

**Metabolic syndrome risk and mental health:
Relationship with physical activity and physical fitness
in Flemish adults**

by Katrien Wijndaele

Supervisor: Prof. Dr. R. Philippaerts

Co-supervisor: Prof. Dr. J. Lefevre

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Supervisor:

Prof. Dr. R. Philippaerts (UGent)

Co-supervisor:

Prof. Dr. J. Lefevre (KULeuven)

Supervisory board:

Prof. Dr. R. Philippaerts (UGent)

Prof. Dr. J. Lefevre (KULeuven)

Prof. Dr. J. Bouckaert (UGent)

Prof. Dr. G. De Backer (UGent)

Prof. Dr. W. Duquet (VUB)

Examination board:

Dr. U. Ekelund (MRC Epidemiology Unit, Cambridge, UK)

Prof. Dr. F. Boen (KULeuven)

Prof. Dr. S. De Henauw (UGent)

Prof. Dr. G. Cardon (UGent)

Prof. Dr. R. Philippaerts (UGent)

Prof. Dr. J. Lefevre (KULeuven)

Prof. Dr. J. Bouckaert (UGent)

Prof. Dr. G. De Backer (UGent)

Prof. Dr. W. Duquet (VUB)

Prof. Dr. I. De Bourdeaudhuij (UGent)



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SAMENVATTING

Het metabool syndroom vertoont wereldwijd een hoge, stijgende prevalentie, en gaat gepaard met een verhoogd risico op cardiovasculaire aandoeningen, type II diabetes en vroegtijdige dood. Psychologische stress vormt eveneens een belangrijke publieke gezondheidsbedreiging omwille van de hoge prevalentie en de geassocieerde gezondheidsrisico's, waaronder depressie, angststoornissen, en het metabool syndroom. Op basis van bepaalde biologische processen, zouden, naast stress, ook fysieke activiteit en fysieke fitheid, een causale rol kunnen hebben in de ontwikkeling van het metabool syndroom. Bovendien ondersteunen bepaalde theorieën mogelijke positieve effecten van fysieke activiteit op stress. De studie van de onderlinge relaties tussen fysieke activiteit, fysieke fitheid, stress en het metabool syndroom is dus een belangrijke bron van informatie voor de ontwikkeling van effectieve preventiestrategieën tegen stress en het metabool syndroom. Het voornaamste doel van deze thesis bestond eruit deze onderlinge relaties te onderzoeken in een populatie van Vlaamse volwassenen tussen 18 en 75 jaar. Voorafgaand werden echter een aantal computergestuurde psychologische vragenlijsten en een nieuw geconstrueerde continue risicoscore voor het metabool syndroom onderzocht op respectievelijk betrouwbaarheid en validiteit.

De eerste studie toonde aan dat de computergestuurde versie van vijf verschillende psychologische gezondheidsvragenlijsten als een betrouwbaar alternatief voor de originele versie mag gebruikt worden in een algemene volwassen populatie. Vervolgens werd aangetoond dat een continue risicoscore van het metabool syndroom, geconstrueerd om een aantal beperkingen van reeds bestaande binaire definities op te vangen, een valide instrument is voor epidemiologisch onderzoek. In de vier relatiestudies konden we, evenwel hun cross-sectioneel karakter in het achterhoofd houdend, vooreerst besluiten dat sportparticipatie door middel van positieve effecten op sociale steun en coping, een vermindering van stress, angst en depressie kan veroorzaken. Verder kan een vermindering van sedentair gedrag resulteren in een risicoverlaging voor het metabool syndroom, supplementair op een risicoverlaging door een toename in matige tot intense fysieke activiteit. Wat betreft fysieke fitheid kan een hogere spierkracht bij vrouwen eveneens beschermend zijn tegen het metabool syndroom, bovenop een beschermend effect van een goede aerobe fitheid, terwijl bij mannen enkel een mogelijk beschermend effect van aerobe fitheid tegen het metabool syndroom werd gevonden. Tenslotte toonde een causaal model aan dat het beschermend effect van matige tot intense fysieke activiteit tegen het metabool syndroom voornamelijk zou veroorzaakt worden door een toename in fysieke fitheid.

1.

**GENERAL INTRODUCTION AND
OUTLINE OF THE THESIS**

1. Introduction

1.1. Metabolic syndrome

A central health outcome within the scope of this thesis is the metabolic syndrome. The metabolic syndrome represents a constellation of metabolic abnormalities that co-occur in individuals more often than might be expected by chance. In a Consensus Statement from the International Diabetes Federation,² the general features of the metabolic syndrome were defined to be 1) abnormal body fat distribution, 2) insulin resistance, 3) atherogenic dyslipidaemia, 4) elevated blood pressure, 5) proinflammatory state, and 6) prothrombotic state. When clustering, they are associated with an increased risk for cardiovascular morbidity^{36, 101, 104, 116, 122, 128, 155, 179} and mortality,^{88, 89, 93, 108, 118, 169} type 2 diabetes^{83, 101, 105, 128, 155, 179} and all-cause mortality.^{88, 89, 108, 118, 169}

The concept of the metabolic syndrome has already been described in the 1920's.²⁷ However, it was Reaven's Banting Medal award lecture in 1988¹⁴⁵ that served as a landmark publication, and was followed by intensive investigation on the metabolic syndrome, formerly also described as "syndrome X",¹⁴⁵ "insulin resistance syndrome",⁴⁸ or "the deadly quartet".⁹⁹

The pathogenesis of the metabolic syndrome and of its components is complex and remains unclear. However, two features appear to stand out as potential causative factors: *abnormal fat distribution (central obesity)* and *insulin resistance*. Other important factors also influence the development of the metabolic syndrome, including genetic profile, physical inactivity, ageing, a proinflammatory state and hormonal dysregulation. The role of all these causal factors may vary depending on ethnic group.² One hypothesis concerning hormonal changes suggests that elevated levels of serum cortisol, caused by chronic stress, may contribute to the development of visceral obesity, insulin resistance and dyslipidemia.^{47, 153}

As mentioned above, a first potentially important causative factor is *abnormal fat distribution (central obesity)*. General obesity contributes to hyperglycemia, hypertension, high serum triglycerides, low HDL cholesterol and insulin resistance. However, it has been documented that individuals with a normal BMI may nevertheless be characterized by an excess of visceral adipose tissue and show the features of the metabolic syndrome. Therefore, abdominal obesity in particular and more specifically an excess of visceral fat may have a

pathophysiological role. In a recent study, visceral fat has been independently associated with each of the metabolic syndrome components.³⁰ Although much further research is needed to elucidate the association between central obesity and the other metabolic syndrome components, it is hypothesized that adipose tissue (particularly visceral adipose tissue) is a source of several molecules that induce insulin resistance, including excess nonesterified fatty acids and tumor necrosis factor- α . Furthermore, excessive adipose tissue is associated with a decreased production of adiponectin, a molecule that is found to have anti-diabetic, anti-atherosclerotic and anti-inflammatory functions.^{2, 80}

Insulin resistance is widely believed to be a central feature of the metabolic syndrome, although the mechanistic link between insulin resistance and most of the metabolic syndrome components is not fully understood. It is strongly associated with atherogenic dyslipidemia and a proinflammatory state. However, its associations with hypertension and the prothrombotic state are less tight and remain unclear. Further research is needed examining these associations.^{2, 80}

1.1.1. Defining the metabolic syndrome

The concept of the metabolic syndrome has existed for at least 80 years.²⁷ However, before 1998, there had been no initiative to develop an internationally recognized definition. The first proposal was made by an expert panel of the *World Health Organization (WHO)* as a working definition to be improved upon in the future.¹⁸⁰ This definition was designed based on the assumption that insulin resistance may be the common etiological factor for the individual risk factors of the metabolic syndrome. Therefore, the presence of diabetes mellitus, impaired fasting glycaemia, impaired glucose tolerance or insulin resistance was a *sine qua non* for the diagnosis to be made, together with two or more of the other risk factors shown in Table 1.

In 1999, the *European Group for the Study of Insulin Resistance (EGIR)* suggested a modified version of the WHO definition, which was simpler to use in epidemiological studies since it did not require an euglycaemic clamp to measure insulin sensitivity.⁸ EGIR proposed the use of fasting insulin levels to estimate insulin resistance and impaired fasting glucose as a substitute for impaired glucose tolerance. Waist circumference only was used as a measure of central obesity, and microalbuminuria was omitted from the definition. They also preferred

the term "insulin resistance syndrome", and restricted their definition to non-diabetic individuals. The WHO and EGIR definition however agree in that they both focus on the trait of insulin resistance/hyperglycemia as an essential component (Table 1).

Subsequently, the *National Cholesterol Education Program Adult Treatment Panel (NCEP ATPIII)* provided a new definition of the "metabolic syndrome" in 2001, as part of an educational program for the prevention of coronary heart disease.⁶¹ In contrast with both earlier proposed definitions, the presence of insulin resistance was not taken into account in this new definition. A second major difference was the non "glucose-centric" character of the definition, since all risk factors were treated of equal importance in making the diagnosis.² Furthermore, this definition was intended to be easily applicable in clinical practice, since it was based on fasting values of a few laboratory parameters (triglycerides, HDL cholesterol, plasma glucose) and measurement of waist circumference and blood pressure (Table 1).⁹²

Table 1. Comparison of three definitions of the metabolic syndrome (adapted).⁵⁵

WHO (1999) ¹⁸⁰	EGIR (1999) ⁸	NCEP ATPIII (2001) ⁶¹
Diabetes or impaired fasting glycaemia or impaired glucose tolerance or insulin resistance (hyperinsulinaemic, euglycaemic clamp-glucose uptake in lowest 25%)	Insulin resistance – hyperinsulinaemia: top 25% of fasting insulin values from non-diabetic population	3 or more of the following:
Plus 2 or more of the following:	Plus 2 or more of the following:	
Obesity: BMI > 30 or waist-to-hip ratio > 0.9 (male) or > 0.85 (female)	Central obesity: waist circumference ≥ 94 cm (male) or ≥ 80 cm (female)	Central obesity: waist circumference >102 cm (male) or > 88 cm (female)
Dyslipidaemia: triglycerides ≥ 1.7 mmol/L or HDL cholesterol < 0.9 (male) or < 1.0 (female) mmol/L	Dyslipidaemia: triglycerides > 2.0 mmol/L or HDL cholesterol < 1.0 mmol/L	Hypertriglyceridemia: triglycerides ≥ 1.7 mmol/L Low HDL cholesterol: < 1.0 mmol/L (male) or < 1.3 mmol/L (female)
Hypertension: blood pressure > 140/90 mm Hg	Hypertension: blood pressure ≥ 140/90 mm Hg and/or medication	Hyperension: blood pressure ≥ 135/85 mm Hg or medication
	Fasting plasma glucose ≥ 6.1 mmol/L	Fasting plasma glucose ≥ 6.1 mmol/L
Microalbuminuria: albumin excretion > 20 µg/min		

In 2002, the *American Association of Clinical Endocrinology (AACE)* released a position statement on the "insulin resistance syndrome", deliberately not providing a specific definition but allowing the diagnosis to rely on clinical judgement.⁵⁷ This position statement, together with the EGIR definition, were the least frequently used, although they contributed to the creation of an ICD-9 code (International Classification of Diseases) for the metabolic syndrome (code 277.7 Dysmetabolic syndrome X).¹

The lack of a standard definition led to confusion and made comparisons between studies difficult. Estimation of the prevalence of the metabolic syndrome differed, according to the definition used.^{9, 18, 68, 144} As shown in Figure 1, within the same population, different individuals were diagnosed using different criteria.² Finally, studies comparing the predictive power of different definitions for subsequent diabetes mellitus or cardiovascular disease produced contradictory results.^{105, 115} Another important problem was that applicability of the existing definitions was not equal for diverse ethnic groups, especially cutoffs for obesity.²

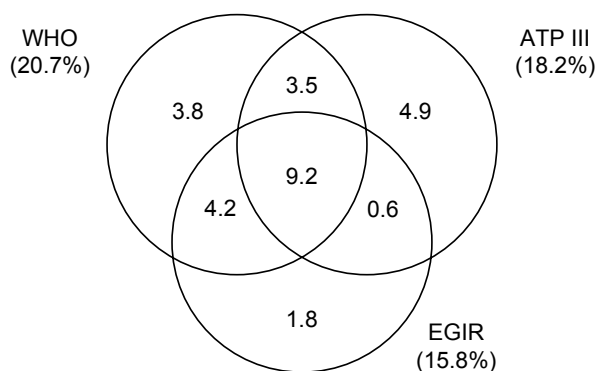


Figure 1. Prevalence of the metabolic syndrome according to three different definitions in an Australian non-diabetic population.⁵³ Data shown are percentage prevalences within the total population.²

The *International Diabetes Federation (IDF)* felt a strong need for one unifying definition that 1) enabled identification of individuals at high risk of developing cardiovascular disease and diabetes, 2) was useful for clinicians and researchers world-wide, and 3) made international comparisons possible. Therefore, it was decided to use the NCEP ATP III definition⁶¹ as a starting point and to modify and update it to reflect these objectives.^{2, 3} In this new IDF definition, central obesity, as assessed by waist circumference, was agreed as an essential component for diagnosis (Table 2).¹⁷⁰ This was based on evidence showing that central obesity is more strongly associated with all other metabolic syndrome risk factors

than any other parameter, and is highly correlated with insulin resistance.³⁰ Although it was recognized that insulin resistance is an important component of the metabolic syndrome, its measurement was not seen as essential to this new definition, given the latter findings and the fact that central obesity is much easier to measure than insulin resistance. The definition was optimized by providing ethnic-specific cutoffs for waist circumference. Furthermore, a number of additional parameters (e.g. tomographic assessment of visceral adiposity and liver fat, inflammatory markers, thrombotic markers) were highlighted by the IDF to be included in research studies, in order to further optimize the definition in the future.^{2, 3}

Table 2. International Diabetes Federation metabolic syndrome definition (adapted)¹⁷⁰

Central obesity: waist circumference ≥ 94 cm for European men or ≥ 80 cm for European women, with ethnicity specific values for other groups

Plus 2 or more of the following:

Triglycerides > 1.7 mmol/L, or specific treatment for this lipid abnormality

HDL cholesterol < 1.0 mmol/L (male) or < 1.3 mmol/L (female), or specific treatment for this lipid abnormality

Systolic blood pressure ≥ 130 mm Hg or diastolic blood pressure ≥ 85 mm Hg, or treatment of previously diagnosed hypertension

Fasting plasma glucose ≥ 5.6 mmol/L, or previously diagnosed type 2 diabetes

1.1.2. Epidemiology of the metabolic syndrome

The lack of a standard definition of the metabolic syndrome until 2005 does not facilitate comparison of prevalence rates between studies. Furthermore, studies from various countries differ in study design, sample selection, year that they were undertaken, and age and sex structure of the population. Although the obesity criteria in the NCEP-ATPIII definition⁶¹ may not be appropriate for Asian populations³, Figure 2 provides an overview of world-wide prevalence rates based on this definition.²⁷

Despite methodological differences between these studies, some interesting trends can be found.⁵⁵ First of all, as can be seen in Figure 2, prevalence rates vary widely across populations. For example, in studies including subjects 20-25 years and older, prevalence varies from 8% (India) to 24% (USA) in men, and from 7% (France) to 43% (Iran) in women. Within the same country prevalence rates also differ substantially between race/ethnic groups. In a large representative sample of the United States population (National Health and Nutrition Examination Survey (NHANES III)) for example, Mexican Americans

show the highest prevalence (31.9%), in comparison with non-Hispanic whites (23.8%) and African Americans (21.6%).^{69, 148} Furthermore, in some populations the age-adjusted prevalence of the metabolic syndrome is higher among men, whereas in other populations it is higher among women.⁵⁵

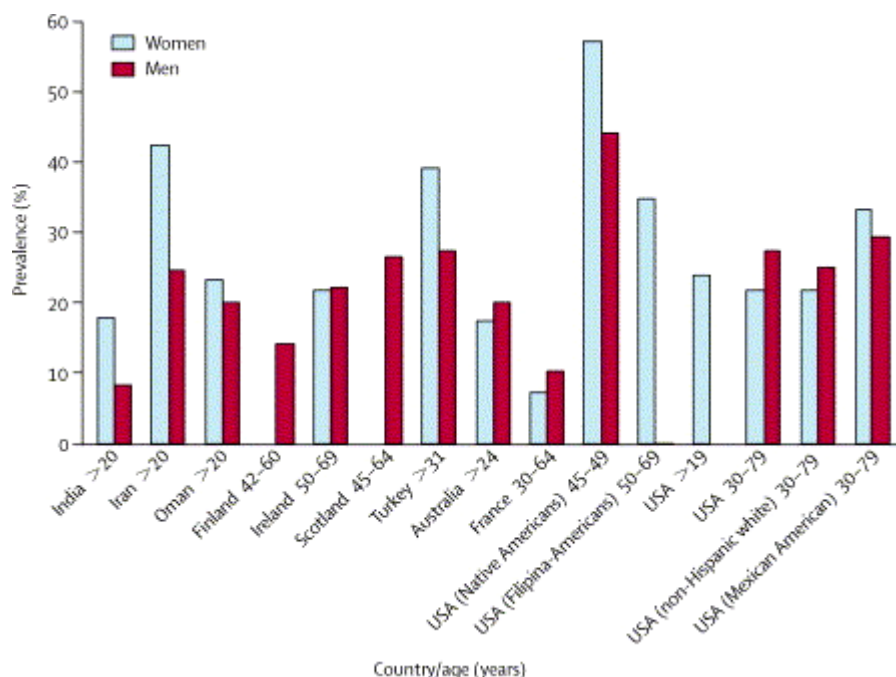


Figure 2. Prevalence of the metabolic syndrome according to the NCEP ATPIII definition.²⁷

A very consistent finding is the fact that metabolic syndrome prevalence is highly age-dependent. In the United States (NHANES III) for example, prevalence increased from 6.7% in the 20-29 year age-group to 43.5% and 42.0% for those aged 60-69 years and at least 70 years, respectively.⁶⁹ Furthermore, the prevalence of the metabolic syndrome increases dramatically with higher BMI. For men participating in the NHANES III, the prevalence of the metabolic syndrome was 4.9-fold (4.5 in women) and 13-fold (8.1 in women) higher for those classified as overweight or obese compared with those of normal weight.¹³⁷ With the current worldwide obesity epidemic, a prevalence increase in the metabolic syndrome is expected. Studies in the United States population aged 20 years and older already showed evidence for an increase in prevalence during the past two decades.^{70, 116}

Populations undergoing a rapid lifestyle change characterized by increased energy intake and decreased physical activity (including south Asians, Hispanics, Arabs, Chinese) also show a higher tendency to develop the metabolic syndrome. Furthermore, even within particular

ethnic groups, prevalence of the metabolic syndrome appears to be higher in urban regions. Therefore, with increasing urbanization in developing countries like India, the prevalence of the metabolic syndrome is expected to increase several-fold in the coming years.¹⁴²

1.1.3. Risks associated with the metabolic syndrome

An increasing number of longitudinal studies provide evidence for certain health risks associated with the metabolic syndrome. The metabolic syndrome is predictive for the development of cardiovascular morbidity^{36, 101, 104, 116, 122, 128, 155, 179} and mortality,^{88, 89, 93, 108, 118, 169} type 2 diabetes^{83, 101, 105, 128, 155, 179} and all-cause mortality.^{88, 89, 108, 118, 169} Since the definitions of the metabolic syndrome comprise established cardiovascular disease risk factors and impaired fasting glucose/impaired glucose tolerance, this might not be unexpected. Although evidence is still poor, presence of the metabolic syndrome might also be associated with a higher risk for other co-morbidities, including chronic kidney disease^{37, 46} and prostate cancer.¹¹¹

In the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study⁸⁸ for example, 6156 men and 5356 women from 11 prospective European cohort studies, aged 30 through 89 years and all non-diabetic at baseline, participated with a mean duration of follow-up of 8.8 years. In individuals with the metabolic syndrome (modified WHO definition) compared with individuals without it, the overall hazard ratios for all-cause and cardiovascular mortality were 1.4 and 2.3 ($P < 0.05$) respectively in men and 1.4 and 2.8 ($P < 0.05$) respectively in women, after adjustment for age, blood cholesterol levels, and smoking. In a population of 958 middle-aged Finnish men, participating in a four-year follow-up study, Laaksonen et al.¹⁰⁵ found odds ratios ranging between 5.0 and 8.8 ($P < 0.05$) depending on the definition used, for the development of type II diabetes in subjects with the metabolic syndrome at baseline versus those without, after adjustment for age. Moreover, a number of studies provided evidence for an increased risk of incident cardiovascular disease and type 2 diabetes, as a function of the number of metabolic syndrome risk factors present at baseline.^{101, 118, 122, 128, 155}

Depending on the choice of metabolic syndrome definition, population studied and exclusion criteria used, length of follow-up and variables adjusted for, different risk estimates are found

between studies (e.g. for cardiovascular disease, increased risk ranges from 30 to 400%). Ford⁶⁷ made a critical review and meta-analysis of studies using the exact or modified versions of the NCEP ATPIII⁶¹ or WHO definition,¹⁸⁰ to determine summary risk estimates for all-cause mortality, cardiovascular disease, and type II diabetes. He concluded that these definitions were modestly associated with incident all-cause mortality and cardiovascular disease, and more strongly with diabetes incidence. The binary character of the definitions was suggested as a possible explanation for the rather low estimates of relative risk. Individuals not diagnosed as having the metabolic syndrome, but being obese or having hypertension, dyslipidemia or hyperglycemia, are included in the reference group, and potentially raise the incidence rate in the reference group, thereby lowering the relative risk estimates. This might also partially explain why multivariate score systems based on continuous variables (e.g. Framingham risk model) outperform the metabolic syndrome in predicting cardiovascular disease, diabetes or mortality.⁹⁷

1.1.4. Metabolic syndrome in epidemiological analyses: binary or continuous?

Although for clinical settings, a binary definition of the metabolic syndrome enabling a yes or no diagnosis is useful, increasing evidence and arguments exist for a more gradual or even continuous approach of the metabolic syndrome in epidemiological analyses.⁹⁷ From a pure methodological point of view, it is clear that dichotomizing a continuous outcome variable reduces the statistical power of the analysis to detect associations with this outcome variable.¹⁴³ So when there is no real need to dichotomize a continuous outcome variable, this should be avoided. In the currently used definitions of the metabolic syndrome,^{8, 61, 170, 180} a dichotomization has been made on two different levels: 1) every individual risk factor is dichotomized using thresholds (e.g. systolic blood pressure \geq 130 mmHg); and 2) the diagnosis of the metabolic syndrome is made in case a certain number of risk factor is present (e.g. in case of \geq 3 risk factors, with or without a certain risk factor as a sine qua non). For epidemiological analyses, the necessity of both forms of dichotomization can be countered. First of all, cardiovascular disease risk increases progressively with higher levels of several metabolic syndrome risk factors,¹⁶⁸ or as stated by Kahn⁹⁷: “Risk is a progressive function of, for example, hyperglycemia and hypertension and cannot simply be regarded as present or absent, depending on whether thresholds are exceeded or not.”. Second, cardiovascular and

diabetes risk increase progressively with an increasing number of metabolic syndrome risk factors,^{101, 118, 122, 128, 155} as shown in Table 3.¹⁵⁵

Table 3. Hazard ratios for coronary heart disease and diabetes as characteristics of the metabolic syndrome accumulate in an individual with zero characteristics as the referent (adapted).¹⁵⁵

N° of Metabolic Characteristics	CHD		Diabetes	
	n (%)	HR (95% CI)	N (%)	HR (95% CI)
0	695 (10.8%)	1	645 (10.8%)	1
1	2077 (32.2%)	1.79 (1.11, 2.89)*	1932 (32.3%)	2.36 (0.71, 7.93)
2	1984 (30.8%)	2.25 (1.40, 3.60)**	1819 (30.5%)	4.50 (1.39, 14.6)*
3	1339 (20.8%)	3.19 (1.98, 5.12)**	1256 (21.0%)	7.26 (2.25, 23.4)**
≥ 4	352 (5.4%)	3.65 (2.11, 6.33)**	322 (5.4%)	24.4 (7.53, 79.6)**

* $P < 0.05$; ** $P > 0.001$

Therefore, one major drawback of the existing definitions is the fact that dichotomization reduces their predictive power for adverse outcomes^{67, 97} or statistical power to find associations with other variables (e.g. physical activity, physical fitness).¹⁴³ A second major limitation is that each risk component is weighted equally in these definitions⁹⁷ (although in the WHO and IDF definitions substantially more weight is given to the sine qua non risk factors). These binary definitions neglect the interaction between all risk components. All risk components are involved in a complex cascade of physiological processes, and therefore appear in a clustered way. By applying factor analysis to the risk components, the factors underlying the clustering of these risk components can be determined, and are an indication of the underlying pathophysiological processes. Furthermore, the association between the individual risk factors with each of these factors is expressed by means of factor loadings. Therefore, using this analytical strategy to quantify the metabolic syndrome results in a better representation of the physiological interaction between these risk components.

To address both limitations of binary definitions of the metabolic syndrome in epidemiological analyses, a continuous metabolic syndrome risk score (cMSy) was computed within the scope of this thesis, in a sample of 18-75-year-old Flemish adults, including 571 men (aged 46.7 ± 11.2 years) and 449 women (aged 45.8 ± 10.8 years), free from cardiovascular disease and diabetes using principal component analysis.

As this score is a continuous indicator for metabolic syndrome risk, the term “metabolic syndrome risk” will be used in studies including this risk score in analyses, instead of the term “metabolic syndrome”, which is generally used in case this syndrome is diagnosed by means of an internationally recognized binary definition.^{8, 61, 170, 180}

1.2. Stress and stress-related health problems

A secondary health outcome discussed in this thesis includes stress and (mental) health problems related to stress. *Stress* has been defined by Lazarus and Folkman¹¹² as “the perception that events or circumstances have challenged or exceeded one’s ability to cope”. *Coping* is defined as “the person’s constantly changing cognitive and behavioral efforts to manage specific external and/or internal demands that are appraised as taxing or exceeding the person’s resources”.¹¹² According to Lazarus and Folkman,¹¹² perceiving stress is the result of two processes. When an individual is confronted with a certain stimulus or situation, a primary appraisal (first process) occurs, in which this stimulus is defined as irrelevant/benign or as a potentially stressful stimulus. In case of a potentially stressful stimulus, a secondary appraisal (second process) occurs in which the individual evaluates his coping resources. If the individual perceives his coping resources as adequate, no stress response occurs. However, if the individual perceives that he won’t be able to cope with the potentially stressful stimulus, he will experience stress. The stress-buffering theory introduces the role of social support in the perception of stress. *Social support* is defined as “a multidimensional construct that refers to the psychological and material resources available to individuals through their interpersonal relationships”.¹⁵¹ An individual’s perception that social support is available may contribute to a less negative primary and secondary appraisal.¹⁰⁷ To explain this theory, the example can be used of an overweight middle-aged woman, who’s physician strongly recommends to start doing some exercise. A threatening primary appraisal for this woman might be: “My health is in serious danger if I don’t lose some pounds.”. A negative secondary appraisal might be: “I’m not the sporty type, I will never be able to start or maintain this exercise schedule.”. However, if she perceived that she was surrounded by a group of loving, helpful and committed people, the primary appraisal might be modified to: “No matter how obese or ill I will be, I will always receive the love and commitment of my caring family.”. The secondary appraisal might be changed to: “I have several friends who will want to accompany me to the gym every week. Then my chances to

maintain the program will be higher.”. According to the theory of Lazarus and Folkman,¹¹² these revised appraisals should lead to less perceived stress. The above mentioned theories show strong interrelationships between perceived stress, coping and social support, suggesting that inclusion of coping and social support in studies on perceived stress might provide more profound insights in the associations between perceived stress and other variables (e.g. physical activity). To indicate that stress is not always associated with negative consequences, Selye¹⁶⁰ introduced the terms eustress versus distress. Eustress (“good stress”), refers to stressful situations perceived as challenges which are met successfully and therefore are a source of self-esteem, pride, and greater ability to cope with future stressors. Conversely, distress (“bad stress”) is stress leading to organismic breakdown and is most often just referred to as “stress”.

Prevalence rates of perceived stress are high. In a United States National Health Interview Survey for example, about half of the adult population admitted feeling under at least moderate stress during the previous two weeks.¹⁶³ Moreover, stress often results in different negative health outcomes. Physical diseases which may be caused by stress include cardiovascular disease, cancer, infectious diseases and auto-immune diseases.⁴¹ Furthermore, stress is the most common underlying condition leading to depression and anxiety,⁹⁸ two important public health concerns, because of their high prevalence and detrimental impact on the quality of life.^{132, 133} The WHO Collaborative Study of Psychological Problems in General Health Care screened nearly 26,000 subjects, who attended primary care facilities in 14 countries and reported that 10.4% of patients had current depression or stress-related anxiety. In Europe, the Depression Research in European Society (DEPRES) survey, involving 78,463 adults, showed a 6-month prevalence rate of 17% for depression. The WHO Global Burden of Disease survey estimates that by the year 2020, depression and anxiety disorders, including stress-related mental health conditions will be highly prevalent and will be second only to ischemic heart disease in the scope of disabilities experienced by sufferers.⁹⁸

The human body can survive by several complex mechanisms aiming to maintain a constant equilibrium, or homeostatis, which is continuously threatened by several stressors. Allostasis is a controlled deviation from homeostasis, and refers to the ability to achieve stability through change. Through allostasis, the body is protected for internal and external stressors by controlled responses of the autonomic nervous system, the hypothalamo-pituitary adrenal

axis, and the cardiovascular, metabolic and immune systems.^{121, 159} Acute stress is the reaction to acute, stressful stimuli such as major life events or fight or flight stimuli. Chronic stress is the cumulative load of minor, day-to-day stresses,¹²¹ or the long-term repeated disruption of a homeostatic system.¹⁵³ Chronic stress may result in allostatic load, which is the wear and tear resulting from chronic overactivity of allostatic systems. Furthermore, it is speculated that long term allostatic load may cause the allostatic system to become exhausted, resulting in underactivity.^{121, 159} Both overactivity and underactivity of the allostatic system may lead to a diverse spectrum of disorders, such as severe chronic disease, anorexia nervosa, (melancholic) depression, alcoholism, malnutrition, hyper- or hypothyroidism, Cushing's syndrome, chronic fatigue syndrome and others.^{38, 81}

Recently, hypotheses have been made linking stress to the development of the metabolic syndrome.^{14-16, 153, 159} An acute stress stimulus evokes a set of stereotype neuroendocrine responses, including activation of the hypothalamo-pituitary adrenal axis and of the sympathetic nervous system, resulting in secretion of cortisol and catecholamines, respectively. The combined effects of these neuroendocrine alterations allow a fight or flight response (including a mobilization of lipids from the adipose tissue and glucose from hepatic glycogen, together with an acute state of insulin resistance, vasoconstriction in the splanchnic area and vasodilation in skeletal muscle), an essential reaction in ancient times to escape from predators. Although this threat has now disappeared, these responses remain an important defence against acute trauma or severe infection. However, in case of repeated mental stress or chronic stress, chronic increases in cortisol and catecholamines may appear, which lead to a number of adverse health effects. These include insulin resistance, dyslipidemia, visceral obesity and hypertension. It is not possible to describe all possible physiological pathways explaining the effects of chronic increases in catecholamines and cortisol on these adverse health outcomes, because they affect many complex physiological processes and some processes still need more conclusive evidence. However, those leading to insulin resistance and visceral obesity, two central features of the metabolic syndrome will be mentioned here in a simplified way. Excess cortisol may cause a state of *insulin resistance* through different processes. Cortisol inhibits insulin secretion from pancreatic β -cells, it may induce insulin resistance in adipocytes, it may increase hepatic glucose metabolism and inhibit glycogen synthase in skeletal muscle. These processes may lead to hyperglycemia, which is initially tackled by an increased insulin response. Eventually however, β -cell response becomes insufficient, and the unopposed effects of cortisol further increase metabolic disturbances.

Excess cortisol may also cause *visceral obesity*. Excess cortisol promotes the activity of lipoprotein lipase, resulting in higher levels of free fatty acids and accumulation of triglycerides in adipocytes. Moreover, glucocorticoid receptors are much more dense in visceral adipose tissue as compared to other regions, resulting in predominantly visceral obesity.¹⁵³ Furthermore, acute and chronic stress have also been demonstrated to stimulate the production of pro-inflammatory cytokines, probably through activation of the sympathetic nervous system. Eventually, all these factors may result in the development of the metabolic syndrome.^{153, 159}

A number of studies found evidence for associations between stress and the metabolic syndrome, using a cross-sectional or prospective design.^{35, 79, 149, 174} In a large prospective cohort study (Whitehall II) for example, Chandola et al.³⁵ investigated the association between chronic stress at work and the metabolic syndrome (NCEP ATPIII definition), involving 10,308 men and women, aged 35-55, with a mean duration of follow-up of 14 years. They found a dose-response relation between exposure to work stressors over 14 years (1 exposure, 2 exposures, ≥ 3 exposures) and risk of the metabolic syndrome, independent of other relevant risk factors (P for linear trend < 0.01). Adjusting for age and employment grade, employees with chronic work stress (≥ 3 exposures) were more than twice as likely to develop the metabolic syndrome (odds ratio: 2.25, $P < 0.05$).

