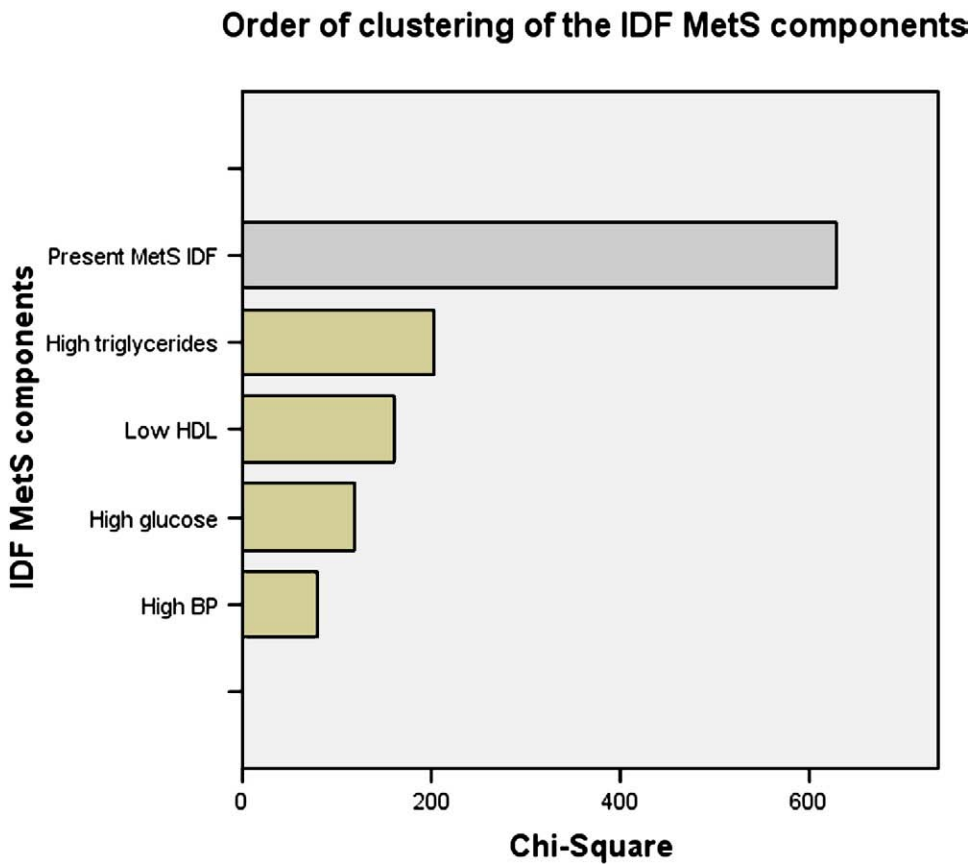

Fig. 2. Hierarchical order of clustering of the IDF MetS components.

inequality method [19], using multiple-adjusted ORs derived from binary logistic regression models, as described above. Subtypes of fat (saturated, polyunsaturated, monounsaturated) and carbohydrate (sugar, starch) intake were used rather than total macronutrient values because of concerns regarding multicollinearity.

3. Results

Of the 1195 participants recruited, data were missing for 12 and 6 participants for ATPIII and IDF classifications, respectively. Data for demographic, physical, and lifestyle factors according to the ATPIII and IDF MetS classifications for the remaining sample appear in Table 1. Prevalence estimates for men classified with present ATPIII MetS and IDF MetS were 37.7% and 41.8%, respectively. The percentages who reported at least 4 medical conditions were significantly higher, as were means for age, percentage abdominal FM, and insulin, whereas means for percentage whole-body LM, muscle strength, total testosterone, bioavailable testosterone, and SHBG were significantly lower for men classified with present MetS according to both ATPIII and IDF criteria. Means for men classified with the ATPIII MetS were also found to be lower for LDL and higher for monounsaturated fat. Components predicting MetS classifications in descending order of importance (according to Wald statistics) were high triglycerides, high glucose, low HDL, central obesity, followed by high blood pressure for ATPIII (Fig. 1), and high triglycerides, low HDL, high glucose, followed by high blood pressure for IDF (Fig. 2).