A large intervariability exists in stress hormone response, so that not all individuals perceiving (the same level of) stress develop these metabolic abnormalities (to the same extent). Gender appears to be an important moderator variable. The stimulation of glucocorticoids and the adrenergic system seems to be less in women than men, maybe because of a suppressive effect of oestrogen. Moreover, heredity, personality, and ability to cope are also important moderating factors.^{153, 159}

1.3. Problem analysis

Based on the prevalence rates and associated risks for comorbidities described above, it is clear that both the metabolic syndrome and stress are large-scale public health problems. The metabolic syndrome already shows a high prevalence world-wide. In 2000, an estimated 55 million adults in the United States had the metabolic syndrome.⁷⁰ The rising epidemic of

obesity will fuel a rapid increase in prevalence rates of the metabolic syndrome in the future. For the US population, that is ageing and in which more than one half of adults are overweight or obese, it has been estimated that the metabolic syndrome soon will overtake cigarette smoking as the primary risk factor for cardiovascular disease.⁵⁶ Because of the associated increased risk for type 2 diabetes, cardiovascular disease (and possibly other co-morbidities such as kidney disease), it is expected that the metabolic syndrome will have a large burden on world economies, without effective interventions.¹⁴⁸

Estimates for the economic impact of stress have already been made. For the case of the United States, stress-related disorders cost the nation more than \$42 billion per year. Furthermore, \$150 billion of revenue is lost to stress annually in lost productivity, absenteeism, poor decision-making, stress-related mental illness, and substance abuse. In the United Kingdom, costs related to stress for the British industry are estimated to be 3 billion pounds per year.⁹⁸

These figures clearly support the need for prevention strategies tackling the epidemic of the metabolic syndrome and stress. Developing these prevention strategies requires a profound knowledge about the modifiable determinants of both the metabolic syndrome and perceived stress. Lifestyle factors, including physical activity are probably linked to the development of the metabolic syndrome.⁹² Moreover, biological pathways might exist to explain and support benign effects of certain physical fitness variables on the metabolic syndrome or its individual risk factors.⁹⁶ Concerning stress, there are psychological and physiological theories supporting benign effects of participation in physical activity on level of perceived stress.¹³⁶ Therefore, studying the interrelationships between physical activity and physical fitness, the metabolic syndrome and stress (a possible aetiological factor for the metabolic syndrome) might provide a fertile soil for developing effective prevention strategies.

Examining these associations is preferably done within a frame of reference, describing possible associations between physical activity, physical fitness and both health outcomes and identifying other factors possibly influencing these parameters or the associations between them. In the next section of this introduction, a theoretical model developed by Bouchard and Shephard²² and functioning as a key model in research studying associations between physical activity, physical fitness and health, will be introduced.

2. Frame of reference

2.1. Consensus model of Bouchard and Shephard

Based on an International Consensus Meeting, Bouchard and Shephard²² proposed a conceptual model specifying the interrelationships between physical activity, fitness and health (Figure 3).

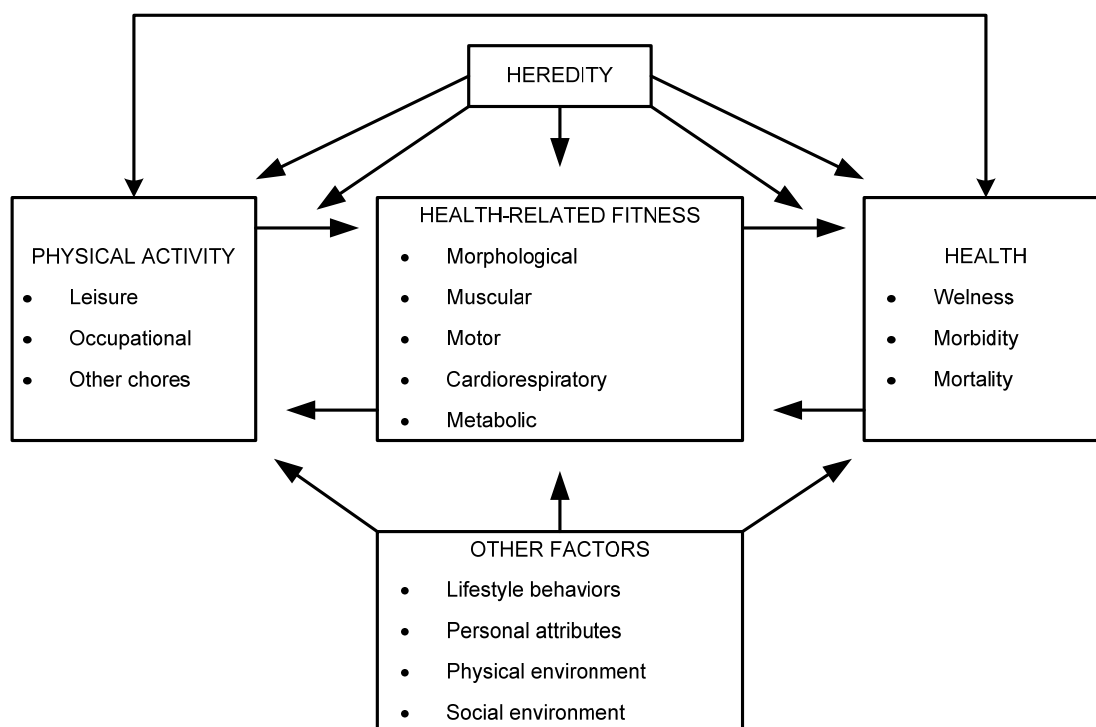


Figure 3. A consensus model describing the interrelationships among physical activity, health-related fitness, and health status.²²

This model shows that all three key concepts show reciprocal relationships. Individuals suffering from chronic disease will be limited in their ability to be physically active, and therefore have lower levels of physical fitness. Individuals being more physically active, show higher fitness levels, better health and even live longer. Moreover, heredity has a substantial influence on all three constructs and their interrelationships. Humans are genetically diverse, inducing individual differences in susceptibility for disease, but also in the level of habitual physical activity and health-related fitness.^{20, 21, 140} Genetic variation also accounts for a substantial fraction of the individual differences in the response to regular exercise of health-related fitness and several risk factors for chronic disease.^{19, 21} Finally,

other lifestyle behaviours (e.g. smoking habits, alcohol and dietary intake), environmental factors including social environment (e.g. social network) and physical environment (e.g. temperature, air quality) and personal attributes (e.g. age, gender, socio-economic status, personality characteristics) influence physical activity, fitness and health. A thorough understanding of this model requires a short introduction of its three main constructs.

Physical activity comprises "any body movement produced by the skeletal muscles that results in a substantial increase over the resting energy expenditure".³³ It is subdivided in categories such as leisure time physical activity, including "exercise", which is "a form of physical activity that is planned, structured, repetitive, and purposive in the sense that improvement or maintenance of one or more components of physical fitness is an objective". Other categories include physical activity during occupation and physical activity during household and other chores.²² During the past several years, the concept of *health-related physical activity* or *health-enhancing physical activity (HEPA)* has received a lot of attention. A large body of evidence has been found for health benefits of regular physical activity.¹⁷¹ However, how much physical activity is needed has been the object of discussion during the past decades. The first physical activity recommendations mainly focused on the improvement and maintenance of physical fitness.⁵ They were demanding, promoting high intensity physical activity, and were rather discouraging for sedentary people to become more active. Moreover, accumulating evidence was found for significant health benefits resulting from regular physical activity of moderate intensity. Therefore, in 1995, the Centers for Disease Control and Prevention and the American College of Sports Medicine (CDC/ACSM) recommended to accumulate 30 minutes or more of moderate-intensity physical activity on most, preferably all, days of the week.¹³⁹ This position statement was followed by similar position statements of other American and European scientific associations.^{59, 131, 171, 175} Generally, they all agree on the fact that moderate intensity physical activity provides sufficient health benefits. Furthermore, physical activity should be incorporated in daily living, and can be accumulated during the day. Additional health benefits can be achieved through greater amounts of physical activity. People who can maintain a regular regime of activity that is of long duration or of vigorous intensity are likely to derive greater benefits. The different types of physical activity assessment methods reflect the complex character of the concept. As physical activity is defined as bodily movement resulting in energy expenditure, in principle "direct calorimetry" (measuring energy expenditure by measuring heat production or heat loss) is the gold standard for physical activity assessment. However,

this technique is not feasible in most research settings due to practical reasons (financial costs, invasiveness, limitation to laboratory situations). Other highly reliable and valid techniques include indirect calorimetry, the doubly labelled water method, and direct observation. These techniques are also used as criterion measurements for validation of other objective and subjective physical activity assessment methods. Objective techniques include activity monitors (pedometers and motion sensors) and heart rate monitoring. Questionnaires and activity diaries are considered subjective methods.^{126, 173}

Physical fitness also is a multi-dimensional concept and has been defined in several ways. One of the most frequently cited definitions describes physical fitness as “the ability to carry out daily tasks with vigor and alertness, without undue fatigue and with ample energy to engage in leisure time pursuits and to meet the above average physical stress encountered in emergency situations”.⁴⁰ Since the beginning of the 1980’s, the concept is operationalized with a focus on two goals: performance and health. Performance-related fitness refers to those fitness components that are necessary for optimal work or sport performance. *Health-related fitness*, the concept of interest for the present discussion, has been defined as “a state characterized by (a) an ability to perform daily activities with vigor and (b) a demonstration of traits and capacities that are associated with a low risk of premature development of hypokinetic diseases and conditions”.^{22, 138} It refers to those components that are affected favorably or unfavorably by habitual physical activity and relate to health status. These include five components: (1) morphological (body mass for height, body composition, subcutaneous fat distribution, abdominal visceral fat, bone density, flexibility); (2) muscular (power, strength, endurance); (3) motor (agility, balance, coordination, speed of movement); (4) cardiorespiratory (submaximal exercise capacity, maximal aerobic power, heart functions, lung functions, blood pressure); and (5) metabolic fitness (glucose tolerance, insulin sensitivity, lipid and lipoprotein metabolism, substrate oxidation characteristics).

Several laboratory and field tests have been designed to measure physical fitness in adults.¹⁶⁶ The Eurofit for Adults is an example of a field test battery to assess health-related fitness in adults aged 18 to 65 years.^{44, 173}

Health was defined at the Consensus Conference in Toronto in 1988 as “a human condition with physical, social, and psychological dimensions, each characterized on a continuum with positive and negative poles. Positive health is associated with a capacity to enjoy life and to withstand challenges; it is not merely the absence of disease. Negative health is associated

with morbidity and, in the extreme, with premature mortality”. Morbidity can be defined as “any departure, subjective or objective, from a state of physical or psychological well-being, short of death”. Wellness is a holistic concept, describing “a state of positive health in the individual, and compromising physical, social and psychological well-being”.²²

Within the scope of this thesis, perceived stress and metabolic syndrome risk will be discussed as two different health outcomes. Strictly following the definitions of Bouchard and Shepard,²² the individual risk factors used in the continuous metabolic syndrome risk score, which were based on existing definitions of the syndrome^{61, 170} are categorized as morphological (waist circumference), cardiorespiratory (blood pressure) or metabolic (fasting plasma glucose, HDL cholesterol and triglyceride levels) health-related fitness variables. However, since the metabolic syndrome has received an ICD-9 code (International Classification of Diseases), it will be discussed as a morbidity in the scope of this thesis.

Although genetic structure is a determinant of metabolic syndrome risk^{7, 28, 86, 114, 124} and perceived stress,¹⁵³ and has a significant impact on physical activity, physical fitness²² and possibly on the associations between them, it is beyond the scope of this thesis to measure the impact of heredity. However, other factors, including lifestyle factors and personal attributes, will be included in analyses.

2.2. Aims of the association studies

In this thesis, six original research studies are included. The first two studies (chapters 2.1.1. and 2.1.2.) are methodological studies on mental health and metabolic syndrome risk. The last four studies (chapters 2.2.1, 2.2.2., 2.2.3. and 2.2.4) examined the associations between physical activity, physical fitness, metabolic syndrome risk and stress using a cross-sectional design in a population-based sample of male and female Flemish adults, aged 18 to 75. In the next section, the aims of these four studies will be introduced, applying the consensus model of Bouchard and Shepard²² to each of them.

2.2.1. Physical activity and stress-related mental health problems

As perceived stress is an important determinant in the development of anxiety, depression and other mental and physical disorders,^{41, 98} the knowledge necessary to develop effective prevention and treatment strategies for stress is valuable. The association between physical activity and perceived stress has been the object of several studies, of which some have shown benign effects of exercise for primary or secondary stress prevention.^{26, 158} In general, two different approaches have been made to explain these benign effects, more specifically a physiological and a psychological approach. Physiological theories mainly focused on the benign effects of regular aerobic exercise. However, as these theories alone were unable to adequately explain the complex relationship between physical activity and stress (e.g. similar health gains achieved by aerobic and anaerobic exercise), it was assumed that psychological processes might also be involved.^{141, 172, 177}

In order to investigate the psychosocial processes through which exercise can result in stress-reduction, the multidimensional, dynamic and complex nature of stress has to be taken into consideration.¹¹³ According to the theories described in paragraph 1.2.,^{107, 112} level of perceived stress is strongly associated with coping and perceived social support. Moreover, other psychological theories suggest mechanisms through which certain types of physical activity may promote the use of more active, problem-focused coping strategies^{66, 113} and enhance the level of perceived social support,⁴³ which are both associated with lower perceived stress.¹²⁷ Therefore, taking into consideration the concepts of coping and social support can result in a more comprehensive understanding of the complex relationship between physical activity and stress. However, until now only a limited number of studies used this approach, by examining the association between stress, coping, social support and leisure activities in general, including physical activity, in certain subpopulations.^{23, 34}

In chapter 2.2.1., we study the association between several types of physical activity and stress in a population-based sample of 18- to 75-year-old Flemish adults, by taking into consideration social support and coping, using a cluster-analytical approach. The second objective consists of investigating whether these subgroups of individuals also differ in anxiety and depression and in different types of physical activity. These objectives are based on the hypothesis that certain types of leisure time physical activity have a stress-reducing effect, because they result in higher perceived social support, and more active, problem focused coping,

which are both associated with lower perceived stress. Gender, age and socio-economic status influence both physical activity and perceived stress.^{11, 22, 42, 72, 102, 117, 120, 167} Therefore, their possible confounding (age, gender) or moderating effect (socio-economic status) is taken into account in the analyses. Figure 4 shows the application of the consensus model of Bouchard and Shephard²² to these research aims.

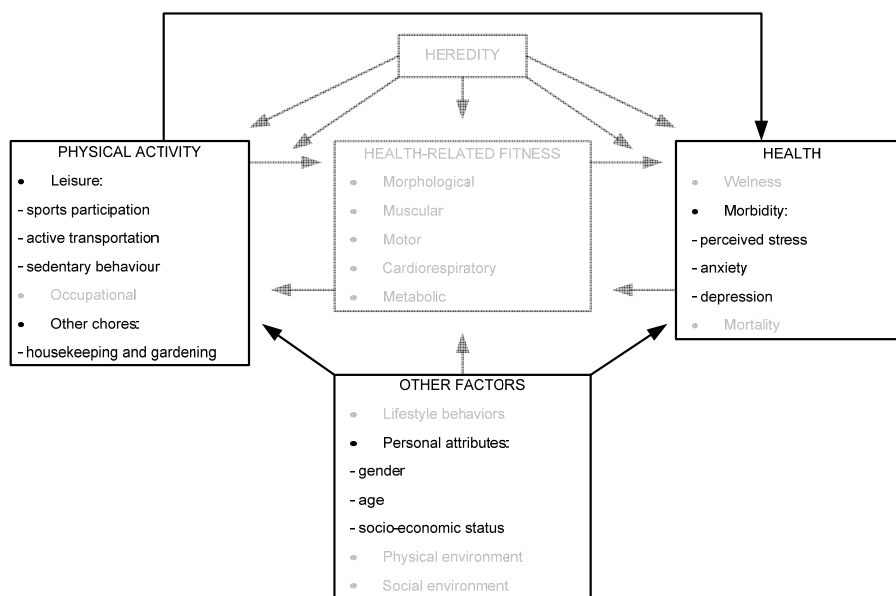


Figure 4. Application of the consensus model of Bouchard and Shephard²² to the research questions addressed in chapter 2.2.1.

All factors presented in the original model of Bouchard and Shephard,²² as shown in Figure 3, are also presented in Figure 4. However, factors included in the current study hypothesis and analyses are presented in bold, whereas other factors mentioned in the original model of Bouchard and Shephard²² but not included in the current study hypothesis, are presented transparently. Arrows starting from or pointing to factors not included in analyses were also presented transparently.

2.2.2. Physical activity and metabolic syndrome risk

The relationship between physical activity and the metabolic syndrome in adults has been the object of intensive research. The majority of these studies report an inverse association between physical activity level and prevalence^{13, 24, 31, 53, 73, 90, 109, 125, 147, 176} or incidence^{58, 106} of the metabolic syndrome.

A few years ago, it has been acknowledged that in finding ways to influence important health outcomes, the study of sedentary behaviour may be as important as the study of physical activity. Sedentary behaviour is a distinct class of behaviours that can coexist and compete with physical activity.¹³⁵ Studies including both sedentary behaviour and physical activity have indicated that both factors may have independent effects on several health outcomes. Television watching, a common form of sedentary behaviour, has been associated with elevated risk for type 2 diabetes, obesity⁸⁷ and cardiovascular disease markers,⁹⁴ all independently of physical activity level. Therefore, finding independent associations for sedentary behaviour and physical activity level with metabolic syndrome risk may provide support for prevention strategies including efforts to decrease sedentary behaviour, besides promotion of physical activity, since both behavioral changes might show additional effects in reducing metabolic syndrome risk. So far, a limited number of studies simultaneously investigated the association between both behavioral parameters and the metabolic syndrome in adults.^{13, 53, 71} Moreover, a binary definition of the metabolic syndrome was used in these studies, which may include some methodological limitations, as described in paragraph 1.1.4.

Referring to the consensus model (see Figure 5),²² in chapter 2.2.2. the association of sedentary behaviour and moderate to vigorous leisure time physical activity with metabolic syndrome risk is examined in Flemish adults aged 18 to 75, using a validated continuous metabolic syndrome risk score. Second, the relationship of both leisure time physical activity and sedentary behaviour with each of the continuous metabolic syndrome risk factors is determined. Since sedentary behaviour and physical activity are associated with obesity,^{13, 87} and obesity predicts the development of several individual risk factors of the metabolic syndrome,⁸² the extent to which obesity mediates the relationship of sedentary behaviour and physical activity with the continuous metabolic syndrome risk factors is also investigated. These associations will be studied based on the hypothesis that sedentary behaviour results in higher metabolic syndrome risk, whereas moderate to vigorous leisure time physical activity reduces metabolic syndrome risk, and that both effects are independent, which implies that both behaviours show additional effects. Metabolic syndrome risk and level of physical activity and sedentary behaviour are associated with gender,^{146, 161, 167} age,^{69, 161, 167} education level,^{60, 165, 167} smoking behaviour,^{134, 157} and alcohol^{63, 154} and dietary intake.^{12, 157} Therefore, analyses are conducted in both genders separately, and corrected for age, education level and these lifestyle factors.

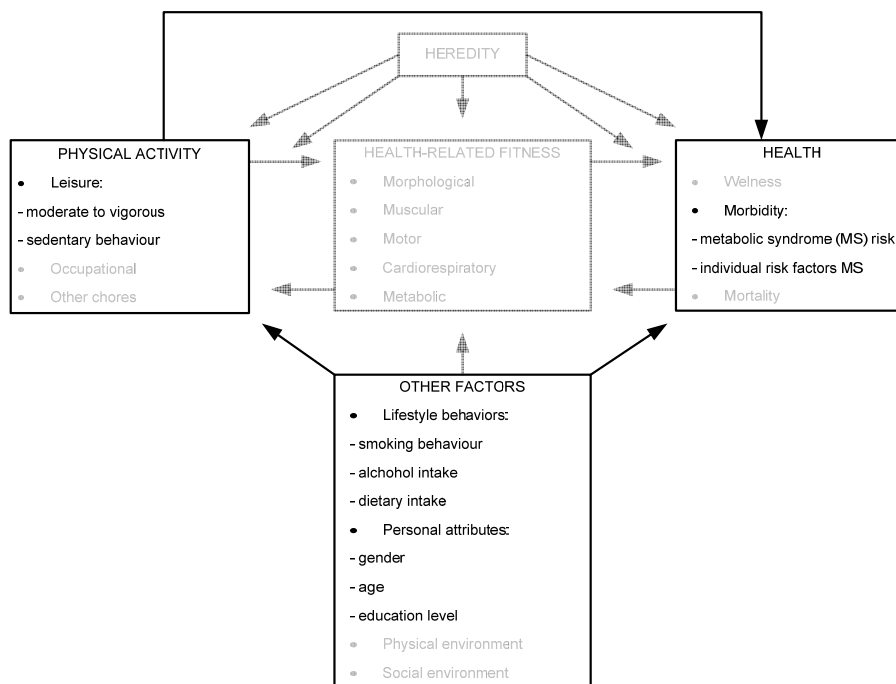


Figure 5. Application of the consensus model of Bouchard and Shephard²² to the research questions addressed in chapter 2.2.2.

2.2.3. Health-related fitness and metabolic syndrome risk

Besides physical activity, aerobic fitness has also been frequently associated with the prevalence^{31, 39, 64, 90, 96, 103, 109, 176, 178} and incidence^{29, 65, 110} of the metabolic syndrome. The inverse association found in these studies support promotion of aerobic exercise, resulting in higher aerobic fitness, as a prevention strategy for the metabolic syndrome. Furthermore, biological pathways might exist to explain and support protective effects of resistance training and muscular strength on the development and treatment of the metabolic syndrome. This assumption is based on the results of some intervention studies, showing benign effects of resistance training on whole body insulin action,⁶ central obesity and body composition,¹⁰ blood pressure,³² triglycerides and HDL cholesterol blood levels.⁶² However, so far, only two studies investigated the association between muscular strength and the metabolic syndrome, both in a population of adult men.^{95, 96} The first (cross-sectional) study provided evidence for an inverse association between muscular strength and prevalence of the metabolic syndrome, independent of aerobic fitness and several confounding variables.⁹⁶ In further longitudinal analyses, muscular strength was inversely associated with incidence of the metabolic syndrome after extensive adjustment for confounders. This association was marginally nonsignificant after additional adjustment for aerobic fitness.⁹⁵ These findings might be

indicative for a protective effect of strength in the development of the metabolic syndrome, that is additional to the benign effect of aerobic fitness. However, both studies showed some limitations. The population studied consisted of males only, so until now, no studies have investigated the independent and combined association of muscular strength and aerobic fitness with metabolic syndrome risk in women. Furthermore, both previous studies used a binary definition of the metabolic syndrome, which may be associated with reduced statistical power (see paragraph 1.1.4).

Therefore, in chapter 2.2.3. the independent and combined association of muscular strength and aerobic fitness with a validated continuous metabolic syndrome risk score is investigated in male and female adults aged 18 to 75. Second, the relationship of muscular strength and aerobic fitness with the individual continuous metabolic syndrome risk factors, and the extent to which obesity mediates this relationship is determined. This will be studied based on the hypothesis that muscular strength and aerobic fitness independently, and therefore additionally, have a protective effect regarding metabolic syndrome risk. Since metabolic syndrome risk, muscular strength and aerobic fitness may be associated with gender, age, education level, and some lifestyle behaviours including smoking, alcohol and dietary intake,^{12, 25, 63, 69, 85, 134, 146, 162, 165} their possible confounding effects are considered in analyses (see Figure 6).

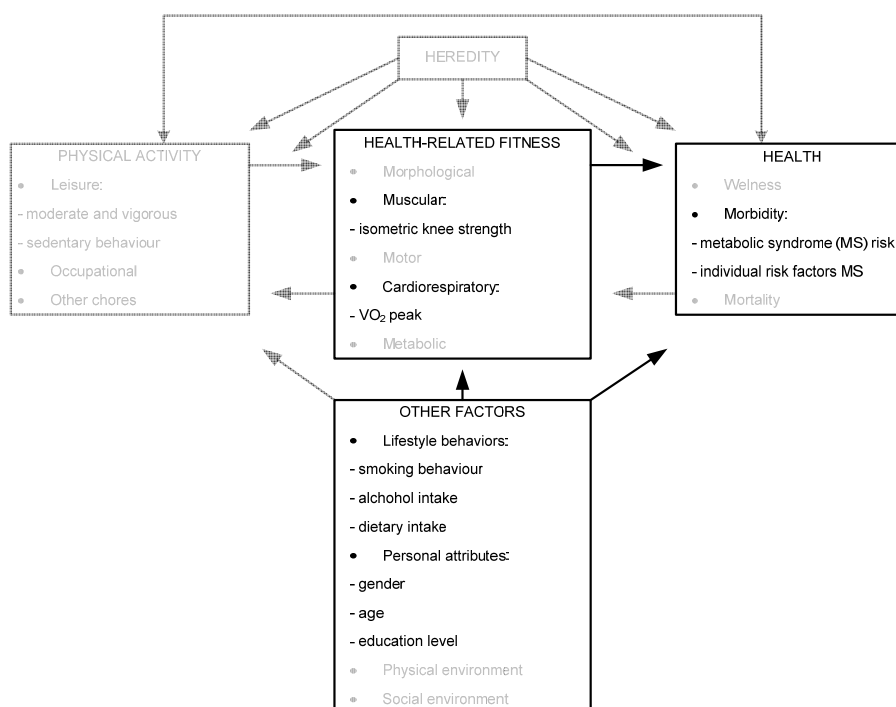


Figure 6. Application of the consensus model of Bouchard and Shephard²² to the research questions addressed in chapter 2.2.3.

2.2.4. Health-related lifestyle, fitness, distress and metabolic syndrome risk

In the search for preventive strategies of the metabolic syndrome, its modifiable determinants need to be thoroughly understood. As can be derived from the previous parts in this introduction, three important modifiable factors that each have been studied in relation with the prevalence or incidence of the metabolic syndrome are health-related lifestyle (including physical activity,^{13, 24, 31, 53, 58, 73, 90, 106, 109, 125, 147, 176} sedentary behaviour,^{13, 53, 71} alcohol^{51, 63, 74, 152, 181} and dietary intake^{12, 75} and smoking behaviour^{76, 91, 129, 134}), physical fitness (predominantly aerobic fitness^{29, 31, 39, 64, 65, 90, 96, 103, 109, 110, 176, 178} and muscular strength^{95, 96}) and distress (including stress,^{35, 79, 149, 174} anxiety and depression^{17, 84, 100}). However, these three factors also show interrelationships, and evidence already exists that some variables (e.g. aerobic fitness) might modify the relationship between other variables (e.g. physical activity^{73, 147}) and the metabolic syndrome. Therefore, it might be interesting to investigate the interrelations between all three factors and between these three factors and metabolic syndrome risk in one theoretical model by means of latent variable structural equation modelling. Until now, no previous studies handled this specific research question. A specific model, partially based on the consensus model of Bouchard and Shephard²² is examined within the scope of this study (chapter 2.2.4.). In Figure 7, an overview is given of all variables included in analyses.

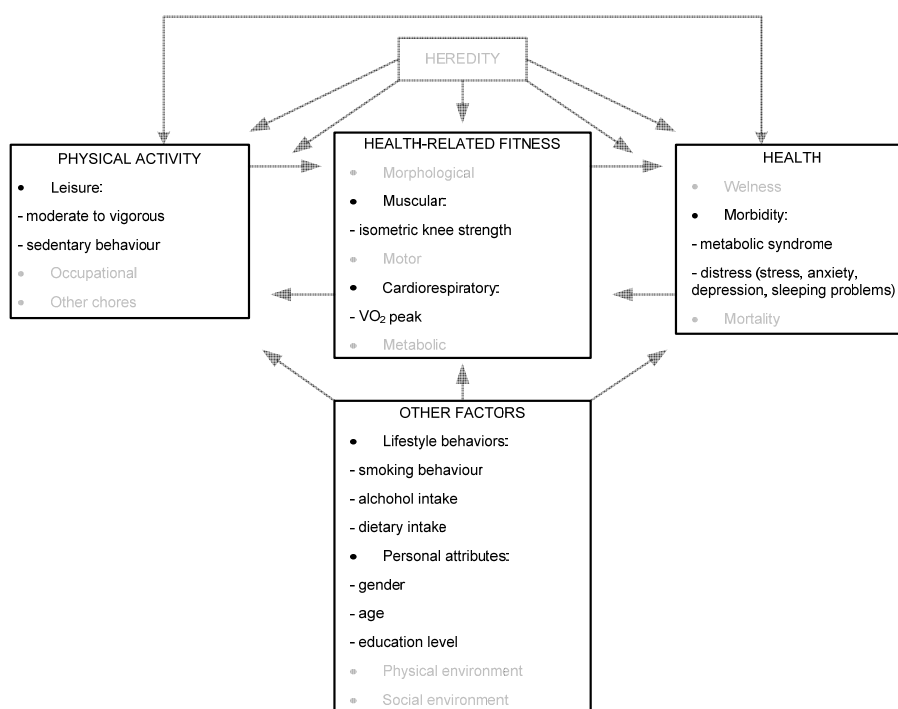


Figure 7. Application of the consensus model of Bouchard and Shephard²² to the research questions addressed in chapter 2.2.4.

In this figure, arrows between boxes are presented transparently, as this figure cannot be used to present all associations between the variables examined within this study.

The path model studied in chapter 2.2.4. is shown in Figure 8. This model causally links psychological distress, health-related lifestyle, physical fitness and a metabolic syndrome factor. Health-related lifestyle is based on measurements of physical activity, sedentary behaviour, alcohol intake and dietary fat intake. Physical fitness is based on measurements of aerobic fitness and muscular strength. Distress is based on measurements of perceived stress, depression, anxiety and sleeping problems. The metabolic syndrome factor is based on measurements of waist circumference, triglycerides, HDL cholesterol, blood pressure and plasma glucose. This model is based on the following hypotheses:

- A higher (lower) level of physical fitness is causally associated with a lower (higher) metabolic risk, independent of health-related lifestyle.
- A lower (higher) level of distress is causally associated with a lower (higher) metabolic risk, independent of health-related lifestyle.
- A healthier (unhealthier) lifestyle is causally associated with a lower (higher) metabolic risk. This effect can be subdivided in an effect that is independent of physical fitness and of distress, an effect that is mediated by physical fitness, and an effect that is mediated by distress.

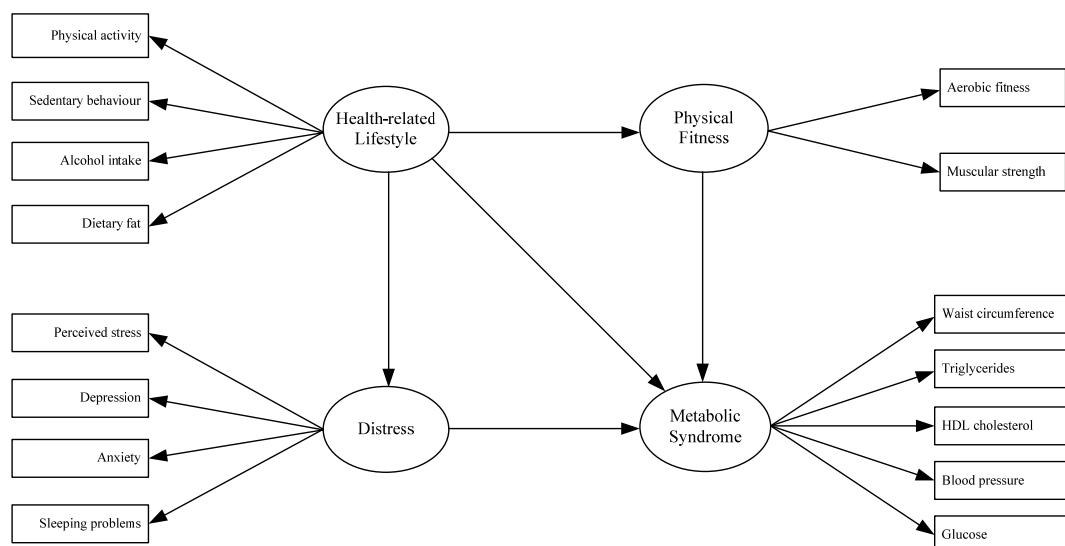


Figure 8. Path model causally linking psychological distress, health-related lifestyle and physical fitness with a metabolic syndrome factor.

3. Outline of the thesis

This thesis is primarily a collection of manuscripts that are published, in press, under editorial review or submitted for publication. All articles were written to stand alone, which may lead to some repetition, mainly in the description of the methods applied.

The next section incorporates original research findings and comprises of two parts. Part 1 exists of two methodological studies. The purpose of the first study (chapter 2.1.1.) was to examine the reliability, equivalence and respondent preference of a computerized version of the General Health Questionnaire (GHQ-12),⁷⁸ Symptom Checklist (SCL-90-R),⁵⁰ Medical Outcomes Study Social Support Survey (MOSSSS),¹⁶⁴ Perceived Stress Scale (PSS)⁴² and Utrecht Coping List (UCL)¹⁵⁶ in comparison with the original version in a general adult population. Since the computerized versions of these questionnaires were developed within the setting of the Policy Research Centre Sport, Physical Activity and Health (see below), their psychometric properties first needed evaluation, before they could be implemented in the different association studies. In the second study, the calculation and validation of the continuous metabolic syndrome risk score is described (chapter 2.1.2.). Part 2 includes the four studies examining the associations between physical activity, physical fitness, stress and metabolic syndrome risk (chapters 2.2.1., 2.2.2., 2.2.3. and 2.2.4.). An overview of the objectives of all six studies presented in the second section of this thesis is provided below:

Part 1. Methodological studies on mental health and metabolic syndrome risk

Objective 1: to evaluate the reliability, equivalence and respondent preference of a computerized version of five mental health questionnaires^{42, 50, 78, 156, 164} in comparison with the original paper-and-pencil version (chapter 2.1.1.).

Objective 2: to validate a continuous metabolic syndrome risk score based on the risk factors of the International Diabetes Federation definition¹⁷⁰ (chapter 2.1.2.).

Part 2. Association studies on physical activity, physical fitness, stress-related mental health, and metabolic syndrome risk

Objective 3: to examine the association between leisure time physical activity and stress, social support and coping, using a cluster analytical approach (chapter 2.2.1.).

Objective 4: to examine the association of sedentary behaviour and moderate to vigorous leisure time physical activity with a validated continuous metabolic syndrome risk score (chapter 2.2.2.).

Objective 5: to examine the association of muscular strength and aerobic fitness with a validated continuous metabolic syndrome risk score (chapter 2.2.3.).

Objective 6: to examine the association between health-related lifestyle, physical fitness, distress and the metabolic syndrome using latent variable structural equation modeling (chapter 2.2.4.).

Finally, in the third section of this thesis general conclusions, limitations, directions for further research and practical implications are formulated.

4. Study sample

All data analyzed in this thesis were collected within the research scope of the *Flemish Policy Research Centre Sport, Physical Activity and Health*. This policy research centre was established in 2001 and is funded by the Flemish Government. It consists of a consortium of three different university departments, more specifically the Department of Movement and Sports Sciences (Ghent University), the Faculty of Kinesiology and Rehabilitation Sciences (KULeuven) and the Faculty of Physical Education and Physical Therapy (Vrije Universiteit Brussel). The main purpose of the Flemish Policy Research Centre Sport, Physical Activity and Health is to provide scientific support to the Flemish Government regarding sports participation, physical activity, physical fitness and health in the Flemish part of Belgium. Four main themes were set up to accomplish this purpose. Data analyzed in this thesis originate from the first two themes.

Theme 1 was designed to investigate the current quantitative and qualitative pattern of physical activity, physical fitness and general health of the Flemish population. For this purpose, the National Institute of Statistics randomly selected a community sample of 18 to 75 year old adults in 46 randomly chosen municipalities in the Flemish region of Belgium. Of all randomly selected individuals invited to participate in the study, 28% agreed to participate (N = 5170), after they were contacted by letter and telephone respectively. A subsample (16%) of individuals not willing to participate in the study completed a questionnaire on

demographic characteristics, height, weight, socio-economic status, physical activity and their reasons for not taking part in the study. For these non-responders, the main reasons for not participating in the study were lack of time (25.9%), health problems (23.2%), work obligations (14.6%), previous engagements (14.1%), other reasons (22.2%). In a municipal (sports) hall in their neighbourhood, participants were asked to give their written informed consent and to complete a medical checklist⁴ and a short paper-and-pencil physical activity questionnaire (IPAQ).⁴⁵ Subsequently, resting heart rate, blood pressure, spirometric and anthropometric characteristics were measured, following standardized procedures. Physical fitness was measured using the Eurofit for Adults⁴⁴ or the Senior Fitness Test Kit.¹⁵⁰ Finally, participants were asked to complete a computerized physical activity questionnaire (FPACQ),¹¹⁹ and computerized general health and mental health questionnaires. At the end of this test session, subjects were asked to take part in a second, more extensive investigation in the lab of the Policy Research Centre, more specifically the theme 2 study.

Theme 2 was set up to study the relationship of physical activity and physical fitness with health in the Flemish population. For this purpose, laboratory measurements were executed in a subsample of the theme 1 study. At the beginning of this test session, a fasting blood sample was taken, and subjects went through a medical screening by a physician. Subsequently, more extensive anthropometric measurements were performed, including bio-electrical impedance analyses.⁷⁷ A Neurocom device¹³⁰ was used, to measure postural control. Aerobic fitness and muscular strength were successively determined by means of a maximal test on an electrically braked Lode Excalibur cycle ergometer,¹²³ and a test battery measuring knee strength on a calibrated Biodex System Pro 3 dynamometer,⁵² respectively. Physical activity during adolescence and adulthood were determined by means of a retrospective questionnaire. Finally, at the end of this session, subjects were asked to complete a three-day diet record at home.⁴⁹

For clarity, a short overview of the samples used in the different studies is given below:

Chapter 2.1.1. Reliability, equivalence and respondent preference of computerized versus paper-and-pencil mental health questionnaires

A number of 245 adults, aged 18 to 75 participated in this study, and were divided into two groups: (1) internal consistency, equivalence and preference for computerized and/or paper-and-pencil administration formats of the mental health questionnaires were analyzed in group

I (n = 130); (2) test-retest reliability of the computerized administration was measured in group II (n = 115). Group I was a smaller subset of theme 1, who completed the paper-and-pencil version of the questionnaires at home. Subjects of group II were part of the theme 2 study, and performed the computerized administration for the second time during their lab-visit.

Chapter 2.1.2. A continuous metabolic syndrome risk score: utility for epidemiological analyses

Theme 2 participants with complete data for all metabolic syndrome risk factors took part in the study of chapter 2.1.2. Subjects were excluded in case of a history or evidence of cardiovascular disease or diabetes. As a result, 1020 adults (571 men, 449 women) aged 18 to 75 were included in the analyses.

Chapter 2.2.1. Association between leisure time physical activity and stress, social support and coping: a cluster-analytical approach

All theme 1 subjects with complete data of the computerized mental health and physical activity questionnaires used for these analyses were included in the study of chapter 2.2.1. This resulted in a total number of 2616 Flemish 18-to75-year-olds, of which 1430 were male and 1186 were female.

Chapter 2.2.2. Sedentary behaviour, physical activity and a continuous metabolic syndrome risk score in adults

For the analyses performed in chapter 2.2.2., only theme 2 participants with complete data for all metabolic syndrome risk factors, sedentary behaviour, leisure time physical activity and for all confounding variables were included. Furthermore, participants were excluded in case of a history or evidence of cardiovascular disease or diabetes. The resulting number of participants were 559 men and 433 women, aged 18 to 75.

Chapter 2.2.3. Muscular strength, aerobic fitness and metabolic syndrome risk in Flemish adults

Similar as in the study of chapter 2.2.2., subjects for this study originated from theme 2. A total of 1019 adults (571 men, 448 women), free from cardiovascular disease and diabetes and with complete data for all (confounding) variables were included in the analyses.

Chapter 2.2.4. A path model of health-related lifestyle, physical fitness, distress and metabolic syndrome risk factors in adults

For the study in chapter 2.2.4., theme 2 subjects with complete data for all mental health, physical activity, physical fitness, metabolic syndrome risk and confounding variables were included. Similar as in both previous studies, individuals with a history or evidence of cardiovascular disease or diabetes were excluded. This resulted in a number of 965 subjects (549 men, 416 women), aged 18 to 75.

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2.

ORIGINAL RESEARCH

Part 1

Methodological studies on mental health and metabolic syndrome risk

CHAPTER 2.1.1.

RELIABILITY, EQUIVALENCE AND RESPONDENT PREFERENCE OF COMPUTERIZED VERSUS PAPER-AND-PENCIL MENTAL HEALTH QUESTIONNAIRES

**K Wijndaele, L Matton, N Duvigneaud, J Lefevre, W Duquet,
M Thomis, I De Bourdeaudhuij, R Philippaerts**

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Abstract

The purpose of this study was to examine the reliability, equivalence and respondent preference of a computerized version of the General Health Questionnaire (GHQ-12), Symptom Checklist (SCL-90-R), Medical Outcomes Study Social Support Survey (MOSSSS), Perceived Stress Scale (PSS) and Utrecht Coping List (UCL) in comparison with the original version in a general adult population. Internal consistency, equivalence and preference between both administration modes was assessed in a group of participants (n=130) who first completed the computerized questionnaire, followed by the traditional questionnaire and a post-assessment evaluation measure. Test-retest reliability was measured in a second group of participants (n=115), who completed the computerized questionnaire twice. In both groups, the interval between first and second administration was set at one week. Reliability of the PC versions was acceptable to excellent; internal consistency ranged from $\alpha=0.52$ to 0.98, ICC's for test-retest reliability ranged from 0.58 to 0.92. Equivalence was fair to excellent with ICC's ranging from 0.54 to 0.91. Interestingly, more subjects preferred the computerized instead of the traditional questionnaires (computerized: 39.2%, traditional: 21.6%, no preference: 39.2%). These results support the use of computerized assessment for these five instruments in a general population of adults.

Key words: computer, paper-and-pencil, assessment, reliability, equivalence, questionnaire

Introduction

For more than two decades, there is a worldwide incremental use of computer-administered questionnaires in a wide range of disciplines, including psychological assessment (Schulenberg & Yutrzenka, 1999; Booth-Kewley, Edwards & Rosenfeld, 1992). This is associated with the numerous advantages of computerized assessment for the clinician, researcher and respondent. These include immediacy of data entry avoiding coding errors (Schmitz, Hartkamp, Brinschwitz, Michalek & Tress, 2000; Klein & Sobol, 1996); possibility of direct scoring, reporting and interpreting of results (Vispoel, Boo & Bleiler, 2001); possibility of branching between questions based on the respondents' prior answers (Webb, Zimet, Fortenberry & Blythe, 1999); reduction of research time and costs (Lukin, Dowd, Plake & Kraft, 1985); increase in flexibility e.g. by adding explanatory messages, error corrections and prompts (Kiesler & Sproull, 1986); protection of respondents' confidentiality because no written record exists (Navaline, Snider, Petro, Tobin, Metzger, Alterman et al., 1994); greater motivation and enjoyment among respondents in comparison with those completing paper-and-pencil surveys (Rosenfeld, Booth-Kewley & Edwards, 1996). These plus-points will undoubtedly help to maintain the growth in number of instruments being computerized.

Some studies, discussing the equivalence between computerized and paper-and-pencil versions of psychological instruments, support the 'common assumption' that both administration modes yield similar results. Others however demonstrate the opposite (overview in Ford, Vitelli, & Stuckless, 1996; Booth-Kewley et al., 1992). This contradiction strongly grounds the American Psychological Association's (1986) recommendation to investigate the equivalence between both versions of a psychological questionnaire in every case. Moreover, equivalence is a sine qua non when norms from a paper-and-pencil version are to be adapted to the computerized one (Schulenberg & Yutrzenka, 2001; King & Miles, 1995; Hofer, 1985). As stated by Ford et al. (1996), equivalence has to be examined for every population (clinical, non-clinical,...) separately. Additionally, one can argue that equivalence also has to be investigated in certain subpopulations (gender, age groups,...) since respondents' characteristics such as gender, age, education level and computer experience appear to act as moderators of administration mode effects (King & Miles, 1995; Wright, Aquilino & Supple, 1998).

The General Health Questionnaire-12 (Goldberg & Williams, 1988), the Symptom Checklist (Derogatis, Lippman & Covi, 1973), the Medical Outcomes Study Social Support

Survey (Sherbourne & Stewart, 1991), the Perceived Stress Scale (Cohen & Williamson, 1988) and the Utrecht Coping List (Schreurs, Van De Willige, Brosschot, Tellegen & Graus, 1993) are five psychological instruments used extensively in different kinds of settings, including epidemiological research in the general population. Literature only reveals two equivalence studies concerning the computerized and traditional versions of one of these questionnaires. One study (Franke, 1999), examining the Symptom Checklist, involved 400 university students (24.3 ± 5 years of age) randomly assigned to one out of two groups: a computer-administered group or a paper-and-pencil administered group. Schmitz et al. (2000) also studied the equivalence between both administration methods for the Symptom Checklist, using a similar design in 282 psychosomatic outpatients. Both previous studies used a randomized design, with subjects only completing one version of the questionnaire. A disadvantage of this design is the potential bias caused by sampling error, induced by inter-individual differences between subjects of different administration groups. Furthermore, they involve two specific populations, which may limit generalizability of the results.

The purpose of the present study was to investigate the reliability and equivalence of the computerized and traditional versions of the General Health Questionnaire-12, Symptom Checklist, Medical Outcomes Study Social Support Survey, Perceived Stress Scale and Utrecht Coping List in a general adult population, using a test-retest design. Furthermore, respondents' general preference between both administration modes was examined. It was hypothesized that the computerized versions of these five psychological questionnaires can serve as a useful alternative for the original paper-and-pencil versions, and that a general preference goes out to the computerized version.

Material and methods

Subjects

In this study, 245 adults (18-75 years of age) participated. They were all part of a larger community sample, randomly selected by the National Institute of Statistics (NIS) for an epidemiological survey on physical activity, physical fitness and health, carried out by the Policy Research Centre Sport, Physical Activity and Health in the Flemish part of Belgium. All subjects were native Dutch speakers and signed an informed consent statement approved by the Ghent University Hospital Ethics Committee before allocation to the study group.

Design

To accomplish the research purpose, subjects were divided into two groups: 1) internal consistency, equivalence and preference for computerized and/or paper-and-pencil administration formats were analyzed in group I (n=130); 2) test-retest reliability of the computerized administration was measured in group II (n=115). In both subsets, the interval between first and second administration was set at one week, to prevent memory bias. Table 1 presents an overview of the composition of both study samples.

Table 1. Composition of both study samples, according to gender, age, education level and computer experience

	Group I (n=130)	Group II (n=115)
Gender (%)		
males	49.2	51.3
females	50.8	48.7
Age (%)		
18-40 years of age	31.5	32.2
41-60 years of age	41.5	34.8
61-75 years of age	27.0	33.0
Education level (%)		
low (secondary school or lower)	56.2	45.2
high (university or college)	43.8	54.8
Computer experience (%)		
low ('totally disagree' or 'disagree')	25.0	
high ('agree' or 'totally agree')	75.0	

Procedures

Both groups received the computerized administration of the instruments, without the knowledge of a possible second administration. This happened in a municipal (sports) hall in their neighborhood. At the end of this session, subjects were asked to take part in a second, more extensive investigation in the lab of the Policy Research Centre. Based on their willingness to visit the lab, they were allocated to one of both groups. Group I, not visiting our lab, was asked to fill out a few additional paper-and-pencil questionnaires (without further specification) at home, which would take one hour at most. They received a sealed envelop and were instructed not to open it during the first seven days and to complete and send back all questionnaires immediately at the end of this interval. Group II received the computerized administration for the second time during their lab-visit.

To avoid possible confounding factors, equality between both administration formats was aimed for as much as possible. The psychological instruments were presented in the same order (General Health Questionnaire-12, Symptom Checklist, Medical Outcomes Study Social

Support Survey, Perceived Stress Scale and Utrecht Coping List). Font styles were identical, large and easy to read in both modes. Back-tracking and changing previous answers in the computerized questionnaire was possible, as is in the paper-and-pencil mode. A progression indicator, expressed in percentages, at the left bottom side of each screen imitated subjects' possibility to count the number of items left to fill out in a traditional questionnaire. Both computerized and paper-and-pencil administration were initiated with the same introductory text, informing subjects about the anonymity of their answers and instructing them to answer as correct and honest as possible. Finally, wording was identical for both formats, except for some mode specific terms (screen, button,...).

The computerized format was developed using Borland Delphin 6 and can be used in computers with operating system Windows98 and higher. Much attention was paid to user-friendliness, so that computer-illiterate subjects were able to fill out the questionnaire independently as well. Items were answered by clicking with the computer mouse on the appropriate choice field. All items had to be completed, otherwise subjects received an instruction message and could not pass on to the next screen. For back-tracking and paging further, two command buttons ('previous screen', 'next screen') were provided at the bottom of each screen. Depending on their length, one to five items were presented per screen. After finishing all items, a final instruction screen appeared, asking subjects to call in a scientific staff member to save their answers.

The paper-and-pencil package included four items, presented in the sealed envelop in a well defined order: an instruction paper, the five psychological instruments, a post-assessment instrument and a stamped and addressed envelop.

Instruments

The instruments applied in this study included the five psychological questionnaires and one post-assessment measure. Demographic data concerning participants' gender, age and education level were obtained through a questionnaire they received during the first testing session.

General Health Questionnaire (GHQ-12). The GHQ-12 (Goldberg & Williams, 1988) is a valid, self-report instrument for the detection of mental disorders in the community and non-psychiatric clinical settings, consisting of 12 items. Since its development, it has been used extensively all over the world and translated in many languages. Typically for the GHQ-12, an item is scored as pathologic in case of a change in an individuals' own normal functioning. Accordingly, the questionnaire has the following four-point response scale: 'not at all', 'same

as usual', 'rather more than usual', or 'much more than usual'. In this study the bimodal GHQ-scoring method (0-0-1-1) was applied, as recommended by Goldberg & Williams (1988). The resulting total scores range from 0 to 12, with higher scores indicating higher probability of mental health problems. Psychometric literature concerning the GHQ-12 revealed Cronbach's alpha coefficients, ranging from 0.78 to 0.97 (Koeter & Ormel, 1991; Goldberg, Gater, Sartorius, Ustun, Piccinelli, Gureje et al., 1997; Schmitz, Kruse & Tress, 1999).

Symptom Checklist (SCL-90-R). A second psychological instrument is the Symptom Checklist (Derogatis et al., 1973). This worldwide applied instrument is a valid multi-dimensional self-report scale containing the most important psychopathological complaints in adolescents, adults and psychiatric (out)patients. Factor-analysis of all 90-items in diverse normal and psychopathological samples in the Netherlands revealed a different dimensional structure in the Dutch version of the SCL-90-R (Arrindell & Ettema, 1986). Four scales remained identically the same, namely phobic anxiety (defined as agoraphobia in the Dutch version), anxiety, somatization and hostility. Sleeping problems was adopted as a new dimension, based on high correlations between the items 44, 64 and 66. The depression scale was modified in the way that four items were added (items 3, 19, 51 and 59) and one item (item 71) was omitted. In the obsessive-compulsive dimension (defined as insufficiency of thinking and acting in the Dutch version) item 71 was added and items 3 and 51 were omitted. Distrust and interpersonal sensitivity (items 6, 7, 8, 18, 21, 34, 35, 36, 37, 41, 43, 61, 68, 69, 73, 76, 83 and 88) was a conglomerate of three factors from the original American dimensional structure, namely interpersonal sensitivity, paranoid ideation and psychoticism. Adding scores on all 90 items resulted in a total score, defined as psychoneuroticism. These newly formed scales strongly resemble those reported in surveys in several American community samples. All items are rated on a five-point Likert scale of distress, ranging from 'not at all' (1) to 'extremely' (5). Cronbach's alphas in the general Dutch population range from 0.76 (hostility) to 0.97 (psychoneuroticism) (Arrindell & Ettema, 1986).

Medical Outcomes Study Social Support Survey (MOSSSS). The third instrument included in this study is a 20-item self-administered social support survey incorporating four social support scales (emotional/informational, tangible, positive interaction, affectionate), one overall support index and one item concerning the size of social network (Sherbourne & Stewart, 1991). Although this instrument was originally developed for chronic patients, it has been used in healthy community samples as well (Allen, Manuel, Legault, Naughton, Pivor & O'Shea, 2004). Items are rated on a five-point Likert scale of support availability, ranging

from 'none of the time' (1) to 'all the time' (5), except for the first item concerning the number of close friends and relatives. Sherbourne & Stewart (1991) reported very high Cronbach's alphas, exceeding 0.90 for all support scales.

Perceived Stress Scale (PSS). The PSS is a 10-item instrument developed to measure the degree to which situations are appraised as stressful (Cohen & Williamson, 1988). It was designed for use in community samples and assesses to what extent individuals see their lives as unpredictable, uncontrollable and overloaded. In each case, respondents were asked to point out how often they felt a certain way on a five-point Likert scale ranging from 'never' (1) to 'very often' (5). A total score is obtained by adding up all scores after reversion of response scores on four positively stated items. Cohen & Williamson (1988) reported a Cronbach's alpha coefficient of 0.78.

Utrecht Coping List (UCL). The fifth and last psychological measure included in this trial is the UCL, used to determine coping style. Subjects were asked to rate how frequently they adopt each of 47 possible ways of coping behavior on a four-point Likert scale ranging from 'rarely if never' (1) to 'very often' (4). Items are clustered in seven coping scales, namely Active Dealing, Palliative Reaction, Avoidance, Social Support Seeking, Passive Reaction, Expression of Emotions and Comforting Thoughts. Cronbach's alphas in the general Dutch population range from 0.55 (expression of emotions) to 0.79 (active dealing and social support seeking) (Schreurs et al., 1993).

Post-assessment measure. A self-constructed post-assessment measure, consisting of two items was implemented to measure former computer experience and preference between both administration formats. In the first item, subjects were asked to indicate their level of agreement ('totally disagree', 'disagree', 'agree', 'totally agree') with the following proposition: 'I'm familiar with using a computer.'. The second item ('Which version of the questionnaire did you like most to complete?') consisted of two parts. Firstly, subjects had to check one of the following possibilities: 1) computerized, 2) paper-and-pencil and 3) no preference. Secondly, a few lines were provided to write down all reasons supporting their choices.

Statistical analysis

All statistical analyses were performed using the SPSS 12.0 statistical software package (SPSS, Inc., Chicago, IL). Answers to all 179 items were reduced to 23 scales and one item (size of social network). For the traditional administration, a scale was not computed if one or more corresponding items were omitted. Since 10 subjects in group I forgot to send back the

post-assessment measure, analysis of these variables was carried out on a sample of 120 participants. In group I, three statistical methods were applied. Cronbach's alphas were used to determine internal consistency for all 23 scales of the computerized version. Single measure intraclass correlation coefficients (ICC) were calculated to measure the equivalence between both administration formats. This was done at two levels: 1) the total group, 2) nine different subsets (both genders, three age groups (18-40, 41-60, 61-75 years of age), two groups of education level (low-high), two groups of computer literacy (low-high)). To analyze whether mode preference is related to gender, age, education level and computer experience, Pearson Chi-square tests were used. In group II, test-retest reliability for the computerized administration was estimated by calculating single measure ICC's. Statistical significance was set at a level of 0.01.

Results

Internal consistency

Cronbach's alphas, measuring internal consistency of the scales in the computerized version are presented in table 2. This table also includes Cronbach's alphas for the scales of the paper-and-pencil version in the current study and in earlier studies. For the computerized version, Cronbach's alphas exceeded 0.70 in 17 scales. Six scales in the SCL-90-R and the UCL demonstrated alphas lower than 0.70, namely agoraphobia ($\alpha=0.61$), somatization ($\alpha=0.66$), hostility ($\alpha=0.52$), palliative reaction ($\alpha=0.68$), passive reaction ($\alpha=0.64$) and expression of emotions ($\alpha=0.66$).

Table 2. Internal consistency (Cronbach's α) of the computerized (PC) and paper-and-pencil (PP) administration modes of five psychological instruments in comparison with internal consistency of the paper-and-pencil mode found in earlier research

Scales	Cronbach's α			
	Group I		Literature	
	PC	PP	PP	Reference
GHQ-12				
Total score	0.79	0.78	0.78 - 0.97	Koeter & Ormel, 1991; Goldberg et al., 1997; Schmitz et al., 1999
SCL-90-R				
Agoraphobia	0.61	0.69	0.51 - 0.83	Arrindell & Ettema, 1986; Franke & Stäcker, 1995
Anxiety	0.77	0.82	0.75 - 0.88	Arrindell & Ettema, 1986; Franke & Stäcker, 1995
Depression	0.85	0.86	0.91	Arrindell & Ettema, 1986
Somatization	0.66	0.68	0.70 - 0.83	Arrindell & Ettema, 1986; Franke & Stäcker, 1995
Insufficiency	0.79	0.78	0.83	Arrindell & Ettema, 1986
Distrust	0.85	0.86	0.91	Arrindell & Ettema, 1986
Hostility	0.52	0.40	0.62 - 0.76	Arrindell & Ettema, 1986; Franke & Stäcker, 1995
Sleeping problems	0.75	0.81	0.78	Arrindell & Ettema, 1986
Psychoneuroticism	0.94	0.95	0.97	Arrindell & Ettema, 1986
MOSSSS				
Tangible	0.88	0.95	0.92	Sherbourne & Stewart, 1991
Affection	0.93	0.93	0.91	Sherbourne & Stewart, 1991
Positive interaction	0.93	0.95	0.94	Sherbourne & Stewart, 1991
Emotional/informational	0.95	0.98	0.96	Sherbourne & Stewart, 1991
Overall support index	0.98	0.98	0.97	Sherbourne & Stewart, 1991
PSS				
Total score	0.79	0.83	0.78	Cohen & Williamson, 1988
UCL				
Active dealing	0.85	0.87	0.78 - 0.79	Schreurs et al., 1993
Palliative reaction	0.68	0.76	0.71 - 0.76	Schreurs et al., 1993
Avoidance	0.75	0.79	0.65 - 0.74	Schreurs et al., 1993
Social support seeking	0.83	0.88	0.79	Schreurs et al., 1993
Passive reaction	0.64	0.62	0.74	Schreurs et al., 1993
Expression of emotions	0.66	0.74	0.55 - 0.64	Schreurs et al., 1993
Comforting thoughts	0.74	0.70	0.60 - 0.68	Schreurs et al., 1993

Test-retest reliability

Table 3 includes the single measure ICC's, estimating test-retest reliability of the computerized questionnaire. They ranged from 0.58 to 0.92. Lowest ICC's were found for the SCL-90-R scales, ranging from 0.58 to 0.85. The only scale below 0.60 was the hostility scale

Table 3. Intraclass correlation coefficients (ICC) for test-retest reliability of the computerized administration mode (PC) and equivalence between the computerized and paper-and-pencil (PP) administration modes of five psychological instruments

Scales/Item	Test-retest reliability PC ICC Group II		Equivalence PC-PP ICC Group I									
	Total Sample	Gender		Age		Education level		Computer experience				
		Males	Females	18-40	41-60	61-75	Low	High	Low	High		
GHQ-12												
Total score	0.76	0.68	0.79	0.71	0.62	0.72	0.78	0.64	0.71			
SCL-90-R												
Agoraphobia	0.64	0.56	0.59	0.33	0.68	0.62	0.46	0.71	0.50			
Anxiety	0.67	0.72	0.69	0.71	0.72	0.65	0.74	0.65	0.75			
Depression	0.72	0.63	0.71	0.66	0.73	0.76	0.65	0.75	0.64			
Somatization	0.67	0.75	0.70	0.73	0.74	0.84	0.60	0.74	0.75			
Insufficiency	0.80	0.83	0.75	0.74	0.77	0.80	0.78	0.76	0.80			
Distrust	0.77	0.61	0.83	0.81	0.69	0.76	0.73	0.62	0.72			
Hostility	0.58	0.67	0.45	0.50	0.51	0.67	0.44	0.49	0.55			
Sleeping problems	0.78	0.82	0.80	0.81	0.77	0.80	0.81	0.76	0.80			
Psychoneuroticism	0.85	0.80	0.80	0.82	0.75	0.84	0.78	0.72	0.85			
MOSSS												
Social network size	0.92	0.85	0.94	0.94	0.92	0.90	0.94	0.80	0.94			
Tangible	0.83	0.81	0.81	0.87	0.76	0.84	0.71	0.81	0.81			
Affection	0.90	0.85	0.88	0.88	0.80	0.88	0.85	0.87	0.86			
Positive interaction	0.87	0.82	0.88	0.86	0.87	0.91	0.76	0.89	0.87			
Emotional/informational	0.90	0.83	0.88	0.87	0.87	0.90	0.74	0.78	0.89			
Overall support index	0.92	0.87	0.91	0.90	0.91	0.94	0.78	0.87	0.91			
PSS												
Total score	0.87	0.67	0.80	0.74	0.63	0.72	0.78	0.67	0.75			
UCL												
Active dealing	0.78	0.75	0.76	0.74	0.72	0.69	0.83	0.63	0.80			
Palliative reaction	0.74	0.63	0.71	0.69	0.73	0.56	0.77	0.83	0.65			
Avoidance	0.73	0.79	0.67	0.76	0.62	0.63	0.87	0.70	0.75			
Social support seeking	0.83	0.81	0.79	0.86	0.73	0.79	0.81	0.78	0.80			
Passive reaction	0.82	0.74	0.79	0.77	0.85	0.74	0.79	0.81	0.76			
Expression of emotions	0.74	0.62	0.73	0.72	0.57	0.59	0.71	0.75	0.68			
Comforting thoughts	0.76	0.72	0.66	0.77	0.53	0.65	0.74	0.63	0.71			

with an ICC of 0.58. Highest ICC's were for the MOSSSS scales, ranging from 0.83 to 0.92. In the GHQ-12, MOSSSS and PSS, coefficients all exceeded 0.75.

Equivalence

Equivalence between both administration modes was measured by calculating single measure ICC's between corresponding scales at two levels: the total study sample and gender, age, education and computer experience level subsamples. These results are also shown in table 3. ICC's in the total sample were similar with the test-retest coefficients for the PC version in group II, ranging from 0.54 to 0.91. Lowest ICC's were again found in two SCL-90-R scales, namely agoraphobia (ICC=0.59) and hostility (ICC=0.54). All other coefficients had values of 0.69 or higher. In general, the ICC's determined in the nine different subsamples were very similar to those in the total group. For the agoraphobia scale, higher ICC's were found for 61-75 year old, lower educated and lower computer experienced subjects. For the hostility scale, higher ICC's were found for males and lower educated individuals. For palliative reaction and expression of emotions, a higher ICC was found for high educated participants. No specific trends between subgroups, were found for any of the instruments studied.

Preference

Participants in group I were asked to complete a post-assessment instrument concerning their level of familiarity with using a computer and their preference between both administration modes. Preference to the computerized administration was given by 39.2% of all subjects. Most important reasons grounding this choice were (in order of frequency): 'faster', 'more progressive', 'more ecological' and 'easier'. An equal percentage (39.2%) had no preference, and 21.6% liked to complete the paper-and-pencil version most. Some of their reasons were: 'no computer knowledge', 'more surveyable', 'faster' and 'more personal'.

Pearson Chi-squares, testing the relationship of mode preference with gender and education level, were not significant (gender: $\chi^2=1.849$, $df=2$, $P=0.397$; education level: $\chi^2=2.957$, $df=2$, $P=0.228$). A significant Chi-square was found for age ($\chi^2=16.514$, $df=4$, $P=0.002$). Most (62.9%) younger adults (18-40 years of age) preferred the computerized method (no preference: 31.4%, PP: 5.7%). In the 41-60 year old participants, 49.0% had no preference, 27.5% chose the computerized mode and 23.5% the paper-and-pencil mode. In the senior subsample (61-75 years of age) a small majority preferred the paper-and-pencil mode (PP: 35.2%, PC and no preference: 32.4%). Computer experience was also found to be

significantly related to mode preference ($\chi^2=23.516$, $df=2$, $P<0.001$). Half (50.0%) of all subjects with low computer experience chose the traditional questionnaire and 10.0% chose the computerized one (no preference: 40.0%). In the highly experienced individuals the opposite pattern was found (PC-mode: 48.9%; PP-mode: 12.2%; no preference: 38.9%).

Discussion

This study examined the reliability of five computerized psychological health questionnaires, and assessed their equivalence with the traditional paper-and-pencil versions. For all scales, internal consistency measures of the computerized version were very comparable with those found for the paper-and-pencil version, both calculated in group I. Differences for Cronbach's alphas between scale-pairs did not exceed 0.08, except for the hostility scale (0.12). However, in this scale, Cronbach's alpha was higher in the computerized version. Furthermore, alphas of the computerized version also did not differ much from those found in earlier research, using the paper-and-pencil version in similar subject samples (Koeter & Ormel, 1991; Goldberg et al., 1997; Schmitz et al., 1999; Arrindell & Ettema, 1986; Franke & Stäcker, 1995; Sherbourne & Stewart, 1991; Cohen & Williamson, 1988; Schreurs et al., 1993). According to Cicchetti's (1994) guidelines for interpreting Cronbach's alphas, 17 out of the 23 scales demonstrated fair (>0.70), good (>0.80) to excellent (>0.90) internal consistency. Six scales did not meet Cicchetti's (1994) criterion of 0.70, namely the agoraphobia, somatization, hostility, palliative reaction, passive reaction and expression of emotions scales. However, as already mentioned, scales of the paper-and-pencil version show similar alphas in the current study and in earlier research (Franke & Stäcker, 1995; Schreurs et al., 1993).

When measuring test-retest reliability of psychological instruments, an ICC between 0.60 and 0.74 is considered good, between 0.75 and 1.00 is considered excellent (Cicchetti, 1994). In this study ICC reliability measures ranged from 0.58 to 0.92, thus showing fair (hostility scale), good to excellent test-retest reliability for the computerized psychological instruments studied. Lowest ICC's were found in some of the SCL-90-R scales. This can probably be explained by the lower internal consistency found for these scales, as mentioned above. Another possible reason is the short recall period used in this particular instrument. Subjects were asked to what extent they suffered from certain physical and mental complaints 'during the past week, including today'. Since the test-retest interval was set at one week to prevent memory bias, it is likely that in some subjects complaints had changed between first

and second administration, resulting in lower ICC's. Stability coefficients for the SCL-90-R found in this study are comparable with those reported by Arrindell & Ettema (1986), ranging from 0.68 to 0.85.

Equivalence results for the total group were very promising, ranging from good (>0.60) to excellent (>0.75) (Cicchetti, 1994). As expected, equivalence in the agoraphobia and hostility scales was fair, which is probably due to the same factors already mentioned, namely a lower internal consistency and a short recall period. The majority of studies does not report separate equivalence results for subgroups. However, since some subgroups were rather small, these results should be interpreted with caution. In all scales, equivalence level in the subgroups was similar to that in the total group. A few noticeable differences in equivalence level between subgroups were found for agoraphobia, hostility, palliative reaction and expression of emotions. Again the somewhat lower reliability of these scales can probably account for this. These results support the equivalence of the computerized and hard copy versions of these questionnaires, not only at the total group but also at the subgroup level.