Table 2 presents set of demographic, physical, and lifestyle factors that best explained the increased odds for ATPIII MetS classification. The odds for present ATPIII MetS classification (in order of importance) decreased for lower insulin levels (86% Q1, 69% Q2, and 34% Q3) and increased for lower percentage whole-body LM (234% Q1, 151% Q2, and 61% Q3), for lower muscle strength (115% Q1 and 91% Q2), and for having 3 (113%) and 4+ (126%) medical conditions. Findings indicate that high insulin levels, low percentage whole-body LM, and low muscle strength were the significant factors associated with an increased risk of the ATPIII MetS classification. Significant PAR estimates suggest that 44% of the ATPIII MetS prevalence among men was prevented because of low insulin levels (approximately 50% less for Q1 than Q4); and approximately 18% and 14% of the ATPIII MetS prevalence would have been theoretically prevented if adults increased muscle mass and strength by approximately 10 and 17 percentage points (from Q2 to Q4 levels), respectively.

Table 2
Odds ratios for present ATPIII MetS, prevalence by risk factor exposure, and PAR%

Risk factors	Exposure levels	Present, n	Absent, n	Prevalence, %	Wald	*P* value	OR	(99.5% CI)	PAR%	(99.5% CI)
Insulin (mIU/L)	Q1 (0.50-5.75)	31	267	7	54	.000	0.14	(0.07, 0.29)	−0.44	(−1.00, −0.17)
	Q2 (5.89-8.32)	82	230	18	30	.000	0.31	(0.17, 0.56)	−0.41	(−0.90, −0.14)
	Q3 (8.51-13.18)	146	146	33	4	.041	0.66	(0.37, 1.17)	−0.17	(−0.56, 0.05)
	Q4 (13.49+)	186	95	42			1			
Whole-body LM (%)	Q1 (51.6-65.1)	153	106	39	22	.000	3.34	(1.63, 6.84)	0.27	(0.15, 0.33)
	Q2 (65.2-68.9)	116	144	30	14	.000	2.51	(1.25, 5.04)	0.18	(0.06, 0.24)
	Q3 (69.0-73.3)	80	178	20	4	.061	1.61	(0.79, 3.28)	0.08	(−0.05, 0.14)
	Q4 (73.4+)	43	230	11			1			
Peak handgrip strength (kg F/[kg LM arm])	Q1 (8.2-12.4)	121	120	31	11	.001	2.15	(1.14, 4.04)	0.17	(0.04, 0.24)
	Q2 (12.5-13.8)	112	140	29	8	.004	1.91	(1.02, 3.60)	0.14	(0.00, 0.21)
	Q3 (13.9-15.3)	84	179	22	1	.289	1.28	(0.67, 2.45)	0.05	(−0.11, 0.13)
	Q4 (15.4+)	68	205	18			1			
Medical conditions (n)	4+	112	83	25	10	.002	2.26	(1.09, 4.68)	0.14	(0.02, 0.20)
	3	72	78	16	8	.005	2.13	(1.00, 4.53)	0.09	(0.00, 0.13)
	2	104	151	23	2	.120	1.44	(0.74, 2.80)	0.07	(−0.08, 0.15)
	1	85	217	19	0	.589	0.88	(0.46, 1.71)	−0.03	(−0.23, 0.08)
	None	73	209	16			1			

Odds ratio, prevalence ORs with 99.5% CIs, and *P* values were determined using binary logistic regression with stepwise selection (starting with a full model including all factors listed in Table 1, with backward elimination: entered if $P < .05$; removed if $P > .01$). Data were age standardized to the Australian male population distribution according to the 2001 Census of Population and Housing. Q1 indicates the lowest quarter.

Approximately 9% and 14% of the ATPIII MetS prevalence would have been theoretically prevented if men had no prior exposure to 3 and 4+ medical conditions, respectively.

Table 3 presents set of demographic, physical, and lifestyle factors that best explained the increased odds for IDF MetS classification. The odds for present IDF MetS classification (in order of importance) decreased for lower insulin levels (87% Q1 and 76% Q2); increased for lower percentage whole-body LM (385% Q1, 445% Q2, and 196% Q3), lower muscle strength (169% Q1 and 138% Q2), SHBG