Another goal consisted of determining individuals' preference between both administration modes. A majority of subjects preferred completing the computerized in comparison with the traditional questionnaire, which is in line with previous study results (Lukin et al., 1985; Schulenberg & Yutrzenka, 2001; Vispoel et al., 2001). Remarkable is the high percentage (39.2%) of participants not able to choose between both modes. A possible explanation for this could be the fact that the paper-and-pencil questionnaires were completed in a different, more quiet environment, namely at home. In this way some subjects, not preferring the computerized administration mode, could have made their choice based on the association they made between the more quiet environment and the traditional administration mode, instead of judging the administration mode itself. This hypothesis can be supported by the relatively high number of environment-related reasons ('more at ease', 'more time to think', 'less cold accommodation', 'able to complete at home') these subjects gave (34% environment-related versus 66% method-related reasons). Mode preference was not found to be related with education level or gender, as already proven by Schulenberg & Yutrzenka (2001) for the Beck Depression Inventory-II. In the literature, arguments exist to support the positive relationship of computer experience with computer attitudes (Dyck & Smither, 1994). Moreover, it is presumed that a high level of computer experience is the most determining factor for having positive computer attitudes (Smith, Caputi, Crittenden, Jayasuriya & Rawstone, 1999). Our data support this assumption, as individuals showing

high levels of computer experience strongly prefer completing the computerized questionnaires, as opposed to their counterparts who choose the traditional one. Age was also related to computer preference, however in a negative and gradual way. Generally, the youngest group was in favor of the PC administered questionnaire, the middle-aged group had no preference and the oldest group still preferred the traditional questionnaire. In earlier research (Couper & Rowe, 1996) it has already been shown that the older individuals are, the less comfortable they are with completing computerized questionnaires. However, it seems reasonable that in the future computer usage in seniors will be as common as it is now in younger and middle-aged adults (Cutler, Hendricks & Guyer, 2003). This could indicate that within a few years computerized psychological assessment may be favorable not only for clinicians, researchers and younger subjects, but also for middle-aged and senior subjects.

The current study offers several important strengths in comparison with previous studies. First of all, reliability and equivalence was assessed for five extensively used psychological health instruments. Until now, four of them had never been an object of equivalence study. The fifth one had only been studied in a population of students and psychosomatic outpatients, which leads us to the second major advantage, namely the study sample. The use of a general population sample aged 18 to 75, with a well-balanced composition according to age, gender and education level, allows a high level of generalization of these results.

However, this study also has some limitations. As hypothesized above, the fact that the traditional questionnaire sets were completed at home could have influenced subjects' preference choice. The next logical question to be asked is whether equivalence results could have been affected. This is highly doubtful, since they closely resemble the test-retest results, measured in group II. A second possible restriction is the concise character of the instrument used for measuring computer experience. Existing instruments (Potosky & Bobko, 1998; Smith et al., 1999) were not used to avoid subjects being overloaded with questionnaires, since they already had to fill out five other instruments.

In conclusion, the results in this study indicate that the computerized versions of the GHQ-12, SCL-90-R, MOSSSS, PSS and UCL are reliable psychological health instruments that can be used as a practical alternative for the traditional versions in a general population of adults. Additional research should be conducted to determine their reliability and equivalence in other (clinical) populations.

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CHAPTER 2.1.2.

A CONTINUOUS METABOLIC SYNDROME RISK SCORE: UTILITY FOR EPIDEMIOLOGICAL ANALYSES

**K Wijndaele, G Beunen, N Duvigneaud, L Matton, W Duquet,
M Thomis, J Lefevre, RM Philippaerts**

Diabetes Care 2006, 29: 2329 (letter to the editor)

This study was designed to validate a continuous metabolic syndrome risk score (cMSy) using the International Diabetes Federation (IDF) risk factors (1). Increasing evidence supports using a cMSy instead of a binary definition for epidemiological analyses: a) dichotomizing continuous outcome variables reduces statistical power (2); b) cardiovascular risk is a progressive function of several metabolic syndrome (MSy) risk factors, eliminating the need to dichotomize these factors (3); c) cardiovascular and diabetes risk increase progressively with increasing numbers of MSy risk factors, eliminating the need to dichotomize MSy (3-4).

The National Institute of Statistics randomly selected a community sample of 18- to 75-year-old Flemish adults. In total, 571 men ($46.7 \pm 11.2y$) and 449 women ($45.8 \pm 10.8y$), tested between October 2002-April 2004, without cardiovascular disease and diabetes, were included.

Calculation of cMSy involved 2 steps. First, principal component (PC) analysis (varimax rotation) was applied to the normalized risk factors, to derive PCs representing large fractions of MSy variance, revealing 2 PCs (eigenvalue ≥ 1.0). In men, PC1 and PC2 explained 33% and 28% variance respectively (loadings PC1 (PC2): waist circumference: 0.51 (0.55); triglycerides: 0.82 (0.16); HDL-C: -0.85 (0.09); blood pressure: 0.12 (0.72); glucose: -0.08 (0.73)). In women, PC1 and PC2 explained 33% and 27% variance respectively (loadings PC1 (PC2): waist circumference: 0.61 (0.54); triglycerides: 0.42 (0.49); HDL-C: 0.12 (-0.90); blood pressure: 0.83 (0.01); glucose: 0.62 (0.04)). Second, cMSy was computed by summing both individual PC scores, each weighted for the relative contribution of PC1 and PC2 in the explained variance. Resulting cMSy was 0 ± 1.42 in men and 0 ± 1.41 in women.

cMSy was higher ($P < 0.001$) in subjects with IDF-MSy (men (12.8%): 2.03 ± 1.00 ; women (8.5%): 2.63 ± 1.28) versus subjects without (men: -0.30 ± 1.21 ; women: -0.24 ± 1.16). Moreover, cMSy increased progressively (Tukey-HSD, $P < 0.001$) with increasing numbers of risk factors in men: 0 (30.1%): -1.21 ± 0.96 ; 1 (33.8%): -0.26 ± 0.87 ; 2 (21.2%): 0.67 ± 0.84 ; 3 (11.2%): 1.76 ± 0.73 ; ≥ 4 (3.7%): 3.04 ± 0.94 ; and women: 0 (47.7%): -0.96 ± 0.79 ; 1 (28.3%): 0.16 ± 0.82 ; 2 (16.3%): 1.21 ± 0.82 ; 3 (5.3%): 2.17 ± 0.81 ; ≥ 4 (2.4%): 4.09 ± 0.99 .

cMSy is a more appropriate (2-4) and valid alternative for epidemiological analyses, although the binary definition (1) remains useful for clinical practice.

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Part 2

**Association studies on physical activity, physical fitness,
stress-related mental health and metabolic syndrome risk**

CHAPTER 2.2.1.

ASSOCIATION BETWEEN LEISURE TIME PHYSICAL ACTIVITY AND STRESS, SOCIAL SUPPORT AND COPING: A CLUSTER-ANALYTICAL APPROACH

**K Wijndaele, L Matton, N Duvigneaud, J Lefevre, I De Bourdeaudhuij,
W Duquet, M Thomis, RM Philippaerts**

Psychology of Sport and Exercise, in press

Abstract

Objectives: Identifying risk clusters of stress, anxiety and depression, taking into consideration social support and coping, 2 important factors through which leisure time physical activity may have stress-reducing effects, may lead to more effective exercise treatment strategies for stress. The aim of this study was to investigate whether stress, social support and coping cluster in meaningful ways in the general adult population, and whether individuals of these clusters also differ in anxiety, depression and different types of leisure time physical activity.

Method: A sample of 2616 Flemish adults, aged 18 to 75, completed 2 self-report computerized questionnaires on mental health, physical activity and demographic characteristics in the presence of a scientific staff member.

Results: Three reliable clusters were identified in both males and females. The first cluster showed high levels of stress and ineffective coping and low levels of social support. The second one showed the opposite, and the third one an intermediate profile. Anxiety and depression were highest in persons of the stressed cluster and diminished gradually over the intermediate and the nonstressed ones. Sports participation and not other types of leisure time physical activity was significantly lower in the stressed cluster.

Conclusions: By means of cluster analysis, risk groups of stress, anxiety and depression in adult males and females can be identified. Sports participation may have a beneficial effect in these at-risk groups.

Key Words: mental health, sports, exercise, anxiety, depression, risk groups

Introduction

There is ample evidence to support the beneficial effects of regular physical activity on health (Paffenbarger, Hyde, Wing, & Hsieh, 1986; U.S. Department of Health and Human Services, 1996). A sedentary lifestyle increases the risk for physical disorders such as coronary heart disease, hypertension, colon cancer, diabetes, obesity and stroke (Powell & Blair, 1994). Furthermore, exercise benefits mental health (Paluska & Schwenk, 2000; Weyerer & Kupfer, 1994).

Some studies examining the relationship between exercise and stress, showed evidence for preventive or stress-reducing effects of physical activity (Buckworth & Dishman, 2002; Scully, Kremer, Meade, Graham, & Dudgeon, 1998). To explain these effects, different physiological mechanisms are proposed, which mainly focus on the benign effects of regular aerobic exercise (Weyerer & Kupfer, 1994). However, these physiological theories alone cannot adequately explain the complex relationship between physical activity and stress. For example they cannot account for the similar mental health gains that can be achieved through either aerobic and anaerobic exercise (Plante & Rodin, 1990). This resulted in the assumption that the benign effects of exercise on stress may also be explained by psychological processes (Van Doornen, De Geus, & Orlebeke, 1988). However, more research is needed to fully understand these mechanisms (Plante & Rodin, 1990).

In order to investigate the psychosocial processes through which exercise can result in stress-reduction, the multidimensional, dynamic and complex nature of stress has to be taken into consideration (Long, 1993). One mechanism through which physical activity is thought to have stress-reducing effects is by being able to master difficult exercise tasks. This results in psychological processes which enhance self-esteem, self-efficacy and energy. First of all, this may evoke feelings of competence and mastery, through which individuals appraise a stressor as less threatening or harmful, and as a result perceive less stress (Long, 1993). Secondly, individuals with a higher self-esteem and energy are also believed to use more active, problem-focused coping strategies (Fleishman, 1984), which are also associated with lower perceived stress (Muller & Spitz, 2003). This emphasizes the construct of coping as an important mechanism in the exercise-stress relationship. Furthermore, leisure time physical activity can be an important source of social support (Ewart, 1985; Mills, 1985). Evidence exists that leisure-generated social support can have stress-reducing effects. By engaging in leisure activities that enable social interaction, people develop larger social

networks and closer friendships, and hence are more likely to perceive that they will be supported in case of problems (Coleman & Iso-Ahola, 1993). So, taking into consideration the concepts of coping and social support can result in a more comprehensive understanding of the complex relationship between leisure time physical activity and stress. Furthermore, it is very likely that certain types of leisure physical activity, that can provide social support and/or can result in a higher self-esteem and self-efficacy, will be more strongly associated with lower levels of perceived stress than others. Stephens (1988) also found that recreational physical activity instead of household chores resulted in a better psychological well-being in four population surveys in the United States and Canada. He concluded that choice of activity or quality of time may be an important element in achieving psychological benefits from physical activity. In addition, besides leisure time physical activity, low socio-economic status may also be related with stress, depression, anxiety and other pathologies (Baum, Garofalo, & Yali, 1999; Krieger, 2001). Furthermore, evidence exists for an inverse association between socio-economic status and participation in physical activity (Ford, et al., 1991; Lynch, Kaplan, & Salonen, 1997). Therefore, the association between physical activity and stress may be influenced by socio-economic status.

Stress often results in different negative physical and psychological health outcomes (Carmack, Boudreaux, Amaral-Melendez, Brantley, & de Moor, 1999). Identifying risk groups showing high levels of perceived stress in the general adult population is therefore a necessity for the primary and secondary prevention of several (mental) health problems. Two often described psychological disorders which may originate from stress are depression and anxiety (Cohen, Kessler, & Underwood, 1995; Lovallo, 1997). Both remain important public health concerns, because of their high prevalence, large financial burden and detrimental impact on the quality of life (O'Connor, Raglin, & Martinsen, 2000; O'Neal, Dunn, & Martinsen, 2000).

Cluster analysis enables us to investigate what levels of perceived stress, social support and different coping behaviours naturally coexist. An advantage of this technique is that it can provide new insights in the interactive processes between stress, social support and coping, through the possible appearance of subgroups with unique or unexpected profiles. Moreover, the possibility of identifying risk groups for perceived stress by means of cluster analysis also including social support and coping, may lead to more effective exercise treatment strategies for stress, because social support and coping are two factors through which exercise can alter the process of actually perceiving stress.

The aim of our study was twofold: (a) firstly, we examined whether perceived stress, social support and coping cluster in meaningful ways in a large population-based sample of adult males and females; (b) secondly, we investigated whether these subgroups of individuals also differ in anxiety, depression and different types of leisure time physical activity. We also examined whether differences in leisure time physical activity between clusters of individuals are dependent on socio-economic status.

Method

Participants and Procedure

This study is based on research data collected by the Flemish Policy Research Centre Sport, Physical Activity and Health (SPA) between 2002 and 2004. The sample consisted of 2616 adults aged 18 to 75. They were respondents of an epidemiological study of the SPA, aiming to investigate the relationship of physical activity, sports participation and physical fitness with general health parameters in adults. Therefore the National Institute of Statistics (NIS) randomly selected a community sample of 18- to 75-year-olds in 46 randomly chosen municipalities in the Flemish part of Belgium. Of all randomly selected individuals invited to participate in the study, 28% agreed to participate. For the non-responders, the main reasons for not participating in the study were lack of time (25.9%), health problems (23.2%), work obligations (14.6%), previous engagements (14.1%), other reasons (22.2%). This participation rate and the reasons for not participating in the study can probably be explained by the fact that the test battery was quite comprehensive (given the context of a large epidemiological study), also including physical measurements of anthropometric, fitness, and health parameters, besides questionnaires.

Responders included 1430 males (49.3 ± 13.0 yrs of age) and 1186 females (47.8 ± 12.3 yrs of age). The proportion of participants with high education level (university or college) was 49.6% in males, and 51.4% in females. Concerning occupation status, 68.3% of males and 62.8% of females were employed. All respondents signed an informed consent statement approved by the Ethics Committee of the Ghent University. We collected the data by means of two self-report computerized questionnaires, one on mental health and another one on physical (in)activity and demographic characteristics. Participants completed them either in the Policy Research Centre lab or in a municipal (sports) hall in their neighbourhood, in the presence of a scientific staff member.

Measures

Cluster Variables

Perceived stress. We measured perceived stress using the Perceived Stress Scale (PSS), a 10-item questionnaire assessing the degree to which situations in one's life are appraised as stressful (Cohen & Williamson, 1988). Respondents had to indicate how often they felt or thought in the described way during the last month (e.g., "how often have you been upset because of something that happened unexpectedly"). Answer categories were on a 5-point Likert scale (*never to very often*). A total score was calculated by summing all items and dividing this sum score by ten. In this way, the total score ranged from 1 to 5, which corresponds to the original 5-point answering scale. A higher score indicates a higher level of perceived stress.

Social support. The Medical Outcomes Study Social Support Survey (MOSSSS) was used to measure social support (Sherbourne & Stewart, 1991). This 20-item instrument measures how often each of several kinds of support are available if needed. Items (e.g., "someone you can count on to listen to you when you need to talk") were rated on a 5-point Likert scale of support availability (*none of the time to very often*). An Overall Support Index was obtained by summing all items and dividing this sum by the number of items. Consequently, the Overall Support Index ranged from 1 to 5, with higher scores denoting more social support.

Coping. The Active Dealing, Passive Reaction and Avoidance Coping scales were adopted from the Utrecht Coping List (UCL) (Schreurs, Van De Willige, Brosschoot, Tellegen, & Graus, 1993). These three scales represent the three main coping constructs identified by Endler and Parker (1990). Respondents indicated in general how frequently they adopt the described examples of coping behaviour on a 4-point Likert scale (*rarely if never to very often*). Active Dealing was assessed by seven items (e.g., "taking instant action in case of a problem", "looking at the problem from every angle") describing a direct, rational problem solving strategy. Passive Reaction measures a tendency of being totally preoccupied by problems without being able to do something about it (seven items, e.g., "not feeling capable of doing something", "worrying about the past"). The Avoidance scale was assessed by eight items, including "trying to back out of a situation", "letting things run their course". A score for each of the three scales was obtained by summing the corresponding items, and dividing this sum score by the number of items the scale consists of. In this way, all three scale scores ranged from 1 to 4. A higher score denotes a higher frequency of adopting this coping behaviour.

Anxiety, Depression, Physical (in)Activity and Demographic Variables

Anxiety and depression. Levels of anxiety and depression were derived from the Symptom Checklist (SCL-90-R), a multi-dimensional self-report scale containing the most important psychopathological complaints in adolescents, adults and psychiatric (out)patients (Arrindell & Ettema, 2003). The Anxiety and Depression scales consist of 10 and 16 items respectively symptomatic of a higher anxiety level and the clinical depression syndrome. All items are rated on a 5-point Likert scale of distress, ranging from *not at all* to *extremely*. The resulting sum scores for anxiety and depression were also recoded into the original answering scale, ranging from 1 to 5, with higher scores indicating a higher level of anxiety and depression.

A computerized version of all four psychological instruments was applied. Reliability and equivalence of the computerized and traditional paper-and-pencil version were evaluated preliminary in two separate samples of 18- to 75-year-old Flemish adults, as described in more detail by Wijndaele et al. (in press). Briefly, test-retest reliability of the computerized version, measured by calculating intraclass correlation coefficients (*ICC*) in a first group of 115 individuals, was good to excellent, according to Cicchetti's (1994) guidelines (perceived stress: *ICC* = 0.87, social support: *ICC* = 0.92, active dealing: *ICC* = 0.78, passive reaction: *ICC* = 0.82, avoidance: *ICC* = 0.73, anxiety: *ICC* = 0.67, depression: *ICC* = 0.72). Results on the internal consistency (Cronbach's α) of the computerized scales and equivalence with the traditional version, evaluated with intraclass correlation coefficients in a second group of 130 participants were also good to excellent (perceived stress: α = 0.79, *ICC* = 0.75; social support: α = 0.98, *ICC* = 0.90; active dealing: α = 0.85, *ICC* = 0.76; passive reaction: α = 0.64, *ICC* = 0.77; avoidance: α = 0.75, *ICC* = 0.74; anxiety: α = 0.77, *ICC* = 0.70; depression: α = 0.85, *ICC* = 0.70).

Physical (in)activity and demographic variables. Physical (in)activity levels and demographic characteristics (gender, age, occupation, and education level) were assessed applying the Flemish Physical Activity Computerized Questionnaire (FPACQ) (Matton et al., in press). This questionnaire was designed to evaluate the levels of physical activity in several domains. Sports participation was assessed by asking respondents to select their 3 most frequently practiced sports out of a list of 196 sports with different intensities, and both organized and nonorganized. For each of these sports, frequency (from once a year to more than once a day) and duration (from some hours per year to more than 20 hours per week) were reported. A *sports participation* index was computed by summing hours per week spent in sports with an intensity level of 4 METs or higher, according to the classification of

Ainsworth, Haskell, and Whitt (2000). An *active transportation in leisure time* index was obtained by asking the amount of time spent in walking and cycling as transportation in leisure time, during an average week. A *housekeeping and gardening* index was calculated by summing the time spent in low (e.g., cooking, doing the dishes), moderate (e.g., hoovering, mowing the lawn) and vigorous intensity (e.g., scrubbing the floor, digging) activities. A *total active leisure time* index was composed by summing up the sports participation, active transportation in leisure time and housekeeping and gardening indices. A *sedentary behaviour* index was calculated by summation of the time spent on watching television or video or playing computer games during an average week day and during an average weekend day. All (in)activity indices were expressed in hours per week. To classify respondents based on reaching the norm of engaging in at least *30 minutes of moderate activity/day* (Pate et al., 1995), the sports participation index, time spent in cycling as transportation in leisure time, and time spent in gardening and housekeeping of vigorous intensity were summed.

Statistical Analyses

Analyses were carried out using the SPSS 12.0 statistical software package (SPSS, Inc., Chicago, IL). In order to evaluate the necessity of gender specific analysis, differences in mental health (perceived stress, social support, coping behaviour, anxiety and depression) and physical (in)activity between men and women were evaluated using the independent samples *t* test. Pearson bivariate correlation coefficients were calculated between all mental health variables.

To identify and classify naturally occurring patterns of perceived stress, social support and coping, we used cluster analysis after transforming scores into standardized *z*-scores. This cluster analysis involved three successive steps: (a) K-means cluster analysis classified cases into $n = k$ clusters by maximizing between-cluster differences and minimizing within-cluster variance in perceived stress, social support, active dealing, passive reaction and avoidant coping behaviour scores (Hartigan, 1975); (b) the reliability of the resulting cluster solution was evaluated by randomly splitting the sample into two complementary subgroups of 50 % each, and repeating the same clustering procedure in these subgroups. The level of agreement for cluster allocation of subjects between the total group and each of the subgroups, was measured by means of the kappa statistic; (c) multivariate analysis of variance (MANOVA) and one-way analysis of variance (ANOVA)

with Tukey's honestly significant difference (HSD) post hoc test was used to confirm whether individuals of clusters differed significantly for all variables included in the cluster analysis.

Differences in anxiety, depression, physical (in)activity and demographic characteristics between subjects of clusters were analyzed by means of one-way ANOVA, analysis of covariance (ANCOVA) with age as covariate and the HSD post hoc test, and the chi-square (χ^2) test. Data on occupation status were reduced from five to two levels, namely being employed ("I have a job") and being unemployed ("I'm out of work", "I consciously do not work", "I do not work because of a handicap", "I'm retired"). For education level, data were reduced from 13 to 2 levels, namely low (secondary school and lower) and high (university or college) education level.

To examine whether differences in leisure time physical activity between subjects of clusters are dependent on socio-economic status, two-way ANOVA were executed, including socio-economic status as one of both categorical factors. In a first set of analyses, education level was included as a measure of socio-economic status, in a second set of analyses, occupation status was included as a measure of socio-economic status.

To improve the normality of the distribution of positively skewed variables (anxiety, depression, sports participation and active transportation) a logistic transformation (\log_{10}) was used. Social support was normalized by raising it to the 5th power. Minimal statistical significance was set at a level of $p < .05$.

Results

Gender Differences

As shown in Table 1, men reported significantly more social support, $t(2614) = 2.87, p < .01$, and active dealing, $t(2614) = 9.27, p < .001$, than women did. The latter reported significantly higher levels of perceived stress, $t(2614) = -9.24, p < .001$, passive reaction, $t(2614) = -4.18, p < .001$, avoidance, $t(2614) = -3.93, p < .001$, anxiety, $t(2614) = -6.32, p < .001$, and depression, $t(2614) = -8.05, p < .001$. When looking at the differences in physical activity, men participated significantly more in sports, $t(3613) = 8.88, p < .001$, and in active transportation in leisure time, $t(2270.46) = 28.08, p < .001$. Women however spent more time in housekeeping and gardening, $t(2567) = -19.60, p < .001$, and total active leisure time,

$t(2560.75) = -6.59, p < .001$. No difference was reported in sedentary behaviour, $t(2484.99) = 1.89, ns$. Based on these results, all subsequent analyses were executed separately in males and females.

Table 1. Descriptive statistics ($M \pm SD$) and differences between men and women for mental health and physical (in)activity variables

Variable	Total group ($N = 2616$)	Men ($n = 1430$)	Women ($n = 1186$)	t
Perceived stress ^a	2.13 ± 0.60	2.03 ± 0.57	2.25 ± 0.62	-9.24***
Social support ^a	4.32 ± 0.67	4.35 ± 0.65	4.28 ± 0.68	2.87**
Active dealing ^b	2.72 ± 0.54	2.81 ± 0.54	2.62 ± 0.52	9.27***
Passive reaction ^b	1.49 ± 0.40	1.46 ± 0.39	1.53 ± 0.41	-4.18***
Avoidance ^b	1.87 ± 0.41	1.84 ± 0.42	1.91 ± 0.40	-3.93***
Anxiety ^a	1.27 ± 0.36	1.23 ± 0.32	1.31 ± 0.40	-6.32***
Depression ^a	1.32 ± 0.41	1.27 ± 0.37	1.38 ± 0.45	-8.05***
Sports participation ^c	2.46 ± 3.31	2.96 ± 3.71	1.85 ± 2.62	8.88***
Active transportation in leisure time ^c	2.00 ± 2.36	2.97 ± 2.78	0.83 ± 0.75	28.08***
Housekeeping and gardening ^c	12.05 ± 7.61	9.57 ± 7.26	15.08 ± 6.90	-19.60***
Total active leisure time ^c	17.21 ± 8.87	16.19 ± 9.50	18.45 ± 7.85	-6.59***
Sedentary behaviour ^c	15.29 ± 8.29	15.57 ± 8.35	14.95 ± 8.21	1.89

^aRated on a 5-point Likert scale. ^bRated on a 4-point Likert scale. ^cExpressed in hours per week.

** $p < .01$. *** $p < .001$.

Intercorrelations

Table 2 presents an overview of the correlations between the scores on all mental health variables in men and women, which were all significant ($p < .05$).

Table 2. Intercorrelations between mental health variables in men (women)

Variable	Social support	Active dealing	Passive reaction	Avoidance	Anxiety	Depression
Perceived stress	-.38** (-.40**)	-.39** (-.39**)	.58** (.64**)	.16** (.10**)	.60** (.63**)	.65** (.68**)
Social support	-	.16** (.19**)	-.36** (-.33**)	-.19** (-.07*)	-.28** (-.30**)	-.39** (-.43**)
Active dealing		-	-.20** (-.30**)	-.19** (-.13**)	-.18** (-.22**)	-.21** (-.26**)
Passive reaction			-	.32** (.23**)	.59** (.59**)	.68** (.66**)
Avoidance				-	.17** (.10**)	.21** (.14**)
Anxiety					-	.73** (.77**)

* $p < .05$. ** $p < .01$.

For the variables included in the cluster analysis, the highest correlations were found in both genders between perceived stress and passive reaction, perceived stress and active dealing and finally perceived stress and social support (r between .38 and .64, $p < .01$). All other intercorrelations were .36 and lower. Correlations between the coping scales were .32 and lower. For anxiety and depression, strong intercorrelations were found in both genders with perceived stress and passive reaction (r between .59 and .68, $p < .01$).

Cluster Analyses

The three-cluster solution was identified as the most reliable and adequate representation of the naturally occurring patterns of perceived stress, social support and the three different coping behaviours among both male and female participants. After repeating the same clustering procedure in two randomly selected complementary subgroups of 50% each, the level of agreement for cluster allocation of subjects between the total group and each of the subgroups, measured by the kappa statistic, was .87 and .92. in males and .89 and .87 in females. A significant MANOVA, $F(10, 2846) = 369.83, p < .001, F(10, 2358) = 313.83, p < .001$, was found for men and women respectively. Figures 1 and 2 show the cluster profiles expressed in standardized scores among both genders.

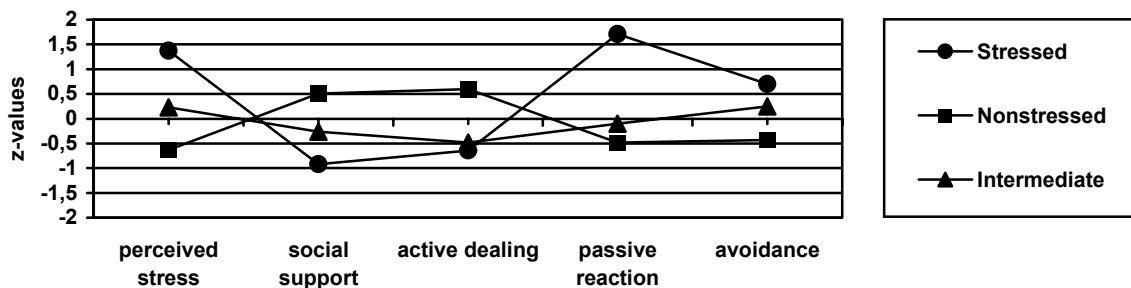


Figure 1. Standard scores of clusters on perceived stress, social support and three coping styles in 18- to 75-year old men ($n = 1430$)

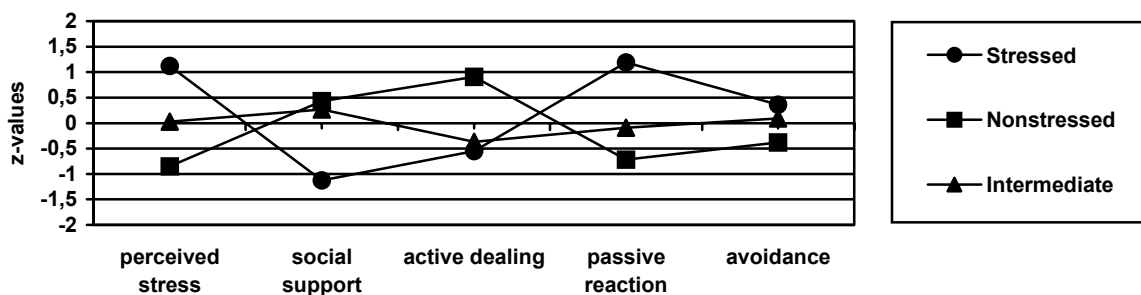


Figure 2. Standard scores of clusters on perceived stress, social support and three coping styles in 18- to 75-year old women ($n = 1186$)

Actual values and test statistics are presented in Table 3. The one-way ANOVA with HSD test revealed that all clusters were significantly different ($p < .001$) for all five cluster variables. However when comparing Figure 1 and 2, it shows that similar clusters were found for men and women. Cluster 1 was labeled *stressed ones with low social support and high passive and avoidant coping behaviour*, abbreviated to *stressed* (15.2% and 22.8% in men and women respectively). Individuals in Cluster 2 (46.7% and 32.2% in men and women respectively) were labeled *nonstressed ones with high social support and active coping behaviour*, abbreviated to *nonstressed*. Respondents in Cluster 3 were labeled *intermediates* (38.1% and 45.0% in men and women respectively), because they reported intermediate levels of perceived stress, social support and the three coping behaviours.

Table 3. Actual values (M \pm SD) and differences between clusters for cluster variables, anxiety and depression in men and women

Variable	Men			F	Women			F
	Stressed (n = 217)	Nonstressed (n = 668)	Intermediate (n = 545)		Stressed (n = 271)	Nonstressed (n = 381)	Intermediate (n = 534)	
Perceived stress ^a	2.81 \pm 0.50 _a	1.67 \pm 0.38 _b	2.16 \pm 0.40 _c	697.13***	2.94 \pm 0.52 _a	1.72 \pm 0.38 _b	2.27 \pm 0.41 _c	641.17***
Social support ^a	3.75 \pm 0.81 _a	4.69 \pm 0.34 _b	4.18 \pm 0.63 _c	273.71***	3.51 \pm 0.76 _a	4.57 \pm 0.46 _b	4.46 \pm 0.44 _c	366.95***
Active dealing ^b	2.46 \pm 0.50 _a	3.14 \pm 0.42 _b	2.55 \pm 0.45 _c	336.89***	2.33 \pm 0.45 _a	3.09 \pm 0.41 _b	2.43 \pm 0.37 _c	384.76***
Passive reaction ^b	2.13 \pm 0.34 _a	1.27 \pm 0.23 _b	1.42 \pm 0.26 _c	896.82***	2.02 \pm 0.39 _a	1.23 \pm 0.22 _b	1.49 \pm 0.28 _c	576.68***
Avoidance ^b	2.14 \pm 0.42 _a	1.67 \pm 0.34 _b	1.94 \pm 0.38 _c	160.30***	2.05 \pm 0.41 _a	1.75 \pm 0.38 _b	1.94 \pm 0.37 _c	50.64***
Anxiety ^a	1.62 \pm 0.54 _a	1.11 \pm 0.16 _b	1.21 \pm 0.23 _c	290.38***	1.70 \pm 0.55 _a	1.13 \pm 0.19 _b	1.25 \pm 0.27 _c	283.49***
Depression ^a	1.80 \pm 0.60 _a	1.12 \pm 0.15 _b	1.24 \pm 0.23 _c	495.52***	1.88 \pm 0.59 _a	1.14 \pm 0.16 _b	1.30 \pm 0.28 _c	431.13***

Note. Means in the same row that do not share subscripts differ at $p < .001$ in the Tukey honestly significant difference comparison.

^aRated on a 5-point Likert scale. ^bRated on a 4-point Likert scale.

*** $p < .001$.

Differences in Anxiety and Depression Between Clusters

The one-way ANOVA with Tukey's HSD test revealed that individuals of all three clusters demonstrated significantly different levels of anxiety, $F(2, 1427) = 290.38$, $p < .001$, $F(2, 1183) = 283.49$, $p < .001$, and depression, $F(2, 1427) = 495.52$, $p < .001$, $F(2, 1183) = 431.13$, $p < .001$, in men and women respectively (see Table 3). The same pattern was found for both variables among clusters. Subjects in the stressed cluster reported the highest levels of anxiety and depression, followed by the intermediates, and finally the nonstressed ones, who were the least anxious and depressed.

Cluster Group Characteristics

As shown in Table 4, stressed males were significantly younger, $F(2, 1427) = 11.98$, $p < .001$, than their counterparts in the nonstressed and intermediate clusters. Therefore, differences in physical (in)activity between male clusters were evaluated by means of ANCOVA, correcting for age. In women, neither age, $F(2, 1183) = 2.03$, ns , nor occupational status, $\chi^2(2, n = 1186) = 1.09$, ns , were discriminating characteristics between clusters. In men however, more employed participants were found in the stressed cluster in comparison with both the nonstressed and intermediate cluster, $\chi^2(2, n = 1430) = 9.41$, $p < .01$. Education level did differentiate between subjects of clusters, $\chi^2(2, n = 1430) = 17.53$, $p < .001$, $\chi^2(2, n = 1186) = 9.19$, $p < .05$, in men and women respectively. The nonstressed individuals had the highest percentage of high educated participants in both genders. The lowest percentage of high educated participants in male adults was found in the intermediates, in female adults a similar percentage was found in the stressed and the intermediate clusters.

Table 4. Actual values (M \pm SD) and differences between clusters for demographic variables in men and women

Variable	Men			F	Women			F
	Stressed (n = 217)	Nonstressed (n = 668)	Intermediate (n = 545)		Stressed (n = 271)	Nonstressed (n = 381)	Intermediate (n = 534)	
Age (years)	45.39 \pm 12.38 _a	50.10 \pm 12.92 _b	49.98 \pm 13.14 _b	11.98***	47.88 \pm 12.26	48.77 \pm 12.44	47.11 \pm 12.10	2.03
Occupation				9.41***				1.09 ^a
Employed (%)	77.0	67.5	65.7		60.5	62.5	64.2	
Unemployed (%)	23.0	32.5	34.3		39.5	37.5	35.8	
Education				17.53***				9.19**
Low (%)	49.3	45.2	57.2		52.8	42.3	50.9	
High (%)	50.7	54.8	42.8		47.2	57.7	49.1	

Note. Means in the same row that do not share subscripts differ at $p < .001$ in the Tukey honestly significant difference comparison.

^aResult of χ^2 test.

* $p < .05$. ** $p < .01$. *** $p < .001$.

Differences in Physical Activity and Sedentary Behaviour Between Clusters

Differences in physical activity and sedentary behaviour were also examined, as shown in Table 5. Significant differences between the male clusters were found for sports participation, $F(2, 1426) = 5.09$, $p < .01$. On average, the stressed group engaged half an hour to three quarters of an hour less in sports, in comparison with the nonstressed and the intermediate group. No differences between the male clusters were found for active

transportation in leisure time, housekeeping and gardening, and total active leisure time. However sedentary behaviour was reported less in the nonstressed males, $F(2, 1407) = 5.19$, $p < .01$, in comparison with their counterparts in both other clusters.

In females, significant differences were found for sports participation, $F(2, 1182) = 3.68$, $p < .05$. The pattern found in males reoccurred, with stressed females doing less sports in comparison with both other clusters. No other differences in physical (in)activity between subjects of clusters were found in females.

The percentage of participants reaching the norm of at least 30 minutes of moderate activity/day was not significantly different among the three clusters for men, $\chi^2(2, n = 1429) = 4.40$, *ns*, nor for women, $\chi^2(2, n = 1184) = 5.13$, *ns*.

Table 5. Actual values (M \pm SD) and differences between clusters for physical activity and sedentary behaviour in men and women

Variable	Men				Women			
	Stressed (<i>n</i> = 217)	Nonstressed (<i>n</i> = 668)	Intermediate (<i>n</i> = 545)	<i>F</i>	Stressed (<i>n</i> = 271)	Nonstressed (<i>n</i> = 381)	Intermediate (<i>n</i> = 534)	<i>F</i>
Sports participation ^a	2.48 \pm 3.45 _a	2.94 \pm 3.64 _b	3.17 \pm 3.88 _b	5.09**	1.67 \pm 2.88 _a	1.87 \pm 2.32 _b	1.94 \pm 2.68 _b	3.68*
Active transportation in leisure time ^a	2.74 \pm 2.42	2.93 \pm 2.86	3.10 \pm 2.81	1.37	0.78 \pm 0.76	0.84 \pm 0.73	0.85 \pm 0.77	1.37
Housekeeping and gardening ^a	9.57 \pm 7.37	9.58 \pm 7.35	9.54 \pm 7.12	0.25	15.72 \pm 6.87	14.45 \pm 6.71	15.21 \pm 7.01	2.81
Total active leisure time ^a	15.28 \pm 8.67	16.17 \pm 9.76	16.58 \pm 9.49	0.39	18.78 \pm 7.52	17.96 \pm 7.72	18.64 \pm 8.10	1.10
Sedentary behaviour ^a	15.96 \pm 8.59 _a	14.93 \pm 8.32 _b	16.19 \pm 8.24 _a	5.19**	15.40 \pm 8.83	14.13 \pm 7.86	15.30 \pm 8.11	2.73
≥ 30 min moderate activity/day				4.50 ^b				5.13 ^b
Yes (%)	53.9	61.4	61.8		42.4	44.9	50.2	
No (%)	46.1	38.6	38.2		57.6	55.1	49.8	

Note. Means in the same row that do not share subscripts differ at $p < .01$ in the Tukey honestly significant difference comparison.

^aExpressed in hours per week. ^bResult of χ^2 test.

* $p < .05$. ** $p < .01$.

The two-way ANOVA, did not reveal a significant interaction effect of education level and cluster membership, or occupation status and cluster membership, on any of the physical activity indexes, in men nor women.

Discussion

This study examined whether perceived stress, social support and coping behaviour cluster in meaningful ways in a population-based sample of 2616 adults aged 18 to 75. Furthermore, we investigated whether these subgroups of individuals differed in anxiety, depression and different types of leisure time physical (in)activity. The use of cluster analysis allowed to take into consideration social support and coping behaviour in the investigation of the physical activity-stress relationship. By identifying risk groups of stress and mental health and evaluating their physical (in)activity level, they may be the focus of future exercise interventions, that are based on the mechanisms of coping and social support.

The bivariate correlation coefficients between all mental health variables were similar for men and women. For the cluster variables, a strong positive correlation was found between perceived stress and passive reaction. Active dealing and perceived stress on the contrary showed a strong negative correlation. Both results are consistent with the findings of Muller and Spitz (2003) that functional coping strategies (e.g., active coping) are linked to lower perceived stress, whereas less functional strategies (e.g., denial) are linked to high perceived stress. Social support also showed a strong negative correlation with perceived stress, which can be supported by the stress-reducing effect social support is believed to have (Cohen, Gottlieb, & Underwood, 2000). A very strong positive relation was found between perceived stress, anxiety and depression. The fact that both mental disorders may originate from perceived stress, can probably account for this (Cohen et al., 1995; Lovallo, 1997). Similar high and positive correlation coefficients were seen between passive reaction and anxiety and depression, as found by Arrindell and Ettema (2003).

An important finding of this study is that three meaningful clusters of stress, social support and coping can be found in the general adult population. Moreover, repeated cluster analysis in two randomly selected, complementary subgroups of 50% each, confirmed that this three-cluster solution is reliable (Landis & Koch, 1977). These three clusters, appearing in both genders, consisted of: (a) the stressed ones with low social support and high passive and avoidant coping behaviour; (b) the intermediates; (c) and the nonstressed ones with high social support and active coping behaviour. Although these clusters are significantly different, they do show a high level of homogeneity when looking at the way stress, social support and the three coping behaviours appear together in each cluster. For example, we did not find any clusters simultaneously showing a high level of stress and social support, or a

high level of stress and active coping. The stressed adults display the most negative profile, followed by the intermediates and the nonstressed adults, who showed the most positive profile. In addition, subjects in the stressed cluster reported the highest level of anxiety and depression, which decreased gradually over those in the intermediate and the nonstressed clusters respectively. This indicates that by making use of cluster analysis based on perceived stress, social support and coping, risk groups for anxiety and depression can be identified.

A central question in this study was whether these clusters differed significantly for several types of leisure physical (in)activity. Sports participation was the only type that could discriminate between the three subgroups in both men and women. A first important characteristic of sports participation is that in many cases it is a social activity (Ewart, 1985; Mills, 1985). Social relationships generated through sports participation and other leisure time activities can reduce stress, because people become embedded in a larger and stronger social network and are more likely to perceive that they will be supported in case of problems (Coleman & Iso-Ahola, 1993). The present results support this idea. The subgroup with the least sports participation also experienced the lowest level of social support and the highest level of stress. Moreover, time spent in household chores and active transportation, two activities with a less social character, did not differ between subgroups. A second feature of sports activities is that they are generally much more challenging and often show graded increments of difficulty when practiced regularly in comparison with active transportation or housekeeping and gardening. In this way, our results may also be supportive of the theory that individuals who master a difficult exercise task, develop a higher self-esteem and self-efficacy for strenuous tasks in general. They experience feelings of mastery and competence through which a potential stressful situation will look less threatening, and lower levels of perceived stress occur (Long, 1993). Additionally, because feelings of mastery and competence have to be reinforced frequently (Long, 1993), the continuously challenging aspect of sports participation also has a major advantage over other types of physical activity. Furthermore, a higher self-esteem is also associated with greater active, problem-focused coping, through which coping effectiveness is increased as well (Fleishman, 1984). In our study, the subgroup with the least sports participation also shows the least active coping behaviour. Instead, they display a passive and avoidant coping style. Clusters did not differ in percentage of participants achieving the norm of at least 30 minutes of moderate activity/day. This was not completely unexpected as this norm is rather based on the

physiological benefits of exercise on health (Pate et al., 1995), while the categorization of our individuals is based on the possible psychosocial mechanisms through which exercise can result in a better psychological health.

Low socio-economic status is an important predictor of stress, anxiety, depression and other illness outcomes (Baum et al., 1999; Krieger, 2001). Furthermore, men and women of a higher socio-economic status in childhood or adulthood spend significantly more time in leisure time physical activity as an adult (Ford et al., 1991; Lynch, 1997). Therefore, the association between leisure time physical activity and cluster membership may depend on socio-economic status. In the present study, no significant interaction effects between socio-economic status and cluster membership on level of physical activity were found. This indicates that the association between leisure time physical activity and cluster membership was similar in low and high socio-economic status subjects, as measured by education level or occupation status, and therefore independent of socio-economic status. However, since both socio-economic status indicators were measured in a rather rudimentary way, this result should be interpreted with caution.

Consistent with the literature, women in our study perceived significantly more stress (Cohen & Williamson, 1988; Matud, 2004), anxiety and depression (Angst et al., 2002; Bebbington, 1998; Kessler et al., 1994), compared to men. They also reported significantly less social support and more passive and avoidant coping in comparison with men, who reported significantly more active dealing (Matud, 2004; Ptacek, Smith, & Zanas, 1992). This is also reflected by the higher percentage of females in the stressed cluster in comparison with the corresponding percentage in males. On average, women report one hour less of sports participation per week in comparison with men, which may partly account for the higher percentage of stressed women.

Clusters were also compared for demographic characteristics. The stressed males were significantly younger in comparison with both other subgroups. Cohen and Williamson (1988) also found a small but significant negative correlation between perceived stress and age in a sample of adult Americans. Secondly, stressed males showed the highest level of employment in comparison with both other subgroups, whereas the female clusters did not differ in employment status. Earlier research revealed that women experience more stressful events associated with health and family, and men report more stressful events associated with work and finance (Billings & Moos, 1984), which could explain these results. Finally, the negative correlation between education level and perceived stress found in earlier

research (Cohen & Williamson, 1988) rather consistently reappears in our results, showing the highest percentage of high educated individuals in the least stressed cluster.

This study shows some important strengths. First of all, the large population-based sample covered a wide age range (18 to 75 years old) and analyses were carried out in both genders separately. Secondly, no earlier studies investigated the physical activity-stress relationship by means of cluster analysis including social support and coping. The use of this technique offers some promising results. First of all, risk groups of stress, anxiety and depression can be identified in adult males and females. Furthermore, sports participation instead of other types of leisure time physical activity can discriminate between these subgroups. This may be affirmative for the present knowledge of social support and coping as mechanisms for the psychological benefits of exercise on stress. Based on this information, it is possible that sports participation and other types of physical activity, providing sources of higher social support, self-esteem and self-efficacy, could be effective intervention strategies to deal with stress, anxiety and depression.

However, one limitation of this study is the use of self-report measures. Second, given the participation rate and the reasons of the non-responders for not participating in the study, it is possible that the present study sample has a somewhat selective character for both mental health and participation in leisure time physical activity, which may partially limit external validity of the results. A more heterogeneous sample, reporting more extreme values for mental health and leisure time physical activity would probably yield stronger associations. A third limitation of this study is the cross-sectional design, through which we cannot make assumptions about temporal sequence. In this study, we present and possibly found support for theories in literature, suggesting that leisure time physical activity, and more specifically sports participation, beneficially effect social support and coping strategies, and consequently stress, anxiety and depression. However, it is possible that the effects found operate in the opposite direction, because bidirectional relationships can exist among the variables. First, as suggested by Cohen et al. (1995), individuals perceiving more stress tend to engage in poor health behaviours, including less frequent physical activity. Second and consequently, social support and coping behaviour may, indirectly via perceived stress, influence physical activity participation. Because social support is thought to have a stress-buffering role (Cohen et al., 2000), individuals lacking social support may perceive more stress and consequently engage less in physical activity. Similarly, subjects showing low levels of active coping and high levels of passive and avoidant coping may experience

higher levels of stress (Muller & Spitz, 2003) and consequently be more physically inactive. Third, social support may have a direct, also known as main effect, which includes that social relationships beneficially influence health-related behaviours, including physical activity, through mechanisms such as social control; causing positive psychological states resulting in greater motivation to care for oneself; and providing informational, tangible and economic services promoting health-enhancing behaviours (Cohen et al., 2000). Therefore, given the cross-sectional design of this study, the direction of causality of the present results can probably not be taken for granted. Future longitudinal and intervention studies in nonclinical and clinical populations are needed to investigate the efficacy of sports participation as an intervention method. Finally, it would also be useful to further examine whether some (sports) activities are more efficacious than others.

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CHAPTER 2.2.2.

**SEDENTARY BEHAVIOUR, PHYSICAL ACTIVITY AND
A CONTINUOUS METABOLIC SYNDROME RISK SCORE
IN ADULTS**

**K Wijndaele, N Duvigneaud, L Matton, W Duquet, M Thomis,
G Beunen, J Lefevre, RM Philippaerts**

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Abstract

Objective: The association of sedentary behaviour and leisure time physical activity with a validated continuous metabolic syndrome risk score was investigated in adults.

Design: Cross-sectional study.

Setting: Community sample of 18- to 75-year-olds in the Flemish region of Belgium.

Subjects: A number of 992 adults (559 men) without cardiovascular disease or diabetes.

Methods: Subjects reported time spent in leisure time physical activity and TV watching/computer activities. A validated metabolic syndrome risk score, based on waist circumference, triglycerides, blood pressure, fasting plasma glucose and HDL cholesterol, was used. The metabolic syndrome risk score and time spent in sedentary behaviour and physical activity were analyzed as continuous variables using multiple linear regression.

Results: Metabolic syndrome risk was positively associated with time spent watching TV/computer activities (men: $\beta = 0.086$, $P < 0.05$; women: $\beta = 0.143$, $P < 0.01$), irrespectively of physical activity level, and after adjustment for age, height, education level, smoking status and dietary intake. Independently of time being sedentary, moderate to vigorous leisure time physical activity was inversely associated with metabolic syndrome risk (men: $\beta = -0.185$, $P < 0.001$; women: $\beta = -0.128$, $P < 0.01$). Furthermore, similar independent associations were found for sedentary behaviour and leisure time physical activity with several individual metabolic syndrome risk factors, some mediated by obesity, others independently of obesity.

Conclusions: Although cross-sectional, the present results support inclusion of efforts to decrease sedentary behaviour in prevention strategies for metabolic syndrome risk, besides promotion of moderate to vigorous physical activity, since both behavioural changes might show additional effects.

Key Words: insulin resistance syndrome X, television, exercise, obesity, adult, cardiovascular disease

Introduction

The clustering of risk factors, known as the metabolic syndrome, predicts the development of type 2 diabetes (Laaksonen et al, 2002), cardiovascular disease and all-cause mortality (Lakka et al, 2002) in nondiabetic individuals, and is highly prevalent worldwide (Cameron et al, 2004). To develop effective primary and secondary prevention strategies for this global health problem, its modifiable determinants need to be thoroughly understood.

Earlier research revealed an inverse association between physical activity and metabolic syndrome risk in adults (Ekelund et al, 2005). Furthermore, Owen et al. (2000) urged the need to study physical activity and sedentary behaviour as 2 distinct classes of behaviour in finding ways to influence health outcomes, since they may have independent effects on these health outcomes. Television watching, a common form of sedentary behaviour, has been associated with elevated risk for type 2 diabetes, obesity (Hu et al, 2003) and cardiovascular disease markers (Jakes et al, 2003), all independently of physical activity level. Until now, in a limited number of studies the associations of physical activity and sedentary behaviour with the metabolic syndrome were simultaneously investigated in adults. In these studies, a binary definition of the metabolic syndrome was used (Bertrais et al, 2005; Dunstan et al, 2005; Ford et al, 2005).

However, increasing evidence supports the use of a continuous metabolic syndrome risk score in epidemiological analyses, instead of a binary definition (Kahn et al, 2005): a) dichotomizing continuous outcome variables reduces statistical power to detect associations (Ragland, 1992); b) cardiovascular disease risk is a progressive function of several metabolic syndrome risk factors, eliminating the need to dichotomize these risk factors using cut points (Kahn et al, 2005); c) cardiovascular disease and diabetes risk increase progressively with an increasing number of metabolic syndrome risk factors (Klein et al., 2002), eliminating the need to dichotomize the presence of the syndrome, e.g. in case of 3 or more present risk factors (Kahn et al, 2005).

Sedentary behaviour is inversely and physical activity is directly associated with obesity (Bertrais et al, 2005; Hu et al, 2003). Furthermore, obesity predicts the development of several individual risk factors of the metabolic syndrome and of type 2 diabetes (Han et al, 2002). Therefore, the association of sedentary behaviour and physical activity with the individual metabolic syndrome risk factors may (partially) be mediated by obesity.

The aims of the present study were a) to investigate the cross-sectional association of sedentary behaviour and leisure time physical activity with a validated continuous metabolic

syndrome risk score (Wijndaele et al, 2006) in Flemish adults, aged 18 to 75, and b) to determine the relationship of sedentary behaviour and leisure time physical activity with each of the continuous metabolic syndrome risk factors, and the extent to which obesity mediates this relationship.

Methods

Subjects

Data for this study were collected by the Flemish Policy Research Centre Sport, Physical Activity and Health (SPAHE) between October 2002 and April 2004, in a cross-sectional survey on the relationship between physical activity, physical fitness and several health parameters. For this purpose, the National Institute of Statistics randomly selected a community sample of 18- to 75-year-olds in the Flemish region of Belgium. Subjects were asked to visit the SPAHE examination centre to provide a fasting blood sample, to go through a medical examination, anthropometric measurements, physical tests, and some questionnaires. For the present study, participants with complete data for all metabolic syndrome risk factors, sedentary behaviour, leisure time physical activity, and for all confounding variables used in the analyses, were included. Participants were excluded in case of a history or evidence of cardiovascular disease (abnormal heart auscultation or rest electrocardiogram; sudden death of father or brother before the age of 45, or of mother or sister before the age of 55; systolic blood pressure >150 mm Hg or diastolic blood pressure >100 mm Hg; use of antihypertensive or lipid-lowering drugs) or diabetes mellitus. Consequently, results are based on data of 559 men and 433 nonpregnant women, aged 18 to 75. Prior to participation, subjects gave their written informed consent. The study was approved by the Ghent University Ethics Committee and performed in accordance with the Helsinki Declaration.

Data collection

Blood samples. Subjects were asked to fast from 11:00 P.M. the evening before visiting the laboratory. A sample of fasting blood was taken from an antecubital vein of subjects in supine position. All samples were stored at 4°C before they were transferred to the lab at 11:00 A.M. They were analyzed before 5:00 P.M. the same day. Triglyceride was analyzed using the lipase/glycerol kinase/glycerol phosphate oxidase enzymatic method. HDL

cholesterol was analyzed using the homogeneous polyanion/cholesterol esterase/oxidase enzymatic method. Glucose was analyzed using the hexokinase method. Triglycerides, HDL cholesterol and glucose were measured on an Olympus AU5400 analyzer (Olympus Diagnostica, Hamburg, Germany). The coefficients of variation between days were 1.4% (at 2.07 mmol/l) for triglycerides, 3.9% (at 2.04 mmol/l) for HDL cholesterol and 2.0% (at 16.71 mmol/l) for glucose.

Blood pressure. A physician measured blood pressure at the left arm of subjects who had been seated for 10 minutes, using a NOVA Presameter mercury sphygmomanometer (Riester, Jungingen, Germany). Systolic and diastolic blood pressure were measured 3 times with 1-minute intervals, and the mean of these 3 measurements was used in analyses.

Anthropometric measurements. Anthropometric measurements were taken by trained staff with participants barefoot and in underwear. Height was measured using a stadiometer (Holtain, Crymych, UK) to the nearest 0.1 cm. Waist circumference was measured using a metal tape (Rosscraft, Surrey, BC, Canada) to the nearest 0.1 cm, at the narrowest level between lowest ribs and iliac crests, in standing position.

Continuous metabolic syndrome risk score (cMSy). A validated cMSy was calculated as described in more detail by Wijndaele et al. (2006). In short, cMSy is based on the 5 risk factors in the definitions of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2001) and the International Diabetes Federation (2005), namely waist circumference, triglycerides, HDL cholesterol, blood pressure (systolic and diastolic) and fasting plasma glucose. Calculation involved 3 successive steps: a) all variables were normalized (\log_{10}) because of their non-normal distribution. A blood pressure index was computed by averaging systolic and diastolic blood pressure; b) principal component analysis with varimax rotation was applied to the individual risk factors in order to derive components that represent large fractions of the metabolic syndrome variance, and consequently to give each risk factor the most appropriate weight in calculating cMSy. This analysis revealed 2 principal components with eigenvalue ≥ 1.0 in both genders; c) cMSy was computed by summing both individual principal component scores, each weighted for the relative contribution of principal component 1 and 2 in the explained variance. The resulting cMSy was 0 ± 1.42 in men and 0 ± 1.41 in women. This score showed high validity in both genders (Wijndaele et al, 2006).

Sedentary behaviour and leisure time physical activity. Sedentary behaviour and leisure time physical activity were assessed using the Flemish Physical Activity Computerized

Questionnaire (FPACQ). The FPACQ was found to be a reliable and valid questionnaire for the assessment of different dimensions of physical activity in adults (Matton et al, in press).

Participants were asked to indicate time spent watching television/video or playing computer games during an average week day and weekend day (from 0 to ≥ 6 h/day). *Sedentary behaviour* time was then calculated by multiplying average week day and weekend day scores by 5 and 2 respectively, and summing both products.

Levels of leisure time physical activity were evaluated in several domains. Sports participation was assessed by asking subjects to select their 3 most frequently practiced sports out of a list of 196 sports. For each of these sports, frequency (from 1 week/year to more than 7 times/week) and duration (from <1 h/week to >20 h/week) were reported. Active transportation in leisure time was determined by asking time spent in walking and cycling as transportation in leisure time, during an average week day and weekend day (from 0 to >60 min/day). Furthermore, time spent in housekeeping and gardening activities was assessed (from 0 to >14 h/week). Intensity level of all activities, expressed in metabolic equivalent tasks (METs), was defined according to the classification of Ainsworth et al. (2000). Because of the wide age range of this study population, age-specific MET value cut points (US Department of Health and Human Services, 1996) were used to calculate 2 different intensity indexes. *Moderate leisure time physical activity* was computed by summing the number of hours per week spent in activities of the following intensity: aged 18-39: $4.8 \leq \text{METs} \leq 7.1$; aged 40-64: $4.5 \leq \text{METs} \leq 5.9$; aged 65-75: $3.6 \leq \text{METs} \leq 4.7$. Activities of a higher intensity were included in the *vigorous leisure time physical activity* index, i.e. aged 18-39: METs ≥ 7.2 ; aged 40-64: METs ≥ 6.0 ; aged 65-75: METs ≥ 4.8 (US Department of Health and Human Services, 1996). Consequently, with these indices the association between cMSy and moderate and vigorous leisure time physical activity could be analyzed separately, since vigorous activity entails additional health benefits in comparison with moderate activity (US Department of Health and Human Services, 1996). By summation of moderate and vigorous leisure time physical activity, *total leisure time physical activity* was computed, thus including activities of at least moderate intensity, as proposed in the current physical activity recommendations (US Department of Health and Human Services, 1996).

Confounding variables. Several confounding variables were included in analyses, more specifically age (years), height (cm), education level (low, high), smoking status (current, former, never), and dietary intake (total energy (kcal), saturated fat (%), sugars (%), fibre (g/1000kcal), alcohol (%)). Education level was assessed using the FPACQ (Matton et al., in

press). Data were reduced from 13 to 2 levels, more specifically secondary school or lower and university or college. Smoking status was determined by means of the WHO Monica Smoking Questionnaire (World Health Organization, 1997). To assess dietary intake, subjects completed a validated 3 day diet record (Deriemaeker et al, 2006). Diet records were analysed using Becel Nutrition software (Unilever Co., Rotterdam, the Netherlands).

Statistical methods

All analyses were carried out using the SPSS 12.0 statistical software package (SPSS, Inc., Chicago, IL). The metabolic syndrome risk factors were logarithmically transformed (\log_{10}), owing to their positively skewed distribution, as shown by the Shapiro-Wilk test for normality. Differences between sexes were analyzed by means of independent samples t-tests and Pearson χ^2 -tests. All further analyses were carried out in both genders separately.

Separate multiple linear regression models were used to assess the association for the predictor variables sedentary behaviour and total leisure time physical activity with cMSy. Model A contained sedentary behaviour or total leisure time physical activity and was adjusted for all confounding variables, more specifically age, height, education level, smoking status and dietary intake. Model B was additionally adjusted for the other predictor variable. In addition, the interaction effect of sedentary behaviour and total leisure time physical activity with cMSy was verified, adjusted for the same confounding variables. Using these models, the independent association of both predictor variables with cMSy and their interaction on cMSy was tested.

To examine the association of moderate leisure time physical activity with cMSy, participants who reported vigorous leisure time physical activity (men: 57.4%, women: 41.3%) were excluded to minimize the potential confounding effect of vigorous activity. Subjects reporting moderate leisure time physical activity (men: 63.0%, women: 55.9%) were excluded in analyzing the association of vigorous leisure time physical activity with cMSy. Consequently, analyses for moderate leisure time physical activity were executed in 238 men and 254 women, and analyses for vigorous leisure time physical activity included 207 men and 191 women. Again, 2 multiple linear regression models were used, more specifically Model A containing moderate leisure time physical activity or vigorous leisure time physical activity and adjusted for all confounding variables, and Model B additionally adjusted for sedentary behaviour.

In assessing the association of sedentary behaviour and total leisure time physical activity with the individual metabolic syndrome risk factors, 2 models were applied. Model A

contained both sedentary behaviour and total leisure time physical activity and was adjusted for all confounding variables. Additional adjustment for waist circumference was made in Model B, to analyze the extent to which obesity mediates this relationship.

Sedentary behaviour and physical activity were entered as continuous variables in all analyses. Standardized β -coefficients are provided, which express the number of standard deviations the outcome (cMSy or metabolic syndrome risk factors) changes as a result of 1 standard deviation change in the predictor (sedentary behaviour or leisure time physical activity). Minimal level of statistical significance was set at $P < 0.05$.

Results

Descriptive statistics of subjects are shown in Table 1.

Table 1. Descriptive characteristics of male and female participants

	Men (<i>N</i> = 559)	Women (<i>N</i> = 433)	<i>P</i>
Age (years)	46.8 ± 11.3	45.8 ± 10.7	0.186
BMI (kg·m ⁻²)	25.5 ± 2.9	24.1 ± 3.7	<0.001
Waist circumference (cm)	89.2 ± 8.8	77.4 ± 9.0	<0.001
Triglycerides (mmol·l ⁻¹)	1.30 ± 0.82	1.03 ± 0.47	<0.001
HDL cholesterol (mmol·l ⁻¹)	1.43 ± 0.32	1.75 ± 0.39	<0.001
Systolic blood pressure (mm Hg)	129.3 ± 12.4	122.6 ± 14.0	<0.001
Diastolic blood pressure (mm Hg)	80.4 ± 6.7	76.4 ± 8.0	<0.001
Glucose (mmol·l ⁻¹)	5.17 ± 0.49	4.92 ± 0.48	<0.001
Sedentary behaviour (h/week)	14.8 ± 8.1	13.2 ± 7.9	<0.01
Total leisure time physical activity (h/week)	4.5 ± 5.0	2.4 ± 2.9	<0.001
Moderate leisure time physical activity (h/week)	2.3 ± 3.8	1.6 ± 2.5	<0.01
Vigorous leisure time physical activity (h/week)	2.2 ± 3.4	0.8 ± 1.6	<0.001
Education level			
Low (%)	47.6	42.3	0.095
High (%)	52.4	57.7	
Smoking status			
Current (%)	15.9	13.2	<0.001
Former (%)	27.0	15.0	
Never (%)	57.1	71.8	
Dietary intake			
Total energy (kcal)	2571.7 ± 689.1	1978.2 ± 519.3	<0.001
Saturated fat (%)	13.0 ± 3.3	13.4 ± 3.2	0.153
Sugars (%)	10.5 ± 5.6	10.3 ± 5.3	0.570
Fibre (%)	8.1 ± 2.5	8.8 ± 2.7	<0.001
Alcohol (%)	4.5 ± 4.7	3.2 ± 4.1	<0.001

Data are means ± SD (independent samples *t*-test) or proportions (Pearson Chi²-test).

Waist circumference, triglycerides, glucose, systolic and diastolic blood pressure were higher in men, whereas HDL cholesterol was higher in women. Men also reported more sedentary behaviour, total, moderate and vigorous leisure time physical activity.

Associations of sedentary behaviour and leisure time physical activity with cMSy

As shown in Table 2, sedentary behaviour was positively associated with cMSy in men ($P < 0.05$) and women ($P < 0.01$) after adjustment for age, height, education level, smoking status and dietary intake (Model A). Additional adjustment for total leisure time physical activity did not attenuate these associations in men ($P < 0.05$), nor women ($P < 0.01$) (Model B). An inverse relationship, adjusted for all confounding variables, was found for total leisure time physical activity in both genders (Model A), which remained equally strong (men: $P < 0.001$; women: $P < 0.01$) after additional adjustment for sedentary behaviour (Model B).

Furthermore, in subjects not participating in any vigorous activity, a negative association of moderate leisure time physical activity with cMSy was found in women ($P < 0.05$). In men, this association was marginally significant ($P = 0.051$). For those participants not engaged in any moderate activity, vigorous leisure time physical activity was negatively associated with cMSy (men: $P < 0.01$; women: $P < 0.05$) (Model A). Further correction for sedentary behaviour did not substantially change these associations (moderate leisure time physical activity: women: $P < 0.05$, men: $P = 0.081$; vigorous leisure time physical activity: men: $P < 0.01$, women: $P < 0.05$) (Model B).

Table 2. Associations of sedentary behaviour (h/week) and leisure time physical activity (h/week) with a continuous metabolic syndrome risk score in Flemish adults

	Sedentary behaviour		Total leisure time physical activity		Moderate leisure time physical activity		Vigorous leisure time physical activity	
	Men	Women	Men	Women	Men	Women	Men	Women
Model A ¹	0.100 ³	0.148 ⁴	-0.191 ⁵	-0.133 ⁴	-0.139	-0.156 ³	-0.208 ⁴	-0.171 ³
Model B ²	0.086 ³	0.143 ⁴	-0.185 ⁵	-0.128 ⁴	-0.124	-0.147 ³	-0.211 ⁴	-0.159 ³

Data are standardized β coefficients.

¹Models A are adjusted for age, height, education level, smoking status and dietary intake (total energy, saturated fat, sugars, fibre, alcohol).

²Models B are adjusted for all covariates plus total leisure time physical activity/sedentary behaviour.

³ $P < 0.05$; ⁴ $P < 0.01$; ⁵ $P < 0.001$.

A model including sedentary behaviour, total leisure time physical activity, an interaction term (sedentary behaviour x total leisure time physical activity) and all

confounding variables, revealed no interaction of sedentary behaviour and total leisure time physical activity on cMSy in men ($P = 0.694$), nor women ($P = 0.457$).

Associations of sedentary behaviour and total leisure time physical activity with each of the metabolic syndrome risk factors

Table 3 shows the regression results for the individual metabolic syndrome risk factors. A higher level of sedentary behaviour was associated with more central obesity and less HDL cholesterol ($P < 0.05$) in men, and with a higher waist circumference, systolic and diastolic blood pressure ($P < 0.05$) in women (Model A). Additional correction for waist circumference attenuated the association with HDL cholesterol in men and systolic and diastolic blood pressure in women to a nonsignificant level ($P > 0.05$) (Model B).

For total leisure time physical activity, an inverse association was found with waist circumference in men ($P < 0.001$) and women ($P < 0.05$). Furthermore, a higher level of total leisure time physical activity was associated with a healthier blood lipid profile in men ($P < 0.001$), and a lower diastolic blood pressure in women ($P < 0.01$) (Model A). Waist circumference only partially mediated the associations with triglycerides and HDL cholesterol in men ($P < 0.001$) and diastolic blood pressure in women ($P < 0.05$), since they remained significant (Model B).

Table 3. Associations of sedentary behaviour (h/week) and total leisure time physical activity (h/week) with metabolic syndrome risk factors in Flemish adults

Metabolic syndrome risk factor		Sedentary behaviour		Total leisure time physical activity	
		Men	Women	Men	Women
Waist circumference	Model A ¹	0.093 ³	0.103 ³	-0.149 ³	-0.120 ³
Triglycerides	Model A ¹	0.030	0.071	-0.161 ⁵	-0.034
	Model B ²	-0.006	0.040	-0.108 ⁴	0.002
HDL cholesterol	Model A ¹	-0.093 ³	-0.091	0.178 ⁵	0.067
	Model B ²	-0.061	-0.062	0.129 ⁴	0.034
Systolic blood pressure	Model A ¹	0.018	0.114 ³	0.039	-0.078
	Model B ²	-0.003	0.085	0.071	-0.044
Diastolic blood pressure	Model A ¹	0.002	0.106 ³	-0.037	-0.144 ⁴
	Model B ²	-0.021	0.072	-0.003	-0.104 ³
Glucose	Model A ¹	0.032	0.067	-0.066	-0.059
	Model B ²	0.022	0.048	-0.051	-0.036

Data are standardized β coefficients.