Table 3
Odds ratios for present IDF MetS, prevalence by risk factor, and PAR%

Risk factors	Exposure levels	Present, n	Absent, n	Prevalence, %	Wald	*P* value	OR	(99.5% CI)	PAR%	(99.5% CI)
Insulin (mIU/L)	Q1 (0.50-5.75)	36	265	7	55	.000	0.13	(0.06, 0.29)	−0.48	(−1.09, −0.18)
	Q2 (5.89-8.32)	90	224	18	40	.000	0.24	(0.13, 0.45)	−0.56	(−1.20, −0.22)
	Q3 (8.51-13.18)	170	123	34	2	.140	0.73	(0.39, 1.34)	−0.13	(−0.53, 0.09)
	Q4 (13.49+)	202	79	41			1			
Whole-body LM (%)	Q1 (51.6-65.1)	153	106	39	32	.000	4.85	(2.23, 10.54)	0.31	(0.21, 0.35)
	Q2 (65.2-68.9)	116	144	30	40	.000	5.45	(2.56, 11.6)	0.24	(0.18, 0.27)
	Q3 (69.0-73.3)	80	178	20	16	.000	2.96	(1.38, 6.36)	0.14	(0.06, 0.17)
	Q4 (73.4+)	43	230	11			1			
Peak handgrip strength (kg F/[kg LM arm])	Q1 (8.2-12.4)	138	104	33	17	.000	2.69	(1.37, 5.28)	0.20	(0.09, 0.26)
	Q2 (12.5-13.8)	128	127	30	14	.000	2.38	(1.23, 4.61)	0.18	(0.06, 0.24)
	Q3 (13.9-15.3)	92	173	22	2	.173	1.38	(0.71, 2.69)	0.06	(−0.09, 0.14)
	Q4 (15.4+)	66	206	16			1			
SHBG (nmol/L)	Q1 (6-24)	179	147	36	7	.007	2.02	(0.97, 4.18)	0.18	(−0.01, 0.27)
	Q2 (25-32)	149	166	30	5	.032	1.71	(0.85, 3.43)	0.12	(−0.05, 0.21)
	Q3 (33-43)	92	193	19	0	.526	0.85	(0.42, 1.73)	−0.03	(−0.26, 0.08)
	Q4 (44+)	77	185	15			1			
Age category (per 10 y)	75+	41	38	8	5	.020	2.26	(0.85, 6.02)	0.05	(−0.02, 0.07)
	65-74	81	82	16	10	.001	2.44	(1.11, 5.35)	0.10	(0.02, 0.13)
	55-64	116	119	23	14	.000	2.47	(1.24, 4.92)	0.14	(0.05, 0.19)
	45-54	144	192	29	8	.005	1.84	(1.00, 3.41)	0.13	(0.00, 0.21)
	35-44	115	260	23			1			
Married	Yes	404	553	81	5	.024	0.61	(0.33, 1.13)	−0.52	(−1.65, 0.26)
	No	94	138	19			1			

Odds ratio, prevalence ORs with 99.5% CIs, and *P* values were determined using binary logistic regression with stepwise selection (starting with a full model including all factors listed in Table 1, with backward elimination: entered if $P < .05$; removed if $P > .01$). Data were age standardized to the Australian male population distribution according to the 2001 Census of Population and Housing.

levels (102% Q1 and 71% Q2), and higher age categories (84% to 147%); and decreased for being married (39%). Findings indicate that high insulin levels, low percentage whole-body LM, and low muscle strength were the significant factors associated with an increased risk of the IDF MetS classification. Significant PAR estimates suggest that 48% of the IDF MetS prevalence among men was prevented because of low insulin levels and that 24% and 18% of the IDF MetS prevalence would have been theoretically prevented if muscle mass and strength were increased by approximately 10 and 17 percentage points (from Q2 to Q4 levels), respectively.

4. Discussion

The findings of this report were derived from a comprehensive study of demographic, physical, and lifestyle factors associated with the MetS in a large regionally representative sample of Australian men aged 35 years or older. Prevalence estimates for the ATPIII MetS (37.7%) and IDF MetS (41.8%) among our population of men were high and closely approximate those in a recent report of an Australian population-based survey [6], confirming the national representativeness of our sample. Abnormal levels of triglycerides, glucose, and HDL cholesterol were observed most frequently among those classified with the MetS, indicating that the presence of one condition increases the probability for the presence of other cardiometabolic conditions, an important clinical information for the detection and treatment of multiple cardiovascular disease risk factors.