¹Models A are adjusted for age, height, education level, smoking status, dietary intake (total energy, saturated fat, sugars, fibre, alcohol) and total leisure time physical activity/sedentary behaviour.

²Models B are adjusted for all covariates plus waist circumference.

³ $P < 0.05$; ⁴ $P < 0.01$; ⁵ $P < 0.001$.

Discussion

This study investigated the combined association of television watching or playing computer games, as a parameter of sedentary behaviour, and leisure time physical activity with a validated continuous metabolic syndrome risk score (Wijndaele et al, 2006). After adjustment for confounding factors, sedentary behaviour was associated with a higher metabolic syndrome risk, independently of total leisure time physical activity, in both genders. Furthermore, being active in leisure time was related to a lower metabolic syndrome risk in men and women, independently of sedentary behaviour. These results support the importance of being moderately to vigorously active in relation with metabolic syndrome risk (Bertrais et al, 2005; Dunstan et al, 2005). Moreover, both men and women could benefit from spending less time watching television, and possibly other types of sedentary behaviour, irrespective of their physical activity level. These additive effects might include major opportunities in order to reduce metabolic syndrome risk and related disorders. However, further longitudinal studies or intervention studies are needed to confirm these additive effects. Earlier studies simultaneously examining these relationships (Dunstan et al, 2005; Ford et al, 2005), which all used a cross-sectional design, could not reveal a significant association of sedentary behaviour with the metabolic syndrome, independently of all confounders and total leisure time physical activity in men. However, Dunstan et al. (2005) did reveal independent associations for sedentary behaviour and total leisure time physical activity in women. Differences in results with the present study may partially be explained by the use of a binary definition of the metabolic syndrome in earlier studies, through which statistical power was reduced. In addition, Dunstan et al. (2005) did not include domestic activities, of which exclusion might distort (sex-specific) associations of leisure time physical activity with cMSy.

After extensive adjustment and exclusion of subjects reporting vigorous activity, the metabolic syndrome risk score was negatively related to activities of moderate intensity in women, independently of sedentary behaviour. Furthermore, men and women participating in vigorous intensity activities only, showed a lower metabolic syndrome risk, independently of their time being sedentary. Similar results were found by Bertrais et al. (2005), Dunstan et al. (2005) however did not find significant associations for moderate or vigorous leisure time physical activity in men.

Since watching television or playing computer games is associated with a higher metabolic syndrome risk independently of leisure time physical activity, the effect of

sedentary behaviour cannot be explained by the hypothesis that time spent in sedentary behaviour displaces time spent in moderate to vigorous leisure time physical activity. An alternative hypothesis suggests that high exposure to high-calory food advertisements stimulates people eating unhealthy foods while watching television and even increases overall amount of food consumed a day (Foster et al, 2006). However, the present study shows an association of sedentary behaviour which is independent of dietary intake. Part of the physiological basis to explain the independent risk of sedentary behaviour for metabolic disorders including poor lipid metabolism, might have been found in a high sensitivity of skeletal muscle lipoprotein lipase to be suppressed by muscle inactivity, a process that does not seem to occur in even low-intensity activities such as walking (Bey & Hamilton, 2003; Zderic & Hamilton, 2006).

Sedentary behaviour was associated with unhealthier profiles for waist circumference and HDL cholesterol in men and waist circumference and blood pressure in women, independently of total leisure time physical activity. Since obesity predicts the development of low HDL cholesterol, hypertriglyceridemia, hypertension and type 2 diabetes (Han et al, 2002), additional adjustment for waist circumference was made. Both the association with HDL cholesterol in men and blood pressure in women was mediated by waist circumference, which may suggest a central role of obesity in the pathway between sedentary behaviour and these individual metabolic syndrome risk factors.

This is the first study to examine the combined association of sedentary behaviour and leisure time physical activity with a continuous metabolic syndrome risk score. Although the use of cMSy implies population-specific results, it is more appropriate than using categorical definitions of the metabolic syndrome for epidemiological analyses (Kahn et al, 2005; Ragland, 1992; Wijndaele et al, 2006). Additional strengths of this study are the gender-specific analyses, covering a wide age range. Furthermore, extensive adjustment was made for confounding variables, including dietary intake. Finally, leisure time physical activity was assessed in different domains, including household-related activities.

However, some limitations of this study should be addressed. First of all, because of the cross-sectional design, causality of relationships cannot be determined. However, the exclusion of subjects with a history/evidence of CVD and diabetes reduced the confounding influence of health status on time spent in sedentary behaviour and leisure time physical activity. Secondly, data on sedentary behaviour and leisure time physical activity are reported instead of objectively measured, through which (gender differences in) report imprecision might have influenced the results. Future longitudinal studies, applying objective physical

(in)activity measures are needed to confirm a cause and effect relationship between sedentary behaviour, leisure time physical activity and cMSy.

In conclusion, the present study indicates that high amounts of sedentary behaviour are associated with a higher metabolic syndrome risk in both genders, whereas being moderately to vigorously active is related with a lower risk. Moreover, these associations are independent, which may indicate that both behaviours show additional effects. Furthermore, similar independent relationships exist with several individual metabolic syndrome risk factors. Although cross-sectional, the present results support inclusion of efforts to decrease television watching and playing computer games in prevention strategies for metabolic syndrome risk, besides encouragement to increase moderate to vigorous leisure time physical activity, since both behavioural changes may show additional effects in adult men and women.

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CHAPTER 2.2.3.

**MUSCULAR STRENGTH, AEROBIC FITNESS AND
METABOLIC SYNDROME RISK IN FLEMISH ADULTS**

**K Wijndaele, N Duvigneaud, L Matton, W Duquet, M Thomis,
G Beunen, J Lefevre, RM Philippaerts**

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Abstract

Purpose: To investigate the association of muscular strength and aerobic fitness with a continuous metabolic syndrome risk score in male and female adults.

Methods: This cross-sectional study included 1019 (571 men) Flemish adults, aged 18 to 75. Muscular strength was evaluated by measuring isometric knee extension and flexion peak torque, using a Biodex System Pro 3 dynamometer. Aerobic fitness was quantified as $\dot{V}O_{2\text{ peak}}$, determined during a maximal cycle ergometer exercise test. Both strength and aerobic fitness were scaled for differences in fat free mass, using allometric analyses. A validated metabolic syndrome risk score, based on waist circumference, triglycerides, blood pressure, fasting plasma glucose and HDL cholesterol, was used. The metabolic syndrome risk score, strength and aerobic fitness were analyzed as continuous variables using multiple linear regression.

Results: Metabolic syndrome risk was inversely associated with strength, independently of aerobic fitness, and after adjustment for age, height, education level, smoking status and dietary intake in women ($\beta = -0.172$, $P < 0.001$). In men however, adjustment for aerobic fitness attenuated the inverse association between strength and metabolic syndrome risk ($\beta = -0.044$, $P > 0.05$). Independently of strength, aerobic fitness was inversely associated with metabolic syndrome risk (men: $\beta = -0.309$, $P < 0.001$; women: $\beta = -0.208$, $P < 0.001$). Furthermore, independent associations were found for strength and aerobic fitness with several individual metabolic syndrome risk factors in women, of which most were only partially mediated by central and general adiposity indicators.

Conclusion: Although cross-sectional, the present results support inclusion of strength training in physical activity recommendations, besides aerobic exercise, in women, since both types of activity might show additional effects in reducing metabolic syndrome risk.

Key Words: continuous risk score, adult, aerobic capacity, resistance exercise, obesity

Introduction

The metabolic syndrome, representing the constellation of metabolic abnormalities including central obesity, dyslipidaemia, hypertension, insulin resistance and glucose intolerance, has become one of the major global public-health challenges. The syndrome has a high worldwide prevalence, after a severe increase during the past 2 decades (9). In addition, it predicts the development of type 2 diabetes (18), cardiovascular disease (CVD) and all-cause mortality (19) in nondiabetic individuals. Consequently, there is an urgent need for strategies to prevent an emerging global epidemic of the metabolic syndrome.

The first-line therapy for treatment of the metabolic syndrome is lifestyle modification, including an increase in physical activity (9). Previous cross-sectional studies suggest an inverse association between aerobic fitness, and several risk factors associated with the metabolic syndrome (21, 28). Furthermore, a high level of aerobic fitness in adolescence is protective for the development of diabetes, hypertension, hypercholesterolemia (5) and obesity (10) in adulthood. In addition, aerobic fitness is a strong and independent predictor of metabolic syndrome incidence (5, 20). Therefore, aerobic exercise, resulting in higher levels of aerobic fitness, might play an important role in the primary and secondary prevention of the metabolic syndrome and the associated chronic diseases.

Resistance training has also become part of physical activity recommendations for preventing chronic diseases in adults (2). Some intervention studies suggest beneficial effects of resistance training on whole body insulin action (1), body composition and central obesity (2), blood pressure (6), triglycerides and HDL cholesterol blood levels (12). Consequently, biological pathways might exist to explain and support protective effects of resistance training and muscular strength on the development and treatment of the metabolic syndrome. Nevertheless, until now few studies have examined the association between muscular strength and the metabolic syndrome.

Jurca et al. (15) examined this association in adult men using a cross-sectional design. They found that muscular strength was inversely associated with prevalence of the metabolic syndrome, independently of aerobic fitness and several confounding variables. Further longitudinal analyses in adult men yielded rather comparable results (14). Muscular strength was inversely associated with incidence of the metabolic syndrome after extensive adjustment for confounders. This association was marginally nonsignificant after additional adjustment for aerobic fitness. These findings might be indicative for a protective effect of

strength in the development of the metabolic syndrome, that is additional to the benign effect of aerobic fitness in men. Until now, no studies have investigated the independent and combined association of muscular strength and aerobic fitness with metabolic syndrome risk in women.

Studies examining the association between muscular strength, aerobic fitness and the metabolic syndrome often use a binary definition of the syndrome (5, 20, 14, 15). However, increasing evidence supports the use of a continuous metabolic syndrome risk score in epidemiological analyses, instead of a binary definition (16): a) dichotomizing continuous outcome variables reduces statistical power to detect associations (25); b) CVD risk is a progressive function of several metabolic syndrome risk factors, eliminating the need to dichotomize these risk factors using cut points (16); c) CVD and diabetes risk increase progressively with an increasing number of metabolic syndrome risk factors (17), eliminating the need to dichotomize the presence of the syndrome, e.g. in case of 3 or more present risk factors (16).

Aerobic fitness and muscular strength are both inversely associated with central and general obesity (2, 10). Furthermore, obesity predicts the development of several individual metabolic syndrome risk factors and of type 2 diabetes (13). Therefore, the association of aerobic fitness and muscular strength with the individual metabolic syndrome risk factors may (partially) be mediated by obesity indicators.

The aim of the present study was twofold. First, the independent and combined association of muscular strength and aerobic fitness with a validated continuous metabolic syndrome risk score (30) was examined in both male and female adults aged 18 to 75. Second, the relationship of muscular strength and aerobic fitness with the individual continuous metabolic syndrome risk factors, and the extent to which obesity mediates this relationship was determined.

Methods

Subjects

Data for this study were collected by the Flemish Policy Research Centre Sport, Physical Activity and Health (SPA) between October 2002 and April 2004, for a cross-sectional survey on the relationship between physical activity, physical fitness and several health

parameters. For this purpose, the National Institute of Statistics randomly selected a community sample of 18- to 75-year-old men and women in the Flemish part of Belgium. Subjects were asked to visit the SPAH examination center to provide a fasting blood sample, to go through a medical examination, anthropometric measurements, physical fitness tests, and some questionnaires. Participants with complete data for all metabolic syndrome risk factors, muscular strength, aerobic fitness, and for all confounding variables used in the analyses, were included in the current study. Participants were excluded in case of a history or evidence of cardiovascular disease (abnormal heart auscultation or rest electrocardiogram; sudden death of father or brother before the age of 45, or of mother or sister before the age of 55; systolic blood pressure > 150 mm Hg or diastolic blood pressure > 100 mm Hg; use of antihypertensive or lipid-lowering drugs), diabetes mellitus, or in case they did not achieve at least 85% of the age-predicted maximal heart rate during a maximal cycle ergometer test. Consequently, results are based on data of 571 men and 448 nonpregnant women, aged 18 to 75. The study was approved by the Ghent University Ethics Committee. Prior to participation, the purpose and procedures of the study were explained and subjects gave their written informed consent.

Data collection

Blood samples. Subjects were asked to fast from 11:00 P.M. the evening before visiting the laboratory. A sample of fasting blood was taken from an antecubital vein of subjects in supine position. All samples were stored at 4°C before they were transferred to the lab at 11:00 A.M. They were analyzed before 5:00 P.M. the same day. Triglyceride was analyzed using the lipase/glycerol kinase/glycerol phosphate oxidase enzymatic method. HDL cholesterol was analyzed using the homogeneous polyanion/cholesterol esterase/oxidase enzymatic method. Glucose was analyzed using the hexokinase method. Triglycerides, HDL cholesterol and glucose were measured on an Olympus AU5400 analyzer (Olympus Diagnostica, Hamburg, Germany). The coefficients of variation between days were 1.4% (at 2.07 mmol/l) for triglycerides, 3.9% (at 2.04 mmol/l) for HDL cholesterol and 2.0% (at 16.71 mmol/l) for glucose.

Blood pressure. A physician measured blood pressure at the left arm of subjects who had been seated for 10 minutes, using a NOVA Presameter mercury sphygmomanometer (Riester, Jungingen, Germany). Systolic and diastolic blood pressure were measured 3 times with 1-minute intervals, and the mean of these 3 measurements was used in analyses.

Anthropometric measurements. Anthropometric measurements were taken by trained staff with participants barefoot and in underwear. Waist circumference was measured using a metal tape (Rosscraft, Surrey, BC, Canada) to the nearest 0.1 cm, at the narrowest level between lowest ribs and iliac crests, in standing position. Body weight was recorded with a digital scale (Seca 841, Seca GmbH, Hamburg, Germany) to the nearest 0.1 kg. Height was measured using a stadiometer (Holtain, Crymych, UK) to the nearest 0.1 cm. Body mass index (BMI) was calculated as [body weight (kg)/(height (m))²]. Percentage body fat (%BF) was evaluated by means of bioelectrical impedance analysis (BIA) on the right side of the body with a tetrapolar BIA analyser (Bodystat 1500, Bodystat Ltd, Isle of Man, UK), in subjects who had been in supine position for 5 minutes with the arms and legs in abduction. Fat free mass (FFM, kg) was calculated based on the %BF measured by means of BIA.

Continuous metabolic syndrome risk score (cMSy). A validated cMSy was calculated as described in more detail by Wijndaele et al. (30). In short, cMSy is based on the 5 risk factors in the National Cholesterol Education Program definition (11), namely waist circumference, triglycerides, HDL cholesterol, blood pressure (systolic and diastolic) and fasting plasma glucose. Calculation involved 3 successive steps: a) all variables were normalized (log₁₀) because of their non-normal distribution. A blood pressure index was computed by averaging systolic and diastolic blood pressure; b) principal component analysis with varimax rotation was applied to the individual risk factors in order to derive components that represent large fractions of the metabolic syndrome variance, and consequently to give each risk factor the most appropriate weight in calculating cMSy. This analysis revealed 2 principal components with eigenvalue ≥ 1.0 in both genders; c) cMSy was computed by summing both individual principal component scores, each weighted for the relative contribution of principal component 1 and 2 in the explained variance. The resulting cMSy was 0 ± 1.42 in men and 0 ± 1.41 in women. This score showed high validity in both genders (30).

Muscular Strength. A calibrated Biodex System Pro 3 dynamometer (Biodex Medical Systems, Inc., Shirley, NY) was used to measure isometric strength of the knee. Isometric measurements using this device are found to be reliable and valid (8). Strength of the right knee was measured in a standardized manner. In some subjects with a history of injury in the right knee however, strength of the left knee was evaluated. Subjects were seated upright on the Biodex chair with the axis of the dynamometer corresponding to the knee joint axis. Once positioned, the shoulder, waist, thigh and lower right leg, 2 cm above malleolus medialis, were secured with straps. Participants were asked to cross arms in front of the thorax during

each exercise, in order to avoid compensatory movements. To measure peak torque of isometric extension at an angle of 60° flexion (0° is straight leg), subjects were instructed to extend their lower leg as hard as possible, regardless its fixed position. For peak torque of isometric flexion at an angle of 60° flexion, they were asked to maximally flex their knee. During exercise, both subject and instructor were able to see the strength curve on the monitor. Subjects were given verbal encouragement in generating the highest possible plateau. Both the extension and flexion exercise were performed twice, and for each exercise the highest torque measurement of both trials during plateau was included in analyses. Peak torque values were corrected for the effects of gravity.

Total knee strength was defined as the sum of peak torque of isometric extension and flexion at 60°, divided by FFM, since Pearson correlation coefficients between FFM and absolute total knee strength were higher compared to Pearson correlation coefficients found between body weight and absolute total knee strength in men ($r = 0.56$, $P < 0.001$ for FFM; $r = 0.45$, $P < 0.001$ for body weight) and women ($r = 0.54$, $P < 0.001$ for FFM; $r = 0.26$, $P < 0.001$ for body weight). To optimally scale absolute total knee strength for differences in fat free mass, allometric analyses were performed using log-linear adjustment models, to identify the most appropriate exponent for FFM in dividing absolute total knee strength by FFM (27). These analyses revealed an FFM exponent of $b = 1.014 \pm 0.061$ in men and of $b = 0.975 \pm 0.069$ in women. Consequently, muscular strength was quantified as (absolute total knee strength)·FFM^{-1.014} (N·m·kg_{FFM}^{-1.014}) in men and as (absolute total knee strength)·FFM^{-0.975} (N·m·kg_{FFM}^{-0.975}) in women.

Aerobic fitness. Aerobic fitness was determined by means of a maximal exercise test on an electrically braked Lode Excalibur cycle ergometer (Lode, Groningen, the Netherlands). The standardized exercise protocol started with a workload of 20 W, which was increased stepwise by 20 W·min⁻¹. Participants were instructed to continuously cycle at approximately 70 revolutions per minute. They were verbally encouraged to reach a maximal level of exertion. Oxygen consumption was measured directly with breath-by-breath respiratory gas exchange analysis, using a Cortex Metalyser 3B analyzer (Cortex Biophysic GmbH, Leipzig, Germany), which generates highly reliable results (22). Heart rate was registered continuously with a Polar Smart Heart Rate Monitor Set (Polar Electro Oy, Kempele, Finland). Cardiac function during the test was monitored by means of a 12-channel electrocardiogram (Cardiolyzer Ultra, Cortex Biophysic GmbH, Leipzig, Germany). The exercise test was terminated when subjects were exhausted or when the physician stopped

the test for medical reasons. A high correlation was found between peak oxygen uptake ($\dot{V}O_{2\text{ peak}}$) and exercise duration (men: Pearson $r = 0.85$, $P < 0.001$; women: $r = 0.87$, $P < 0.001$).

For the current analyses, aerobic fitness was quantified as peak oxygen uptake divided by FFM, since Pearson correlation coefficients between FFM and absolute $\dot{V}O_{2\text{ peak}}$ were higher in comparison with those found between body weight and absolute $\dot{V}O_{2\text{ peak}}$ in both genders (men: $r = 0.39$, $P < 0.001$ for FFM; $r = 0.17$, $P < 0.001$ for body weight; women: $r = 0.50$, $P < 0.001$ for FFM; $r = 0.20$, $P < 0.001$ for body weight). Allometric analyses (27) revealed an FFM exponent of $b = 0.820 \pm 0.079$ in men and of $b = 0.973 \pm 0.072$ in women. Therefore, aerobic fitness was quantified as $\dot{V}O_{2\text{ peak}} \cdot \text{FFM}^{-0.820}$ ($\text{mL} \cdot \text{kg}_{\text{FFM}}^{-0.820} \cdot \text{min}^{-1}$) in men and as $\dot{V}O_{2\text{ peak}} \cdot \text{FFM}^{-0.973}$ ($\text{mL} \cdot \text{kg}_{\text{FFM}}^{-0.973} \cdot \text{min}^{-1}$) in women.

Confounding variables. Several confounding variables were included in analyses, more specifically age (years), height (cm), education level (low, high), smoking status (current, former, never) and dietary intake (total energy (kcal), saturated fat (%), sugars (%), fibre (g/1000kcal), alcohol (%)). Education level was assessed using the Flemish Physical Activity Computerized Questionnaire (24), and data were reduced from 13 to 2 levels, more specifically secondary school or lower and university or college. Smoking status was determined by means of the WHO Monica Smoking Questionnaire (29). To assess dietary intake, subjects completed a validated 3-day diet record (7). Diet records were analysed using BeceL Nutrition software (Unilever Co., Rotterdam, the Netherlands).

Statistical analyses

All analyses were carried out using the SPSS 12.0 statistical software package (SPSS, Inc., Chicago, IL). The metabolic syndrome risk factors were logarithmically transformed (\log_{10}), owing to their positively skewed distribution, as shown by the Shapiro-Wilk test for normality. Differences between sexes were analyzed by means of independent samples t-tests and Pearson Chi²-tests. All further analyses were carried out in both genders separately.

Separate multiple linear regression models were used to assess the association of the predictor variables muscular strength and aerobic fitness with cMSy. Model A contained muscular strength or aerobic fitness and was adjusted for all confounding variables, more specifically age, height, education level, smoking status and dietary intake. Model B was additionally adjusted for the other predictor variable to test the independent association of

both predictor variables with cMSy. Moreover, the interaction between muscular strength and aerobic fitness on cMSy, adjusted for the same confounding variables, was verified. To evaluate this interaction effect, muscular strength and aerobic fitness were mean centered and the product of both mean centered variables was computed for each subject. No further adjustment for adiposity was made in assessing the association between metabolic syndrome risk and muscular strength and aerobic fitness, since waist circumference is integral to the metabolic syndrome risk score.

In assessing the association of muscular strength and aerobic fitness with the individual metabolic syndrome risk factors, 2 models were applied. Model C contained both muscular strength and aerobic fitness and was adjusted for all confounding variables. Additional adjustment for obesity was made in Model D, to analyze the extent to which obesity mediates this relationship. Two measures of obesity were successively included in Model D, more specifically waist circumference for central adiposity, and body mass index for general adiposity.

Muscular strength and aerobic fitness were entered as continuous variables in all analyses. Standardized β -coefficients are provided, which express the number of standard deviations the outcome (cMSy or metabolic syndrome risk factors) changes as a result of 1 standard deviation change in the predictor (muscular strength or aerobic fitness). Since all of the standardized β values are measured in standard deviation units, they facilitate the comparison of the (relative) contribution of each predictor in the model. Minimal level of statistical significance was set at $P < 0.05$. A priori power analyses were conducted in order to create a strong study design. The analyses showed that an $N = 168$ and an $N = 156$ in males and females respectively was sufficient to power the study at 0.8 for a detectable β of 0.15 for muscular strength and aerobic fitness, given the 0.05 level of significance, which confirms the adequacy of the present sample size of males ($N = 571$) and females ($N = 448$).

Results

Descriptive statistics of subjects are shown in Table 1. Men showed higher BMI in comparison with women ($P < 0.001$). However, men also displayed higher FFM ($P < 0.001$). Furthermore, waist circumference, triglycerides, glucose, systolic and diastolic blood pressure were higher in men ($P < 0.001$), whereas HDL cholesterol was higher in women ($P < 0.001$). Finally, sex differences were found for muscular strength and aerobic fitness,

expressed in absolute terms, both being higher in men ($P < 0.001$). After scaling both variables for FFM, mean values for muscular strength and aerobic fitness in men were $4.50 \pm 0.77 \text{ N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-1.014}$ and $98.14 \pm 20.19 \text{ mL}\cdot\text{kg}_{\text{FFM}}^{-0.820}\cdot\text{min}^{-1}$, respectively. In women, scaled mean values were $4.84 \pm 0.88 \text{ N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-0.975}$ for muscular strength and $44.76 \pm 8.64 \text{ mL}\cdot\text{kg}_{\text{FFM}}^{-0.973}\cdot\text{min}^{-1}$ for aerobic fitness. No comparison between men and women was made for these scaled values, given the different FFM exponents between sexes for both variables.

Table 1. Descriptive characteristics of male and female participants.

	Men ($N = 571$)	Women ($N = 448$)	P
Age (years)	46.7 ± 11.2	45.8 ± 10.8	0.209
BMI ($\text{kg}\cdot\text{m}^{-2}$)	25.5 ± 2.9	24.1 ± 3.7	< 0.001
Fat free mass (kg)	62.2 ± 7.0	43.8 ± 5.2	< 0.001
Waist circumference (cm)	89.2 ± 8.8	77.3 ± 8.9	< 0.001
Triglycerides ($\text{mmol}\cdot\text{L}^{-1}$)	1.31 ± 0.82	1.03 ± 0.47	< 0.001
HDL cholesterol ($\text{mmol}\cdot\text{L}^{-1}$)	1.43 ± 0.31	1.75 ± 0.40	< 0.001
Systolic blood pressure (mmHg)	129.3 ± 12.4	122.6 ± 14.4	< 0.001
Diastolic blood pressure (mmHg)	80.4 ± 6.8	76.4 ± 8.1	< 0.001
Glucose ($\text{mmol}\cdot\text{L}^{-1}$)	5.16 ± 0.48	4.91 ± 0.48	< 0.001
Muscular strength (N·m)	296.7 ± 61.4	193.0 ± 41.9	< 0.001
Aerobic fitness ($\text{L}\cdot\text{min}^{-1}$)	2.9 ± 0.6	1.8 ± 0.4	< 0.001
Education level			
Low (%)	47.6	42.1	0.077
High (%)	52.4	57.9	
Smoking status			
Current (%)	15.8	12.9	< 0.001
Former (%)	27.1	15.4	
Never (%)	57.1	71.7	
Dietary intake			
Total energy (kcal)	2562.9 ± 691.0	1984.4 ± 519.3	< 0.001
Saturated fat (%)	13.0 ± 3.3	13.4 ± 3.2	0.088
Sugars (%)	10.4 ± 5.5	10.2 ± 5.3	0.606
Fibre (%)	8.2 ± 2.5	8.8 ± 2.7	< 0.001
Alcohol (%)	4.4 ± 4.7	3.2 ± 4.1	< 0.001

Data are means \pm SD (independent samples t-test) or proportions (Pearson Chi²-test).

Associations of muscular strength and aerobic fitness with cMSy

Table 2 presents the individual and combined association of muscular strength and aerobic fitness with cMSy. Muscular strength was negatively associated with cMSy in men ($P < 0.05$) and women ($P < 0.001$) after adjustment for age, height, education level, smoking status and dietary intake (Model A). Additional adjustment for aerobic fitness (Model B)

attenuated this association to a nonsignificant level ($P > 0.05$) in men. In women however, the association between strength and cMSy remained almost equally strong in Model B ($P < 0.001$). For aerobic fitness, an inverse relationship, adjusted for all confounding variables, was found with cMSy in both men and women ($P < 0.001$) (Model A). These associations remained similar ($P < 0.001$) after additional adjustment for muscular strength (Model B).

Table 2. Associations of muscular strength (men: $\text{N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-1.014}$; women: $\text{N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-0.975}$) and aerobic fitness (men: $\text{mL}\cdot\text{kg}_{\text{FFM}}^{-0.820}\cdot\text{min}^{-1}$; women: $\text{mL}\cdot\text{kg}_{\text{FFM}}^{-0.973}\cdot\text{min}^{-1}$) with a continuous metabolic syndrome risk score in Flemish adults.

	Muscular Strength		Aerobic Fitness	
	Men	Women	Men	Women
Model A†	-0.086*	-0.190***	-0.316***	-0.225***
Model B	-0.047	-0.168***	-0.308***	-0.203***

Data are standardized β coefficients.

† Models A are adjusted for age, height, education level, smoking status and dietary intake (total energy, saturated fat, sugars, fibre, alcohol); || Models B are adjusted for all covariates plus aerobic fitness/muscular strength.

* $P < 0.05$; *** $P < 0.001$.

A model including muscular strength, aerobic fitness, an interaction term (muscular strength x aerobic fitness) and all confounding variables, did not reveal an interaction of strength and aerobic fitness on metabolic syndrome risk in men ($P = 0.207$), nor in women ($P = 0.461$).

Associations of muscular strength and aerobic fitness with the metabolic syndrome risk factors

Table 3 shows the regression results for the individual continuous metabolic syndrome risk factors. Model C includes both muscular strength and aerobic fitness and is adjusted for all confounding variables. Model D is additionally adjusted for waist circumference. In men, no associations were found between muscular strength and any of the metabolic syndrome factors ($P > 0.05$). In women, strength was inversely associated with waist circumference, triglycerides ($P < 0.001$) and positively associated with HDL cholesterol ($P < 0.05$) (Model C). The association between strength and triglycerides in women was partially mediated by waist circumference but remained significant ($P < 0.01$). However, additional correction for waist circumference attenuated the association with HDL cholesterol to a nonsignificant level ($P > 0.05$) (Model D).

Additional correction in Model D for BMI, measuring general adiposity, instead of waist circumference, yielded very comparable results for muscular strength (triglycerides: $\beta =$

-0.137, $P < 0.01$; HDL cholesterol: $\beta = 0.064$, $P > 0.05$), indicating a comparable mediating effect of BMI and waist circumference on these relationships.

Furthermore, Table 3 shows that high aerobic fitness was associated with a healthier profile for central adiposity and blood lipids in men ($P < 0.001$) (Model C), which remained equally significant ($P < 0.001$) after additional correction for waist circumference (Model D). In women, high aerobic fitness was associated with a healthier profile for waist circumference ($P < 0.01$), HDL cholesterol ($P < 0.001$), systolic and diastolic blood pressure ($P < 0.01$) (Model C). Waist circumference only displayed a partially mediating effect on the association with HDL cholesterol since it remained significant ($P < 0.01$). However, a stronger mediating effect was found for the associations with systolic and diastolic blood pressure, which were attenuated to a marginally nonsignificant level ($P = 0.063$ and $P = 0.073$, respectively) (Model D).

Adjusting for BMI instead of waist circumference in Model D revealed similar results for aerobic fitness in men (triglycerides: $\beta = -0.185$, $P < 0.001$; HDL cholesterol: $\beta = 0.256$, $P < 0.001$) and women (HDL cholesterol: $\beta = 0.128$, $P < 0.05$; systolic blood pressure: $\beta = -0.072$, $P > 0.05$; diastolic blood pressure: $\beta = -0.074$, $P > 0.05$).

Table 3. Associations of muscular strength (men: $\text{N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-1.014}$; women: $\text{N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-0.975}$) and aerobic fitness (men: $\text{mL}\cdot\text{kg}_{\text{FFM}}^{-0.820}\cdot\text{min}^{-1}$; women: $\text{mL}\cdot\text{kg}_{\text{FFM}}^{-0.973}\cdot\text{min}^{-1}$) with metabolic syndrome components in Flemish adults.

		Muscular Strength		Aerobic Fitness	
		Men	Women	Men	Women
Waist circumference	Model C†	-0.055	-0.156***	-0.249***	-0.158**
Triglycerides	Model C†	-0.062	-0.173***	-0.254***	-0.059
	Model D	-0.042	-0.129**	-0.171***	-0.017
HDL cholesterol	Model C†	-0.009	0.099*	0.317***	0.171***
	Model D	-0.027	0.058	0.224***	0.132**
Systolic blood pressure	Model C†	-0.036	0.021	-0.037	-0.128**
	Model D	-0.024	0.067	0.014	-0.085
Diastolic blood pressure	Model C†	-0.044	-0.001	-0.003	-0.139**
	Model D	-0.030	0.054	0.055	-0.087
Glucose	Model C†	0.039	-0.062	-0.069	-0.095
	Model D	0.046	-0.033	-0.041	-0.067

Data are standardized β coefficients.

† Models C are adjusted for age, height, education level, smoking status, dietary intake (total energy, saturated fat, sugars, fibre, alcohol), and aerobic fitness/muscular strength; || Models D are adjusted for all covariates plus waist circumference.

* $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$.

Discussion

This study examined the combined association of muscular strength and aerobic fitness with metabolic syndrome risk and the independent metabolic syndrome risk factors in both male and female 18- to 75 year old adults. The main findings of this study are: 1) muscular strength and aerobic fitness are independently and inversely associated with metabolic syndrome risk in women after extensive adjustment for confounding factors. In men, the inverse association between strength and metabolic syndrome risk was smaller and not independent of aerobic fitness, for which an independent inverse association with metabolic syndrome risk was found; 2) muscular strength and aerobic fitness are independently associated with a better profile for several individual metabolic syndrome risk factors in women, after extensive adjustment for confounding variables. In men, no independent associations were found for muscular strength, however aerobic fitness was strongly and inversely associated with a better profile for central adiposity and for blood lipids; 3) most of the significant associations with the individual risk factors were only partially mediated by central and general adiposity indicators.

The inverse association between aerobic fitness and metabolic syndrome risk found in the present study is in line with the results of previous investigations (5, 15, 20). So far, only 2 studies investigated the combined association between strength, aerobic fitness and the metabolic syndrome, both in a male adult population. In a first cross-sectional study, Jurca et al. (15) found an inverse association between muscular strength and prevalence of the metabolic syndrome in men, independent of aerobic fitness and after adjustment for age and smoking. In further longitudinal analyses, they found a significant inverse association between strength and incidence of metabolic syndrome, which was marginally not significant when further adjusting for aerobic fitness (14). The present study did show an inverse association in men between strength and metabolic syndrome risk, adjusted for age, height, education level, smoking status and dietary intake. However, this association was attenuated ($P > 0.05$) after further adjustment for aerobic fitness.