High fasting plasma insulin levels (indicating insulin resistance) followed by low muscle mass and strength were the most important set of significant factors that determined the presence of the MetS by either the ATPIII or IDF classifications. These data underline the central role of insulin resistance in the pathophysiology of the MetS and associated abnormalities in plasma glucose and lipid metabolism leading to increases in plasma triglycerides and decreases in HDL cholesterol levels. Although causal pathways are not well established, insulin resistance is believed to increase secretion of very low-density lipoprotein cholesterol as well as impair lipoprotein lipase and hepatic lipase activity, resulting in high triglycerides and low HDL levels [20]. Supporting this notion, insulin-resistant persons were shown to have significantly decreased postprandial muscle glycogen synthesis and increased hepatic de novo lipogenesis, resulting in increased plasma triglycerides and decreased HDL levels compared with non–insulin-resistant controls matched for age, body mass/index, and physical activity [21]. Insulin resistance was also associated with a significantly increased risk of hypertension incidence, independent of body mass [22].

Muscle mass and strength were found to be strong protective factors against being classified with the MetS. Although consistent with observational data showing an association between muscle strength and incident MetS [12], our findings were independent of insulin resistance, abdominal fat, and many other conjectured risk factors simultaneously accounted for. This novel finding suggests that muscle mass and strength are inversely associated with the MetS despite exposure to insulin resistance and abdominal fat accumulation, and is clinically important information for population health given that the prevalence of central and general obesity in Australia is very high [23].

Protective effects of muscle mass and strength were likely due to mechanisms involving both insulin resistance and ectopic fat accumulation. Insulin-stimulated plasma glucose uptake occurs mostly within skeletal muscle, underlining its importance in glucose control [24]. Randomized controlled trials have demonstrated significant strength training effects on muscle mass and strength, insulin resistance, as well as glycosylated hemoglobin in type 2 diabetes mellitus patients [25]. Treatment effects on insulin resistance were likely due to a combination of reduced ectopic fat accumulation into muscle, as muscle strength is inversely associated with muscle lipid depots [26], as well as increased muscle insulin sensitivity due to increases in glucose uptake and metabolism factors [27]. Significant PAR% estimates suggest that the level of increases in muscle mass (~10%) and strength (~17%) needed to eradicate risk factor exposure and prevent approximately 14% to 24% of the MetS prevalence among Australian men would be theoretically achievable with a short-term strength training intervention [25]. Accordingly, this body of evidence attributes muscle mass and strength as the most clinically important targets for treating and preventing the development of the MetS.

Weaker positive associations were found for low SHBG levels, increasing age, being unmarried (IDF), and chronic diseases (ATPIII). The finding for SHBG is consistent with cohort data showing low levels to be associated with an increased risk of the MetS incidence [11], but is likely due to insulin resistance that shows a strong inverse association with SHBG [28]. The association of chronic diseases and increasing age is consistent with the increased risk of the MetS among older populations, whereas the reason for the protective association of being married is unclear. The minor differences in risk factor profiles for each definition are due to the IDF MetS classification being conditional to the presence of central obesity.

Strengths of this study include a large random sample obtained after a high response rate (considering the large participant burden for extensive clinical data collections), which had similar characteristics to men from the general Australian population; the standardized morning blood collection times; and the precise methods used for clinical data collections. Furthermore, study population and characteristics of dropouts and nonresponders have been sufficiently described; and statistical models were adjusted for an extensive list of conjectured risk factors. This report's principle limitation is that PAR% estimates due to risk factors were based on assumptions of causality using

cross-sectional data. This stated, our multiple-adjusted risk ratios for prevalent MetS due to lowest muscle strength quarter closely approximate those reported for incident MetS in the Aerobics Centre Longitudinal Study [12]. Other limitations include seasonal effects from different periods of data collection, reliance of self-report for all lifestyle factors, physical activity type not being discerned (aerobic vs resistance), and our inability to account for other potentially important factors, particularly cardiorespiratory fitness.

In summary, high insulin level, low muscle mass, and low strength were the strongest set of factors significantly associated with an increased risk of ATPIII and IDF MetS classification, independent of abdominal fat and other factors accounted for. If confirmed prospectively, significant PAR% estimates suggest that the level of increases in muscle mass and strength needed to theoretically eradicate risk factor exposure and prevent approximately 14% to 24% of the MetS prevalence among Australian men would be achievable with a short-term strength training intervention. These data also facilitate economic and population health impact modeling for interventions targeting these preventable risk factors associated with the MetS.

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