Differences in results for men between studies may be attributed to several factors. First, in both previous studies (14, 15) muscular strength was scaled for differences in total body weight instead of FFM. FFM however is more strongly correlated with strength. Since fat mass (FM) is highly correlated with waist circumference ($r = 0.88$ for men and $r = 0.87$ for women in the present study, $P < 0.001$), and to a lesser extent also with several other metabolic syndrome risk factors (ranging from $r = -0.19$ for HDL cholesterol in men to $r =$

0.43 for systolic blood pressure in women of the present study, $P < 0.001$), dividing strength by total body weight (including FM and FFM) instead of FFM might (artificially) strengthen the inverse association found between metabolic syndrome and muscular strength. This hypothesis was confirmed by reconducting regression analyses in the present study including muscular strength scaled for total body weight instead of FFM. These analyses revealed stronger associations between strength and metabolic syndrome risk, which remained significant after further adjustment for aerobic fitness in both genders (data not shown). Second, results of the present study were more extensively adjusted for confounding variables in comparison with those of both previous studies (14, 15). Finally, differences between studies in defining the metabolic syndrome, in characteristics and size of the study samples and in measurement procedures for strength, and aerobic fitness might also partially explain differences in study results.

Aerobic fitness was more strongly associated with metabolic syndrome risk in comparison with muscular strength, and correction for aerobic fitness did attenuate the association between strength and metabolic syndrome risk in both genders. However, in women the inverse association between strength and metabolic syndrome risk remained significant, after correction for aerobic fitness. This may suggest a possible protective effect of strength in the development of metabolic syndrome risk, that is additional to the benign effect of aerobic fitness in women. This protective effect may be a function of muscular strength, or may be indicative for the benign effects of regular participation in resistance training, ameliorating both strength and metabolic homeostasis (14). Both hypotheses however support the promotion of resistance training in addition to aerobic fitness training as part of physical activity recommendations in lowering metabolic syndrome risk. Nonetheless, further longitudinal and intervention studies are needed to confirm these assumptions.

Biological pathways through which strength training might lower metabolic syndrome risk include improvements in triglycerides and HDL blood levels (12), blood pressure (6), central adiposity and body composition (2), and whole body insulin action and glucose uptake (1). Insulin resistance is described as a central risk factor in the pathophysiology of the metabolic syndrome (9). Resistance training might protect against insulin resistance by both an increase in muscle quantity and an increase in skeletal muscle insulin action and glucose uptake per unit muscle mass, indicating qualitative muscle adaptations (1). Pathways explaining the protective effects of endurance training closely resemble those suggested for resistance training (5). However, the independent associations of strength and aerobic fitness with metabolic syndrome risk and with several individual risk factors found in women,

suggest that both predictors may have unique benefits. Further research is needed to clearly identify mechanisms explaining these unique benefits.

Adiposity indicators only partially mediated most associations found between strength, aerobic fitness and the independent metabolic syndrome risk factors. Boulé et al. (3), examining the association between aerobic fitness and the individual risk factors, found similar results, except for the association with HDL cholesterol in women that disappeared after controlling for total and abdominal adiposity in their study. The present results may indicate that biological pathways other than obesity are also responsible for the associations found. However, since obesity indicators in the present study depend on anthropometric measurements rather than imaging techniques such as dual-energy x-ray absorptiometry or magnetic resonance imaging systems, these results should be interpreted with caution (26).

To our knowledge, this is the first study to report an inverse association between strength and metabolic syndrome risk in women, and to examine the combined relationship for muscular strength and aerobic fitness with metabolic syndrome risk in women. Furthermore, no previous studies examined the association of muscular strength with a continuous metabolic syndrome risk score. Although the use of cMSy implies population-specific results, it is more appropriate than using categorical definitions of the metabolic syndrome for epidemiological analyses (16, 25, 30). Additional strengths of this study include the objective measurement of both strength and aerobic fitness by means of standardized maximal test protocols using highly reliable measurement devices (8, 22). Furthermore, strength and aerobic fitness were corrected for differences in FFM by means of allometric scaling, the sample studied covered a wide age range, and extensive adjustment in regression analyses was made for confounding variables, including dietary intake. In previous epidemiological studies examining the association of aerobic fitness and muscular strength with the metabolic syndrome, adjustment for dietary intake was rare. However, diet may influence several metabolic syndrome risk factors, and men and women with higher aerobic fitness levels have been shown to have healthier diets than their lower fit counterparts (4).

Some limitations of this study should also be addressed. First of all, causality of relationships cannot be determined because of the cross-sectional design. However, the confounding influence of health status on level of aerobic fitness and muscular strength may have been partially eliminated by excluding subjects with a history/evidence of CVD and type 2 diabetes. Second, the present study sample may represent a more healthy group of adults, which may partially limit external validity of the results. A more heterogeneous sample, including more unhealthy individuals and therefore more extreme values for all

metabolic syndrome risk factors would probably yield stronger associations. Finally, muscular strength was measured by means of lower body strength only. However, a study comparing knee strength and hand grip strength in predicting mortality found similar risk estimates for both strength parameters (23). Future longitudinal studies in both genders are needed to investigate a cause and effect relationship between total body strength and cMSy, including aerobic fitness and all relevant confounding variables in analyses. Furthermore, more controlled experimental studies should be conducted to clearly identify the physiological mechanisms explaining these associations and differences found between men and women.

In conclusion, results of the present study show that muscular strength and aerobic fitness are independently and inversely associated with metabolic syndrome risk in women aged 18 to 75. This may indicate a protective effect of muscular strength on metabolic syndrome risk, that is additive to the benign effect of aerobic fitness. Furthermore, muscular strength and aerobic fitness were associated with a better profile of several individual metabolic syndrome risk factors in women. Most of these associations were only partially mediated by central and general adiposity indicators.

Although cross-sectional, the present results support the inclusion of strength training in physical activity recommendations, besides aerobic exercise, since both types of physical activity may provide unique benefits in the primary and secondary prevention of metabolic syndrome risk. Moreover, resistance training might be a more attractive type of exercise for overweight and obese individuals, who are at higher risk for developing high metabolic syndrome risk and may be aversive from endurance training (1).

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CHAPTER 2.2.4.

A PATH MODEL OF HEALTH-RELATED LIFESTYLE, PHYSICAL FITNESS, DISTRESS AND METABOLIC SYNDROME RISK FACTORS IN ADULTS

**K Wijndaele, M Thomis, L Matton, N Duvigneaud, W Duquet,
G Beunen, J Lefevre, HH Maes, RM Philippaerts**

Psychosomatic Medicine, submitted
The contribution of the first two authors in the present study was equal.

Abstract

Objective: To study a model causally linking psychological distress, health-related lifestyle and physical fitness to a metabolic syndrome (MSy) risk factor structure in adults.

Methods: This cross-sectional study included 965 Flemish adults (549 men), aged 18 to 75, without cardiovascular disease and diabetes. Latent variable structural equation modeling was applied to determine factor structure of distress (stress, depression, anxiety, sleeping problems), health-related lifestyle (physical activity, sedentary behaviour, alcohol intake, fat intake), physical fitness (aerobic fitness, muscular strength) and MSy (waist, triglycerides, HDL cholesterol, blood pressure, glucose) and to estimate contribution of distress, health-related lifestyle and physical fitness in explaining MSy variance.

Results: Factor loadings of indicators on their respective latent variables were significant ($p < .05$), except for health-related lifestyle, on which only physical activity loaded significantly in both genders. Two-group analysis revealed that factor structure of latent variables was sex-specific, whereas causal paths between latent variables could be equated between sexes. In total, 39.6% of MSy variance could be accounted for by distress, health-related lifestyle and physical fitness. Physical fitness contributed the largest part (32.7 %), which was decomposed in a direct physical fitness effect (22.8 %), and an indirect health-related lifestyle effect (9.9 %). Direct contributions of health-related lifestyle (0.8%) and distress (0.068%) were negligible, whereas contribution of all possible covariance pathways contributed another 6.0%.

Conclusions: Although cross-sectional, these results support a protective effect of higher physical fitness and physical activity against the MSy, in which the latter effect is primarily mediated by resulting higher levels of physical fitness.

Key Words: stress; aerobic fitness; insulin resistance syndrome; structural equation modeling; adult; physical activity.

Acronyms: $-2\ln L$ = -2 times log-likelihood; CVD = cardiovascular disease; df = degrees of freedom; MSy = metabolic syndrome; FFM = fat free mass; FPACQ = Flemish Physical Activity Computerized Questionnaire; HDLc = high density lipoprotein cholesterol; HRLS = health-related lifestyle; HRT = hormone replacement therapy; LVSEM = latent variable structural equation modeling; METs = metabolic equivalent tasks; SPAH = Sport Physical Activity and Health; $\dot{V}O_{2\text{ peak}}$ = peak oxygen uptake; WHO = World Health Organization.

Introduction

The MSy has become an important public health concern, mainly for 2 reasons. First, the syndrome shows high prevalence rates worldwide (1). Since MSy risk increases with increasing body mass index (2), the current obesity epidemic will fuel a further prevalence rise in several populations (3). Second, these rising prevalence rates become even more alarming, considering the negative health outcomes of the MSy. It is an important predictor of CVD (4), type 2 diabetes (5), cardiovascular and all-cause mortality (6) in non-diabetic individuals. Therefore, a thorough understanding of its modifiable determinants is currently an important challenge.

Reviewing literature, 3 modifiable determinants that each have been associated with the MSy include psychological distress, HRLS, and physical fitness. Evidence exists that chronic *stress* increases risk for the MSy (7). Furthermore, stress is an important underlying condition leading to anxiety and depression (8), and is associated with sleeping problems (9). Depressive symptoms increase risk for the MSy (10). Sleeping problems are positively associated with obesity (11), diabetes and impaired glucose tolerance (12, 13). Anxiety is positively associated with CVD (14). Concerning *lifestyle*, evidence is accumulating for an inverse association between physical activity level and incidence of the MSy (15, 16). A second lifestyle component associated with the MSy is dietary intake. Besides associations with other nutrients, a positive association exists for dietary total fat with insulin resistance (17) and with the MSy (18). Controversial results are reported on the association between alcohol consumption and the MSy (19, 20). However, in a recent study (21), lifetime drinking intensity was positively associated with MSy prevalence. Finally, time spent in sedentary behaviour, including television watching, shows a positive association with MSy prevalence (22, 23). Two *physical fitness* components associated with the MSy include aerobic fitness and muscular strength. Several prospective studies provide evidence for a predictive role of low aerobic fitness in the development of the MSy (24-26). Finally, muscular strength is associated with MSy prevalence (27, 28).

These findings provide crucial information for preventive strategies. However, psychological distress, HRLS and physical fitness also show interactions. Being physically active for example might result in decreased levels of stress (29), anxiety (30), depression (31) and sleeping problems (32), which may in turn reduce MSy risk. Conversely, stressed individuals tend to adopt adverse lifestyle behaviours, including increased smoking and alcohol intake, poor diet and low exercise level. According to Cohen et al. (8), these poor

health practices may provide a possible pathway explaining adverse physical health outcomes associated with stress. Physical activity might also be a possible pathway between depressive symptoms and metabolic risk (10). Finally, a healthier lifestyle positively influences health-related fitness (33). Moreover, previous research provides evidence for a mediating role of aerobic fitness in the association between physical activity and the MSy (34). Other factors influencing all 3 determinants, the MSy and possibly their interrelationships include gender, age and education level (35-43).

Based on the above stated psychobehavioral theories and other findings, we selected measurements for the latent factors psychological distress, HRLS and physical fitness, and designed a model causally linking these 3 factors to the MSy, as this may provide further information on each of these 3 determinants' relative contribution in explaining MSy variance and their interactions in doing so. To our knowledge, no previous studies have addressed this research question. One study by Vitaliano et al. (44) examined a model including distress, poor health habits and the MSy, besides other latent variables as potential causal factors for coronary heart disease, in a relatively small sample of individuals ≥ 60 years of age, who were primary caregiver for a spouse with Alzheimers's disease. However, unlike distress and poor health habits, physical fitness was not included in the model as a potential causal factor for the MSy. Furthermore, because of the small age range and specific living conditions of these participants, external validity of results may be limited. Therefore, the aim of the present study was to examine the model shown in Figure 1 using LVSEM in a population of male and female adults aged 18 to 75, free from CVD or diabetes.

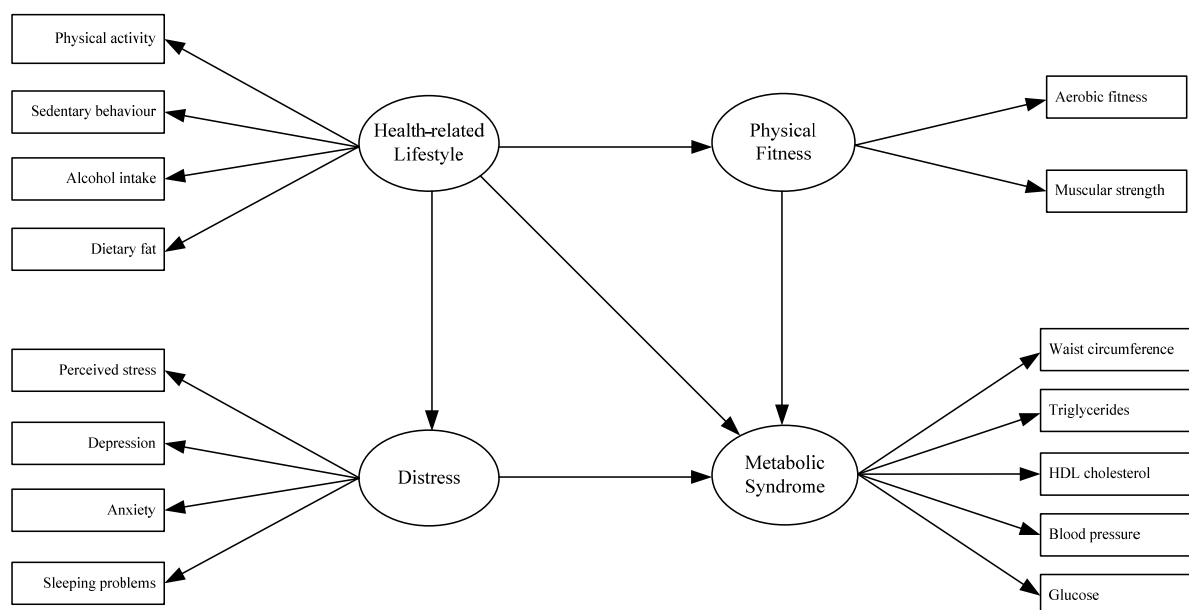


Figure 1. Path model causally linking psychological distress, health-related lifestyle and physical fitness with a metabolic syndrome factor.

More specifically, we investigated 1) what percentage of MSy variance is explained by psychological distress, HRLS and/or physical fitness collectively; 2) whether these relationships are gender-specific; and 3) whether psychological distress, HRLS and/or physical fitness differ in their relative contribution in explaining MSy variance.

Methods

Subjects

Data for this study were collected by the Flemish Policy Research Centre ‘Sport, Physical Activity and Health’ (SPAHE) between October 2002 and April 2004, as part of a cross-sectional survey on the relationship between physical activity, physical fitness and several health parameters. For this purpose, the National Institute of Statistics randomly selected a community sample of 18- to 75-year-old adults in the Flemish part of Belgium. Subjects were asked to visit the SPAHE examination center to provide a fasting blood sample, to go through a medical examination, anthropometric measurements, physical fitness tests, and some questionnaires. Participants with complete data for variables used in analyses, were included in the current study. Participants were excluded in case of history or evidence of CVD (abnormal heart auscultation or rest electrocardiogram; sudden death of father/brother <45, or mother/sister <55 years of age; systolic blood pressure >150 mmHg or diastolic blood pressure >100 mmHg; use of antihypertensive or lipid-lowering drugs), diabetes mellitus, or in case they did not achieve at least 85% of the age-predicted maximal heart rate during a maximal cycle ergometer test. Consequently, results are based on data of 549 men and 416 nonpregnant women. MSy prevalence according to the International Diabetes Federation (45) was 71 (12.9 %) in males and 35 (8.4 %) in females. The study was approved by the Katholieke Universiteit Leuven Medical Ethics Committee. Prior to participation, study purpose and procedures were explained and subjects gave written informed consent.

Data collection

MSy risk factors. The 5 risk factors in the International Diabetes Federation MSy definition (45) were included in analyses, more specifically waist circumference, triglycerides, HDLc, blood pressure (systolic and diastolic) and fasting plasma glucose. A detailed description of measurement procedures of these 5 risk factors is provided elsewhere (28).

Measures of physical fitness. The measurement protocols of muscular strength and aerobic fitness are described in more detail by Wijndaele et al. (28). In short, *muscular strength* was evaluated by measuring isometric knee extension and flexion peak torque, using a Biodex System Pro 3 dynamometer, producing reliable and valid measurements (46). *Aerobic fitness* was quantified as $\dot{V}O_{2\text{ peak}}$, determined during a maximal cycle ergometer exercise test. Oxygen consumption was measured directly using a Cortex Metalyser 3B, generating highly reliable results (47). Both strength and aerobic fitness were scaled for differences in FFM, using allometric analyses (48).

Measures of HRLS. To assess dietary intake, subjects completed a validated 3-day diet record (49). Diet records were analysed using Becel Nutrition software (Unilever Co., Rotterdam, the Netherlands). Both *alcohol* and *fat intake* were expressed as percentage of total energy intake (%). Sedentary behaviour and leisure time physical activity were assessed using the validated Flemish Physical Activity Computerized Questionnaire (FPACQ) (50). Participants were asked to indicate time spent watching television/video or using computer during a usual weekday and weekendday (from 0 to ≥ 6 h/day) to calculate an average week score for *sedentary behaviour* (h/week). Levels of leisure time physical activity were evaluated in several domains. Sports participation was assessed by asking subjects to select their 3 most important sports out of a list of 196 sports. For each of these sports, frequency (from 1 week/year to >7 times/week) and duration (from <1 to >20 h/week) were reported. Active transportation in leisure time was determined by asking time spent in walking and cycling as transportation in leisure time, during a usual weekday and weekendday (from 0 to >60 min/day). Furthermore, time spent in housekeeping and gardening was assessed (from 0 to >14 h/week). Intensity level of all activities, expressed in METs, was defined according to the classification of Ainsworth et al. (51). Because of the wide age range of this study population, age-specific METs cut points were used to include activities of at least moderate intensity, as proposed in the current physical activity recommendations (52). More specifically, *leisure time physical activity* (h/week) was computed by summing time spent in activities of the following intensity: aged 18-39: METs ≥ 4.8 ; aged 40-64: METs ≥ 4.5 ; aged 65-75: METs ≥ 3.6 .

Measures of distress. Level of *perceived stress* was assessed by means of the Perceived Stress Scale (53). The Symptom Checklist (54) was used to measure level of *anxiety*, *depression* and *sleeping problems*. A computerized version of both scales was used. Reliability, internal consistency and equivalence of the computerized and traditional paper-

and-pencil version were evaluated in 2 separate samples of 18- to 75-year-old Flemish adults. A more detailed description of both scales and results on reliability, internal consistency and equivalence are provided elsewhere (55, 56).

Confounding variables. Three confounding variables were included in analyses, more specifically *age* (years), education level (low, high) and smoking status (current, former, never). *Education level* was assessed using the FPACQ (50), and data were reduced from 13 to 2 levels, more specifically secondary school or lower and university or college. *Smoking status* was determined by means of the WHO Monica Smoking Questionnaire (57).

Statistical analyses

Descriptive statistics and data preparation were performed using SPSS12.0 (SPSS, Inc., Chicago, IL). Shapiro-Wilk tests revealed a skewed distribution for some variables. To improve normality, inverse (depression, anxiety, sleeping problems), logarithmic (waist circumference, triglycerides, HDLc, blood pressure, glucose, physical activity, alcohol intake) or square root (perceived stress, sedentary behaviour) transformations were applied. Differences between sexes were analyzed by means of independent samples t-tests and Pearson Chi²-tests.

Gender-specific multiple linear regressions were applied to each observed variable to adjust for the confounding effects of age, education level and smoking status. Variance explained by age, education level and smoking status collectively ranged from $R^2 = .01$ (sleeping problems, anxiety and depression) to $.19$ (aerobic fitness) in men and from $R^2 = .01$ (anxiety and depression) to $.20$ (blood pressure) in women. Smoking status may theoretically be considered as part of the HRLS factor. However, its categorical character precluded its inclusion as an observed variable loading on the HRLS factor. Standardized residuals, resulting from multiple linear regressions were used in further statistical analyses. Pearson correlation coefficients were calculated to investigate bivariate associations between standardized residuals. Subsequently, standardized residuals scores were entered as raw data into the structural equation models, using maximum likelihood analysis of raw continuous data in Mx GUI (58). A two-group (males/females) analysis of the model shown in Figure 1 was tested first with all parameters modeled to be gender-specific. A first submodel tested whether all parameter estimates in males and females could be equated, a second whether causal paths between latent factors showed gender heterogeneity. Alternative models were compared by Chi²-ratio tests with Chi² equal to the difference in $-2\ln L$ of both models and df as the difference in degrees of freedom between both models. Furthermore, a model with a

reversed causal path between distress and HRLS was applied, to examine which of both directions of causation was associated with the best goodness of fit. Finally, path-tracing rules were applied to determine percentage of variance of the MSy factor explained by all 3 determinants and their covariation. Minimal level of statistical significance was set at $p < .05$.

Results

Descriptive statistics

Descriptive statistics of subjects are shown in Table 1.

Table 1. Descriptive characteristics of participants.

	Men (<i>N</i> = 549)	Women (<i>N</i> = 416)	<i>P</i>
Age (years)	46.76 ± 11.24	45.69 ± 10.58	.134
Waist circumference (cm)	89.21 ± 8.84	77.25 ± 8.89	<.001
Triglycerides (mmol·L ⁻¹)	1.31 ± 0.82	1.03 ± 0.47	<.001
HDLc (mmol·L ⁻¹)	1.43 ± 0.32	1.74 ± 0.39	<.001
Systolic blood pressure (mmHg)	129.12 ± 12.25	122.26 ± 13.80	<.001
Diastolic blood pressure (mmHg)	80.41 ± 6.69	76.32 ± 7.89	<.001
Glucose (mmol·L ⁻¹)	5.17 ± 0.49	4.91 ± 0.48	<.001
Perceived stress ^a	2.05 ± 0.60	2.19 ± 0.59	<.001
Depression ^a	1.26 ± 0.38	1.33 ± 0.40	<.001
Anxiety ^a	1.22 ± 0.33	1.27 ± 0.33	<.01
Sleeping problems ^a	1.64 ± 0.75	1.68 ± 0.83	.952
Physical activity (h/week)	4.49 ± 4.98	2.35 ± 2.83	<.001
Sedentary behaviour (h/week)	14.86 ± 8.07	13.12 ± 7.74	<.001
Alcohol intake (%)	4.40 ± 4.64	3.19 ± 4.15	<.001
Dietary fat intake (%)	34.28 ± 7.28	34.99 ± 7.43	.137
Aerobic fitness (L·min ⁻¹)	2.90 ± 0.65	1.77 ± 0.39	<.001
Muscular strength (N·m)	296.32 ± 60.97	193.52 ± 42.41	<.001
Education level			
Low (%)	48.1	42.1	.068
High (%)	51.9	57.9	
Smoking status			
Current (%)	16.2	13.7	<.001
Former (%)	27.1	14.7	
Never (%)	56.7	71.6	

Data are means ± SD (independent samples t-test) or proportions (Pearson Chi²-test).

^aRated on a 5-point Likert scale.

After scaling both variables for FFM, mean values for muscular strength and aerobic fitness in men were $4.77 \pm 0.82 \text{ N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-1.014}$ and $98.09 \pm 20.29 \text{ mL}\cdot\text{kg}_{\text{FFM}}^{-0.820}\cdot\text{min}^{-1}$, respectively. In women, scaled mean values were $4.40 \pm 0.80 \text{ N}\cdot\text{m}\cdot\text{kg}_{\text{FFM}}^{-0.975}$ for muscular strength and $40.30 \pm 7.83 \text{ mL}\cdot\text{kg}_{\text{FFM}}^{-0.973}\cdot\text{min}^{-1}$ for aerobic fitness. No comparison between men and women was made for these scaled values, given the different FFM exponents between sexes for both variables.

Bivariate correlations

Table 2 shows bivariate correlations between standardized residuals of observed variables within each domain and across domains. The negative correlation of perceived stress with depression, anxiety and sleeping problems can be explained by different transformation methods used to normalize these variables (square root for perceived stress and inverse for depression, anxiety and sleeping problems).

LVSEM

Two-group analysis was applied to the model shown in Figure 1, to examine whether parameter estimates in males and females could be equated. As we used raw data as input, goodness of fit of a saturated model including estimates for means and all variances/covariances of both male and female data is used as a baseline fit-value ($-2\ln L = 38491.48$, $df = 14340$). In a first step, all parameters (causal paths between latent variables, factor loadings and residual variances) were set equal between men and women, to test significance for gender-specific parameters estimates. Fit of the model in which all parameters were set free ($-2\ln L = 38675.72$, $df = 14377$, $\text{Chi}^2_{37} = 184.23$, $p < .001$) was compared to the fit of a model fixing all parameters between both sexes ($-2\ln L = 38753.25$, $df = 14430$, $\text{Chi}^2_{90} = 261.76$, $p < .001$). This comparison revealed a significant loss in goodness of fit for the model in which all parameters were fixed ($\Delta-2\ln L (\text{Chi}^2) = 77.53$, $\Delta df = 53$, $p < .05$). In a second step, only causal paths between latent variables were fixed between both genders. No significant loss in goodness of fit was found, comparing this model with the model in which all parameters were set free ($\Delta-2\ln L (\text{Chi}^2) = 7.78$, $\Delta df = 4$, $p > .05$). Therefore, a model for males and females, including gender-specific factor loadings on the latent variables and residual variances, with equal causal pathways between latent variables was retained, as shown in Figure 2.

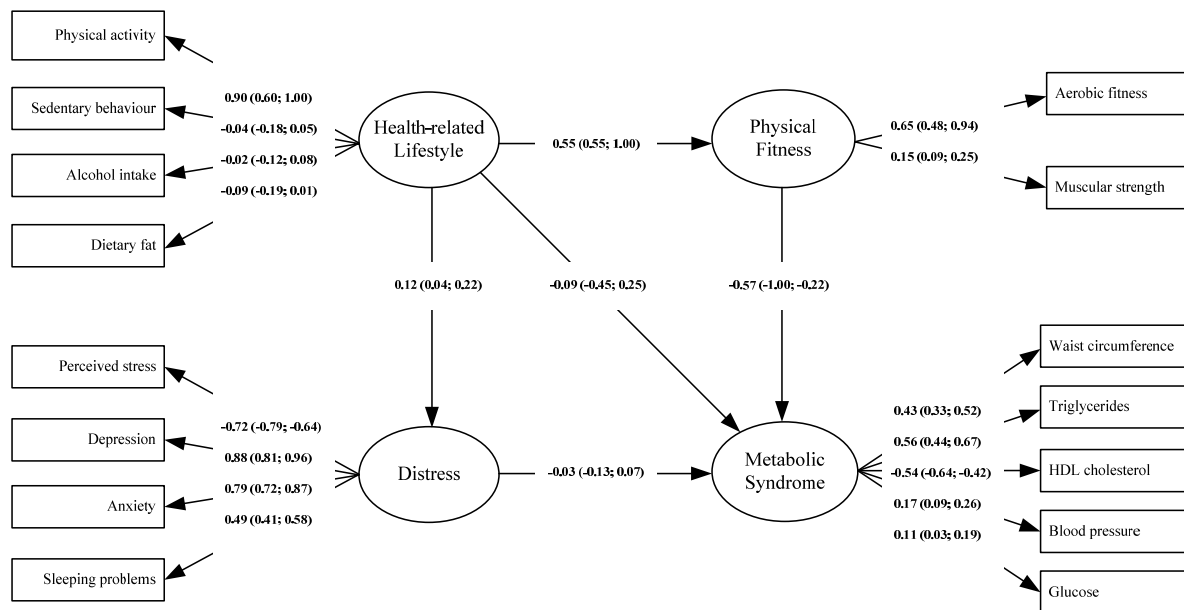
Table 2. Correlations between standardized residuals of the observed variables included in the model

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.
1. Waist circumference		.30**	-.33**	.38**	.22**	.04	.03	.01	.06	-.12*	.08	-.09	.04	-.21**	-.18**
2. Triglycerides	.36**		-.18**	.14**	.06	-.03	.01	.10*	.07	-.01	.06	.01	-.11*	-.08	-.18**
3. HDLc	-.30**	-.48**		-.06	-.10*	-.02	-.01	-.04	-.05	.07	-.07	.18**	-.08	.19**	.14**
4. Blood pressure	.23**	.15**	-.08		.19**	.01	-.01	-.05	.03	-.10*	.16**	-.04	-.06	.15**	-.04
5. Glucose	.13**	.09*	-.04	.15**		.04	-.04	-.03	.01	-.06	.06	-.01	.08	-.11*	-.07
6. Perceived stress	.04	.06	-.03	-.01	.02		-.67**	-.61**	-.39**	-.05	.03	-.01	-.06	.06	-.09
7. Depression	-.03	-.10*	.04	-.02	-.02	-.66**		.72**	.48**	-.01	-.09	.02	.09	-.05	.09
8. Anxiety	-.01	-.07	.02	-.10*	-.02	-.58**	.72**		.45**	.03	-.04	-.01	.06	-.03	.07
9. Sleeping problems	-.04	-.08	-.02	-.02	-.04	-.35**	.44**	.43**		.01	-.06	-.02	.01	.01	.05
10. Physical activity	-.21**	-.20**	.20**	.03	-.03	-.11*	.13**	.11*	.06		-.03	.04	-.04	.27**	.13**
11. Sedentary behaviour	.07	.01	-.13**	.02	.01	.02	-.06	-.02	-.04	-.03		-.06	.05	-.10*	-.02
12. Alcohol intake	.07	.10*	.21**	.09*	.04	-.01	.01	-.03	-.07	-.03	-.12**		-.14**	.04	.12*
13. Dietary fat intake	.06	.04	-.03	-.11*	.01	.01	.02	.06	.01	-.08	-.05	-.11**		-.05	.02
14. Aerobic fitness	-.25**	-.24**	.32**	-.07	-.04	.03	.02	-.02	.02	.33**	-.14**	.01	-.05		.13**
15. Muscular strength	-.09*	-.11*	.05	-.03	.03	-.03	-.01	-.04	.02	.03	-.04	.02	-.02	.14**	

Correlations for female participants are above and for male participants below diagonal.

* $p < .05$, ** $p < .01$

A.



B.

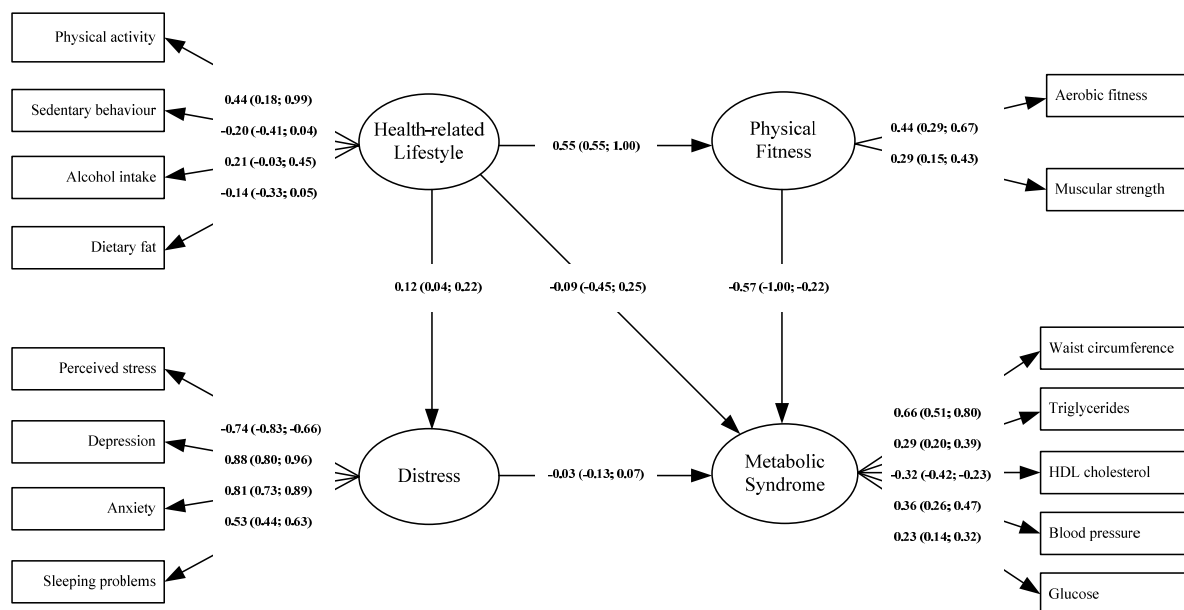


Figure 2. Path models resulting from latent variable structural equation modeling in adult men (A) and women (B).

Measurement model

The measurement model is the model relating observed variables to latent variables or factors, and standardized path coefficients can be interpreted as factor loadings in confirmatory factor analysis. Within the MSy factor, waist circumference loaded substantially higher compared to the other 4 MSy indicators in women, while rather equal loadings were

found for waist circumference, triglycerides and HDLc in men (see Figure 2). HDLc loaded negatively on the MSy factor in both genders. Concerning the distress construct, similar factor loadings were found in both genders (positive loadings for depression, anxiety and sleeping problems should be interpreted keeping in mind they were inversely transformed). More divergent results were found for the HRLS factor. In men, this was predominantly a physical activity factor, as no significant loadings were found for sedentary behaviour, alcohol intake and dietary fat. More equal loadings were found in women, however physical activity was still the only variable significantly loading. In the physical fitness construct, a substantially higher loading was found for aerobic fitness in men, whereas in women loadings between aerobic fitness and muscular strength were more comparable. Residual variances of measured variables were highest for alcohol intake (.99), sedentary behaviour (.99) and fat intake (.98) and lowest for physical activity level (.18) in men. In women, residual variances were highest for fat intake (.97), sedentary behaviour (.95) and alcohol intake (.94), and lowest for depression (.21).

Structural model

The structural model is the regression part of latent variable structural equation modeling. As shown in Figure 2, 3 causal paths between latent variables were significant. The negative causal path from physical fitness to the MSy was the strongest ($\beta = -.57$, CI = -1.00, -.22). This path was preceded by a positive path from HRLS to physical fitness ($\beta = .55$, CI = .55, 1.00). Finally, a marginally significant positive path was found between HRLS and distress ($\beta = .12$, CI = .04, .22). No significant paths were found from HRLS or distress to the MSy.

Reversing direction of causality between distress and HRLS resulted in an equal overall fit. Causal pathways remained almost unchanged (distress to HRLS: .13; distress to MSy: -.03; HRLS to MSy: -.09; physical fitness to MSy: -.57; HRLS to physical fitness: .55).

Applying path-tracing rules, explained variance in the MSy factor can be derived by adding squared path coefficients of direct causal paths to the MSy factor and multiplication of path coefficients of all possible covariation paths. For the resulting model, 39.6% of variation in the MSy factor could be accounted for by the 3 latent factors. Fitness contributed the largest part with 32.7 %, which could be decomposed in a direct physical fitness effect of 22.8 %, and an indirect HRLS effect of 9.9 %. Direct contributions of HRLS (0.8%) and distress (0.068%) were negligible, whereas contribution of all possible covariance pathways contributed another 6.0%.

Discussion

In this study, a model hypothesizing causal pathways between psychological distress, HRLS, physical fitness and a MSy factor was studied using LVSEM in an adult population of males and females, free from CVD and diabetes. Physical fitness was the only latent variable showing a significant direct causal path to the MSy factor, as opposed to HRLS and distress, for which no significant direct paths to the MSy factor were found. In previous research, Vitaliano et al. (44) hypothesized a model including distress, poor health habits and the MSy besides other latent variables (not including physical fitness) as potential causal factors for coronary heart disease. They examined this model using latent variable partial least squares estimation in a small sample of men and women (2 groups, depending on use of HRT), who were primary caregiver for a spouse with Alzheimer's disease ($N = 152$; ≥ 60 years of age). In cross-sectional analyses, the path from distress to the MSy was significant in men and women not using HRT, whereas it was not significant in women using HRT. The path from poor health habits to the MSy was significant in women but not in men. Longitudinal analyses (measurement of distress and health habits was performed 15 to 18 months prior to (new) measurements of MSy risk factors) in men only revealed a significant path between poor health habits and the MSy, but not between distress and the MSy. Differences between study results may be due to several factors. First, in the study by Vitaliano et al. (44), the causal path structure between distress, health habits and the MSy is part of a larger model, through which path coefficients are influenced by antecedent pathways. Furthermore, in the present study, physical fitness showed to be an important mediating variable for HRLS, and was not included in the study of Vitaliano et al. (44). This may explain differences found for the direct path between HRLS and the MSy. Third, study populations differed substantially. We adjusted for the confounding effect of age in the present study, whereas the caregiver sample in the study by Vitaliano et al. (44) shows a specific age structure (≥ 60 years of age). Furthermore, it is highly probable that a population of caregivers shows higher levels of perceived stress and resulting depression, anxiety and sleeping problems, compared to the population based sample in the present study, possibly explaining different results found for the direct path between distress and the MSy. Fourth, although the concept of the distress, HRLS and MSy latent variables was similar, variables used to construct the underlying factors as well as factor loadings on these latent variables were not completely equal. Finally, differences in statistical analysis methods and adjustment for confounding factors (e.g. smoking behaviour) may also account for different study results.

Physical fitness contributed the largest part in explaining MSy variance, compared to HRLS and distress. This is in accordance with results of previous studies showing a strong negative association between aerobic fitness -loading relatively strong on the physical fitness factor especially in men- and MSy, which is independent of other possible determinants, including physical activity (24-26). Furthermore, some studies found evidence for a negative association between strength and the MSy (27, 28). However, part of the large difference between physical fitness, HRLS and distress in their contribution to explain MSy variance may be due to differences in measurement techniques. Measurement error for aerobic fitness and muscular strength was probably smaller, partly as a consequence of the fact that physical fitness indicators were measured objectively, as opposed to distress and HRLS indicators, which were measured by self-report questionnaires.

HRLS mainly contributed in explaining MSy in an indirect way, via physical fitness. Taking into account the large loadings of physical activity and aerobic fitness on the respective latent variables, this result is consistent with previous research showing a mediating role of aerobic fitness in the association between physical activity level and the MSy (34).

Several reasons may account for the rather low overall fit of the model and small causal path estimates between latent variables found in the present study. First of all, most studies applying factor analysis to the different risk factors of the MSy, report at least 2 and usually 3 to 4 factors to underlie overall correlation between risk factors (59). However, as in the present study the MSy was represented by 1 factor only (accounting for part of MSy variance), power to find strong associations with the MSy construct may have been reduced. Similarly, to promote interpretability of the model, distress, HRLS and physical fitness were also represented by 1 single factor. However, even without taking into consideration the conservative representation of all latent factors in the model, measured variables underlying the latent factors for HRLS, fitness and distress only correlate very moderately (ranging between .01 and .32) with most of the individual measured variables of the MSy factor. Second, the HRLS factor, although conceptually derived from 2 MSy-related energy intake measures (overall fat/alcohol) and 2 energy expenditure measures (physical activity/inactivity) was found to be a factor predominantly explained by physical activity, especially in men. Similarly, low associations between health behaviour indicators were found by Vitaliano et al. (44). Whether the high loading on the causal path from physical fitness to MSy risk factors represents linked biological (genetic) pathways or other environmental pathways could not be studied in this sample of unrelated individuals. Also

HRLS, as well as distress probably have an underlying biological (genetic) component besides environmental sources of interindividual variation.

Reversing direction of causal paths between HRLS and distress, did not reveal different results concerning model fit or path estimates. This may be due to the fact that path estimates for causal paths from HRLS and distress to the MSy were both low. Furthermore, although a marginally significant path estimate was found, correlation structure between the indicators of HRLS and distress did not provide strong indication for a strong causal path between both latent variables in either direction.

To our knowledge, this is the first study to include 3 possibly important modifiable determinants of the MSy in 1 model, which enabled to compare relative contributions of all 3 factors in explaining MSy variance. A second major strength of this study was the use of a large sample of adult males and females covering a wide age range. Although only subjects free from CVD and diabetes were included, the use of this sample may provide higher external validity. Furthermore, adjustment was made for confounding variables, including smoking behaviour as opposed to previous research (44), a variable associated with the MSy and other variables included in analyses (60-64).

Some limitations of this study should also be addressed. First of all, although causal paths are estimated using LVSEM, causality of relationships per se cannot be determined because of the cross-sectional design. MSy or its comorbidities may negatively influence level of physical fitness, distress or HRLS, suggesting causality in the opposite direction. However, the possible confounding influence of MSy comorbidities on physical fitness, distress or HRLS is at least partially eliminated by excluding subjects with history/evidence of CVD and type 2 diabetes. Second, the present study sample represents a more healthy group of adults. Although this may render higher external validity of study results, the use of a more heterogeneous sample, showing a higher variability for characteristics examined, would probably yield stronger associations. Third, although only applicable to a smaller part of the study population, the possible modifying effect of HRT on the associations studied was not accounted for.

In conclusion, results of the present study indicate that almost 40% of MSy variance can be accounted for by physical fitness, HRLS and psychological distress in men and women, aged 18 to 75 without CVD or diabetes. In both genders, physical fitness is the most important contributor, with HRLS (primarily defined by physical activity) showing a smaller contribution, which is mediated by physical fitness. No significant contribution was found for psychological distress. Although cross-sectional, these results may support that a higher level

of physical fitness and physical activity may be protective against the MSy, and that the effect of physical activity is primarily mediated by a resulting higher level of physical fitness. Future longitudinal studies, including all 3 determinants in 1 model are needed to confirm these causal relationships.

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3.

**GENERAL DISCUSSION AND
CONCLUSIONS**

This thesis describes four studies aiming to investigate the association between physical activity, physical fitness, stress-related mental health and metabolic syndrome risk, in a population of Flemish male and female adults, aged 18 to 75. These association studies were preceded by two methodological studies, in which the reliability of five computerized mental health questionnaires and the validity of a continuous metabolic syndrome risk score were examined. The third and final section of the thesis starts with an overview and discussion of the main findings of these different studies. Subsequently, limitations and directions for further research are discussed. Finally, practical implications of the results found in these studies will be formulated.

1. Main findings

1.1. Methodological studies on mental health and metabolic syndrome risk

The purpose of the first study (chapter 2.1.1.) was to investigate the reliability, equivalence and respondent preference of a computerized version of the General Health Questionnaire (GHQ-12),¹¹ Symptom Checklist (SCL-90-R),⁶ Medical Outcomes Study Social Support Survey (MOSSSS),²⁹ Perceived Stress Scale (PSS)⁴ and Utrecht Coping List (UCL),²⁸ in comparison with the original version, in two general population samples aged 18 to 75. These samples showed a well-balanced composition according to age, gender and education level. This study demonstrated that for most scales, internal consistency and test-retest reliability of the computerized versions were acceptable to excellent. Equivalence between the computerized and the original paper-and-pencil versions was fair to excellent for the total group. The percentage of subjects preferring the computerized version (39.2%) was higher than the percentage preferring the paper-and-pencil version (21.6%), and 39.2% had no preference. Preference for the computerized administration mode was related to lower age and higher level of computer experience.

In the second study (chapter 2.1.2.), a continuous metabolic syndrome risk score was validated in a population of adults aged 18 to 75, who were free from cardiovascular disease and diabetes. This research question was based on findings that cardiovascular and diabetes risk increase progressively 1) with higher levels of several continuous metabolic syndrome risk factors, and 2) with a higher number of metabolic syndrome risk factors.^{15, 27} In the

existing definitions of the metabolic syndrome,^{2, 8, 32, 36} a dichotomization has been applied on two levels, resulting in a reduced predictive and statistical power. Furthermore, most risk factors are weighted equally in these definitions. Therefore, to address both limitations, a metabolic syndrome risk score was developed, applying principal component analysis (varimax rotation) on the continuous metabolic syndrome risk factors, used in the NCEP⁸ and IDF definitions.³² In both genders, two principal components with eigenvalue ≥ 1 were retained, explaining a similar percentage of metabolic syndrome variance (33% and 28% in men, 33% and 27% in women). The continuous risk score was calculated by summing both individual principal component scores, each weighted for the relative contribution of principal component 1 and 2 in the explained variance. Summing both principal component scores provides a better representation of the "construct" of the metabolic syndrome since more metabolic syndrome variance is explained. Only taking into consideration the first factor for example would be physiologically incorrect, since e.g. variables loading low on the first factor, but high on the second factor would be insufficiently represented. In a study published very recently,¹³ a similar procedure was used to calculate a continuous metabolic syndrome risk score. In this study, principal component analysis was applied to four metabolic syndrome variables, more specifically waist circumference, triglycerides, systolic blood pressure and glucose, and one combined score for men and women was calculated. This analysis revealed a first principal component with eigenvalue of 2.0 and a second one with eigenvalue 0.8. Variance explained by the first principal component was 50%. Therefore, in this study the continuous metabolic syndrome risk score consisted of the first unrotated principal component. These results deviate with the results of chapter 2.1.2. In our results, both for men and women, the first two principal components showed an eigenvalue > 1.0 , indicating that they both explain an important percentage of total metabolic syndrome variance in this sample of adult men and women (percentage of explained variance before rotation was respectively 38% and 23% in men and respectively 39% and 20% in women). Most studies applying factor analysis to metabolic syndrome risk factors report at least 2 and usually 3 to 4 factors to underlie the overall correlation between risk factors,¹⁵ which is in accordance with our study results. As indicated above, because in our sample both first principal components explained an important percentage of metabolic syndrome variance, individual principal component scores of the first and second principal components were summed. Varimax rotation was applied so that the resulting components were orthogonal, and therefore independent. Therefore, the continuous risk score calculated in chapter 2.1.2. explains more metabolic syndrome variance (men: 61%; women: 60%) compared to the risk

score calculated by Hillier et al.¹³ Finally, our risk score was validated against the IDF definition of the metabolic syndrome,³² showing a higher risk score in subjects with IDF-defined metabolic syndrome, which also increased progressively with an increasing number of risk factors, in both genders.

To conclude, the newly developed continuous metabolic syndrome risk score yields some important methodological advantages compared to the existing binary definitions of the metabolic syndrome,^{2, 8, 32, 36} and acknowledges the urgent call of the American Diabetes Association and the European Association for the Study of Diabetes for the development of a multivariate metabolic syndrome score system using continuous variables.¹⁵ First, by using a continuous score, a modest change in only one variable will result in only a modest change in the overall metabolic syndrome risk score. On the contrary, in the existing definitions applying dichotomization at two levels,^{2, 8, 32, 36} a lot of information is lost. Therefore, this continuous approach yields substantially higher predictive power for adverse outcomes (such as cardiovascular disease or diabetes) or statistical power to find associations with other variables (such as physical activity, physical fitness, stress). Second, in the continuous metabolic syndrome risk score, a more realistic weight is given to each risk component, which is not the case in the existing binary definitions.^{2, 8, 32, 36}

The conclusion can be made that the computerized versions of the GHQ-12, SCL-90-R, MOSSSS, PSS and UCL are reliable psychological health instruments that can be used as a practical alternative for the traditional versions in a general population of adults. Furthermore, although a binary metabolic syndrome definition may remain useful for clinical practice, the continuous metabolic syndrome risk score calculated in adults without cardiovascular disease and diabetes is a valid and more appropriate alternative for epidemiological analyses.

1.2. Association studies on stress-related mental health, metabolic syndrome risk, physical activity and physical fitness

The main objective of the third study (chapter 2.2.1.) was to examine the association between stress (-related mental health problems) and leisure time physical activity in a population-based sample of 18- to 75-year-old Flemish adults, applying cluster analysis including social support and coping behaviour, two factors through which exercise can alter the process of

actually perceiving stress. The results of this study indicated that three different and reliable clusters could be identified in both genders, more specifically a cluster consisting of stressed individuals with low social support and high passive and avoidant coping behaviour (“stressed”), a second cluster labelled “intermediates”, and a third cluster consisting of nonstressed individuals with high social support and active coping behaviour (“nonstressed”). These clusters were also discriminative in certain malign psychological health outcomes of stress, as the lowest level of anxiety and depression was found in the nonstressed cluster, and increased progressively in the intermediate and stressed cluster. Furthermore, in both genders, sports participation was higher in the nonstressed and intermediate cluster, compared to the stressed cluster. As sports activities have a more social and a more challenging character compared to other types of physical activity (e.g. active transportation, housekeeping and gardening), sports participation may result in a higher perceived social support, higher self-esteem and self-efficacy and greater active coping behaviour, which are all associated with lower levels of stress. The conclusion can be made that by making use of cluster analysis based on perceived stress, social support and coping in a population-based sample of adults, risk groups for anxiety and depression can be identified. Furthermore, although cross-sectional, these results may indicate that sports participation and other types of physical activity, providing sources of higher perceived social support, self-esteem and self-efficacy, could be effective primary and secondary prevention strategies for stress, anxiety and depression.

The purpose of the fourth and fifth study (chapters 2.2.2. and 2.2.3.) was to examine the associations of sedentary behaviour, moderate to vigorous leisure time physical activity, muscular strength and aerobic fitness with the continuous metabolic syndrome risk score, in Flemish adults free from cardiovascular disease and diabetes. In both studies, analyses were adjusted for the confounding effects of age, height, education level, smoking status and dietary intake. A higher level of sedentary behaviour was associated with a higher metabolic syndrome risk, independently of leisure time physical activity, in both genders. Furthermore, being more active in leisure time was related to a lower metabolic syndrome risk, independently of time spent in sedentary behaviour. Aerobic fitness was inversely associated with metabolic syndrome risk, independently of muscular strength in both genders. An inverse association was found between muscular strength and metabolic syndrome risk in women, independently of aerobic fitness. In men however, the inverse association between muscular strength and metabolic syndrome risk was attenuated after adjustment for aerobic

fitness. Moreover, independent associations were found with several individual metabolic syndrome risk factors for sedentary behaviour and moderate to vigorous leisure time physical activity in both genders, and for muscular strength and aerobic fitness in women. Some of these associations were mediated by adiposity, whereas others were not, suggesting that biological pathways other than obesity are also responsible for the associations found. In conclusion, a low level of sedentary behaviour and a high level of moderate to vigorous leisure time physical activity may provide additional protective effects regarding metabolic syndrome risk in both genders. Furthermore, high levels of aerobic fitness and muscular strength may also provide additional protective effects in women.

For chapter 2.2.3., the total model, including age, height, education level, smoking status, dietary intake, muscular strength and aerobic fitness, could explain 18.5% of metabolic syndrome variance in men and 24.5% in women. In men, variance uniquely explained by aerobic fitness was 7%. In women, variance uniquely explained by aerobic fitness was 3.1%, and by muscular strength 2.5%. For chapter 2.2.2., the total model, including age, height, education level, smoking status, dietary intake, sedentary behaviour and moderate to vigorous leisure time physical activity could explain 14% of metabolic syndrome variance in men and 21.7% in women. Variance uniquely explained by sedentary behaviour was 1.5% in both genders. Variance uniquely explained by moderate to vigorous leisure time physical activity was 3% in men and 1.3% for women. For sedentary behaviour and leisure time physical activity, these figures indicate rather low effect sizes.

The last study (chapter 2.2.4.) was designed to examine a theoretical model, causally linking psychological distress, health-related lifestyle and physical fitness with a metabolic syndrome risk factor in Flemish adults without cardiovascular disease and diabetes, using latent variable structural equation modeling. In structural equation modelling, a model is tested using goodness-of-fit tests to determine if the pattern of variances and covariances in the data is consistent with a structural model, specified by the researcher based on literature and/or theory. Latent variable structural equation modelling (LVSEM) consists of two main parts, more specifically the measurement model and the structural model. The *measurement model* is that part of the LVSEM model dealing with the latent variables and their observed variables. *Latent variables*, are the *constructs* or *factors* which are measured by their respective observed variables. These *observed variables*, also referred to as *manifest variables*, may be scales in a questionnaire, objectively measured characteristics,... The measurement model is based on confirmatory factor analysis and standardized path

coefficients between latent variables and their respective observed variables can be interpreted as factor loadings. The *structural model* is the part of the LVSEM model, applying path analysis between latent variables. In the structural model, latent variables may be independent, mediating and dependent variables, depending on the direction of causal path(s) that can have their origin, end point or both in each latent variable.

Sedentary behaviour and moderate to vigorous leisure time physical activity, as defined in the fourth study, were included as observed variables loading on the health-related lifestyle factor, besides alcohol and fat intake. The observed variables within the construct of physical fitness consisted of aerobic fitness and muscular strength, as defined in the fifth study. Furthermore, perceived stress, depression, anxiety (included in the third study) and sleeping problems were the observed variables loading on the psychological distress construct. The main aim of this study was to investigate the relative contribution of psychological distress, health-related lifestyle and physical fitness in explaining metabolic syndrome variance, and their interactions in doing so. This study indicated that 39.6% of the variance of the metabolic syndrome factor could be accounted for by the physical fitness, health-related lifestyle and psychological distress factors in both genders. Physical fitness was the most important contributor (direct effect of 22.8 %), besides health-related lifestyle (primarily defined by physical activity), showing a smaller contribution (9.9 %), which was mediated by physical fitness. No significant contribution was found for psychological distress. These results may indicate that the inverse association between moderate to vigorous leisure time physical activity and metabolic syndrome risk, found in study four, may be mediated by an increase in physical fitness (primarily aerobic fitness showing a substantially higher loading compared to muscular strength). Previous research already showed a mediating effect of aerobic fitness in the association between physical activity and the metabolic syndrome.²⁴ However, the results of the sixth study should be interpreted with caution.

First of all, measurement error of both physical fitness indicators is much smaller than measurement error for the health-related lifestyle (and psychological distress) indicators. In a prospective study, Ekelund et al.⁷ showed that objectively measured physical activity energy expenditure (showing lower measurement error in comparison with self-reported physical activity) was inversely associated with metabolic syndrome risk, independent of aerobic fitness and other confounding factors in middle-aged men and women without metabolic syndrome at baseline. Moreover, aerobic fitness was not an independent predictor toward metabolic syndrome risk after adjusting for physical activity energy expenditure. Similar results were found by Franks et al.¹⁰ in a cross-sectional study, applying statistical adjustment

for differences in measurement precision between physical activity energy expenditure and aerobic fitness. These studies suggest that the higher contribution of physical fitness in explaining metabolic syndrome variance found in study six, may partially be caused by differences in measurement error between the indicators of physical fitness, health-related lifestyle and psychological distress.

Second, in study six, metabolic syndrome variance was represented by one factor only, whereas the results of the second study of this thesis suggest a better representation of the construct of the metabolic syndrome by taking into consideration two factors. Because of differences in metabolic syndrome representation and general statistical approach, integrating the results of study four, five and six should be done with caution. Similarly, although the significant pathway between health-related lifestyle (or physical activity) and psychological distress might be considered as supportive for the results of the third study, differences in study population, statistical approach and quantification of physical activity should be kept in mind.

From these four studies, the conclusion can be made that cluster analysis, including social support and coping, enables us to identify risk groups of stress, anxiety and depression in a population-based sample of adults and that sports participation may exert beneficial effects in these at-risk groups. Furthermore, avoiding sedentary behaviour may provide additional benefits in lowering metabolic syndrome risk, besides being moderately to vigorously active in adults free from cardiovascular disease and diabetes. In women, high muscular strength may also exert a positive effect, additional to the benign effect of aerobic exercise. Therefore, these results may support inclusion of strength training and a reduction of sedentary behaviour, besides inclusion of moderate to vigorous physical activity and exercise increasing aerobic fitness in physical activity recommendations to reduce metabolic syndrome risk. Finally, the effect of moderate to vigorous activity might be mediated by an increase in physical fitness. However, direction of causality of these associations should not be taken for granted, given the cross-sectional design of all four studies.

2. Reflection, limitations and recommendations for further research

In the following section, results of the epidemiological association studies of chapter 2.2.1., 2.2.2., 2.2.3. and 2.2.4. will be more thoroughly evaluated regarding their validity. Therefore, bias, confounding and chance within these studies will be examined.

2.1. Bias, confounding and chance

2.1.1. Bias

A possible source of bias which may have occurred within these studies, is *selection bias*, which is “error due to systematic differences in characteristics between those who take part in a study and those who do not”.³⁷ Results presented in this thesis were derived from the theme 1 and theme 2 studies of the Flemish Policy Research Centre Sport Physical Activity and Health. For the purpose of the theme 1 study, the National Institute of Statistics randomly selected a community sample of 18- to 75-year-olds in 46 randomly chosen municipalities in the Flemish region of Belgium. However, from those selected individuals, only subjects who were willing to participate in this “large scale study on physical activity, physical fitness and health” could be included in the study sample, resulting in a response rate of 28%. Part of the lower participation rate can probably be explained by the fact that the test battery was rather comprehensive (given the context of a large epidemiological study), and also included physical measurements of anthropometric, fitness, and health parameters, besides questionnaires. The mean duration of a test session was 1.5 hours. This might have put off individuals to participate in the study. Comparable participation rates have been reported for other epidemiological studies in which variables were actually measured instead of using (mailed) questionnaires (e.g., BIRNH study³¹: Belgian population aged 25-74y, participation rate = 36.5%).

As individuals e.g. showing a healthier lifestyle, higher level of physical fitness or free from disease might have been more interested to participate, selection bias might have occurred. To examine whether selection bias had occurred, two different analyses were executed within the frame of the theme 1 study. Both analyses were executed in men and women separately, and age categories with a range of 5 years (e.g. 18-24, 25-29, 30-34) were used.

First, the theme 1 study sample was compared to the general adult Flemish population for two demographic characteristics, more specifically age and education level (data for the general adult Flemish population were provided by the National Institute of Statistics). Regarding age, a significant difference was found between the age structure of the theme 1 study sample and that of the general adult Flemish population in both genders ($P < 0.05$). Generally, individuals 18- to 34 years of age were underrepresented in the theme 1 study sample, whereas individuals 35- to 70 years of age were overrepresented in the theme 1 study. The maximal level of underrepresentation was found in women between 18 and 24 years (2.32%). The maximal level of overrepresentation was found in men between 55 and 59 years of age (1.95%). Women 70 years of age and older were underrepresented (1.87%), whereas in men of this age, no under- or overrepresentation was found. Regarding education level (5 categories), generally the lowest education levels (secondary school degree or lower) were underrepresented, and the highest education levels (college or university degree) were overrepresented ($P < 0.05$). Relatively large differences were found in the youngest age groups. In the older age groups, there was predominantly an underrepresentation of the lowest education level (no degree/primary school).

Second, a subsample of individuals not willing to participate (non responders) completed a questionnaire, which provided the opportunity to compare participants of the theme 1 study and non-responders for certain characteristics of interest. An important reason for this was that no detailed scientific data on physical activity and physical fitness in Flemish adults were available before the Flemish Policy Research Centre Sport Physical Activity and Health was established. These analyses revealed that participants of the theme 1 study spent more time in sports activities, compared to non responders. This difference was significant ($P < 0.05$) in most age groups. Regarding sedentary behaviour, no significant difference was found between participants and non responders, except for 2 groups. In men aged 25 to 29 and women aged 40 to 44, more sedentary behaviour was reported by non-responders ($P < 0.05$). For body mass index, no significant difference was found between participants and non responders, except for individuals older than 70 years of age, in which responders showed a higher body mass index ($P < 0.05$).

These data indicate that in the theme 1 study, selection bias has probably occurred for age (although differences were rather small) and education level. Comparing participants of the theme 1 study with non responders, there is an indication that selection bias may also have occurred for certain physical activity variables. No indication was found for strong selection bias regarding sedentary behaviour or body mass index.

The theme 2 study sample consisted of theme 1 participants who were willing to visit our lab to take part in a more extensive investigation. This investigation comprised a whole-day visit to the lab on a working day. Therefore, selection bias in the theme 2 study sample was probably stronger than in the theme 1 sample, although no data are available on this. Furthermore, we excluded participants with cardiovascular disease and diabetes for analyses in study two, four, five and six, because this extra exclusion renders important advantages, as described in the discussion section of chapter 2.2.4. However, by doing this, the study sample of these studies became even more homogeneous for several metabolic, and probably other variables of interest.

Therefore, as in many large-scale epidemiological studies, the samples used in the present thesis probably show smaller variability for several variables of interest compared to the general population of 18 to 75 year olds. The above stated figures indicate a possible selection of the study sample for physical activity, so that more active people have participated in the theme 1 (and probably theme 2) study. Further, although no comparison analyses with the general adult Flemish population or non responders were possible regarding physical fitness and mental health, it could be assumed that individuals showing higher fitness levels and/or showing a better mental health were more willing to participate. Moreover, exclusion of subjects with cardiovascular disease and diabetes has probably resulted in a metabolically more healthy study sample. Therefore, it is probable that the study sample used in each of the association studies only includes subjects representing a certain part of the entire spectrum of values existing in the general adult Flemish population for the exposure and outcome variables. This selection probably results in associations that deviate to some extent from reality, an effect that is known as selection bias. For example, it could be that the lack of significant contribution of distress in explaining metabolic syndrome variance found in chapter 2.2.4., could be due to the fact that maybe predominantly mentally and metabolically healthy individuals were part of the study sample.

Further, it should be noted that in case selection has occurred in the study sample regarding mental health, the use of the subscales anxiety and depression, may have (partially) caused the lack of significant contribution of distress in explaining metabolic syndrome variance, found in chapter 2.2.4. In case predominantly mentally healthy individuals took part in the study, both scales, which were constructed to detect clinical symptoms in both the general population and

clinical populations, may not be sensitive enough to detect differences in stress-related mental problems between individuals of this select sample.

2.1.2. Confounding

Several variables may distort the associations examined within the scope of this thesis. Therefore, in all association studies, statistical adjustment was made for several possibly confounding variables. In chapter 2.2.1. examining the association between physical activity and mental health, adjustment was made for age. Models in chapters 2.2.2. and 2.2.3., examining the association between sedentary behaviour, physical activity, physical fitness and metabolic syndrome risk were adjusted for age, height, education level, smoking status and dietary intake. Finally, analyses in chapter 2.2.4. were adjusted for age, education level and smoking status. By doing this, the distorting effect of the confounding variable on the estimated associations is removed. However, residual confounding remains in case the adjusted results are still distorted by other confounding variables not included in analyses, or in case the confounding factor was inaccurately measured through which adjustment has not removed the whole distorting effect of that confounding variable. To some extent, this may be applicable to the findings presented in this thesis. Some confounding variables included in analyses may have been crudely measured, such as education level and smoking. Dietary intake was measured by self-report using a 3 day diet record, which may also be subject of measurement error. Further, some confounding variables may not have been taken into account in the current analyses. In the studies considering metabolic syndrome risk as outcome variable, further adjustment could be made for e.g. certain types of medication. The use of neuroleptica might induce a higher metabolic syndrome risk and might be associated with the exposure variables.^{14,25}

2.1.3. Chance

Finally, because of practical reasons, epidemiological studies must always be executed on a sample of the entire population, in the case of this doctoral thesis, the Flemish adult population. Even if there would be no selection bias or confounding, some chance factor may render study results which do not represent the ultimate true values. However, as variation from the true

values are minimized by the size of the study sample used, the rather high number of participants in each of the association studies will possibly have reduced the effects of chance. Furthermore, statistics and probability values (P) were used to determine whether the associations found were due to chance.

2.2. Reliability and validity of exposure and outcome variables

Validity of exposure and outcome variables is important in epidemiological studies. Therefore, in the following section, reliability and validity of some self-report measures and validity of the continuous metabolic syndrome risk score will be more thoroughly discussed.

2.2.1. Physical activity and sedentary behaviour

Test-retest reliability and relative and absolute validity of the FPACQ were examined in a separate validation study, not included in this thesis. Results will be given on activity variables that were used within the scope of this thesis. A complete description of the results on reliability and validity of the FPACQ can be found in the manuscript by Matton et al.¹⁹

This study was executed in a subsample of participants of the theme 1 and theme 2 study. As employed/unemployed and retired people have a different lifestyle structure, which may possibly influence reliability and validity of the FPACQ, data were analyzed separately for both groups. For test-retest reliability, subjects completed the FPACQ for the first time during the theme 1 test session, and for the second time during the theme 2 test session, with an interval of 2 weeks. Reliability analyses were conducted on data of 66 employed/unemployed participants (31 men, mean age = 39.23 ± 11.65 years; 35 women, mean age = 41.46 ± 12.62 years) and 36 retired participants (20 men, mean age = 63.65 ± 6.05 years; 16 women, mean age = 63.31 ± 3.94 years). For relative and absolute validity, participants wore an RT3 Tri-Axial accelerometer^{22, 23} during seven consecutive days, and concurrently kept a written seven-day activity record for a more comprehensive understanding of the accelerometer data. Participants for reliability and validity analyses were the same, except for some participants of which data could not be used for one of both analyses, due to technical problems. Validity analyses were conducted on data of 62 employed/unemployed participants (32 men, mean age = 39.28 ± 11.72

years; 30 women, mean age = 39.13 ± 11.96 years) and 49 retired people (30 men, mean age = 64.47 ± 5.48 years; 19 women, mean age = 65.37 ± 4.98 years). Definition of activity variables was rather similar between this doctoral thesis and the validation study by Matton et al.¹⁹: time spent in *sedentary behaviour* (h/week) (chapters 2.2.1., 2.2.2., 2.2.4.), *active transportation in leisure time* (h/week) (chapter 2.2.1.) and *total active leisure time* (h/week) (chapter 2.2.1.) were defined in exactly the same way. *Sports participation* was defined as time spent in the 3 most frequently practiced sports (h/week) in the study by Matton et al.,¹⁹ whereas in chapter 2.2.1. the same definition was used but only sports with an intensity level ≥ 4 MET were included. The variables *moderate leisure time physical activity* (h/week), *vigorous leisure time physical activity* (h/week) (chapter 2.2.2.), and *(total) leisure time physical activity* (h/week) (chapters 2.2.2., 2.2.4.), were defined in the same way as the variable total active leisure time, but only activities with an intensity level above the age-specific MET value cut points for moderate or vigorous intensity were included. The variable *housekeeping and gardening* (h/week) (chapter 2.2.1.) was not examined as a separate variable in the study by Matton et al.¹⁹ Therefore, (exact) reliability and validity data for the variables housekeeping and gardening, sports participation, moderate, vigorous and (total) leisure time physical activity, used in this doctoral thesis, cannot be provided. Results on the sports participation and total active leisure time physical activity variables from the study by Matton et al.¹⁹ can only be used as an indication for reliability and validity of the variables sports participation, moderate, vigorous, and total leisure time physical activity used in the current thesis, considering the possibility that reliability and validity might differ for self-reported activities of different intensities.³⁵

Test-retest intraclass correlations coefficients (ICC) for employed/unemployed participants and for retired participants are provided in Table 1.

Table 1. Test-retest intraclass correlation coefficients for four physical activity variables calculated from the FPACQ in employed/unemployed and retired Flemish men and women (adapted from Matton et al.¹⁹)

	Employed/unemployed		Retired	
	Men (n = 31)	Women (n = 35)	Men (n = 20)	Women (n = 16)
Sedentary behaviour	0.93	0.92	0.76	0.89
Active transportation in leisure time	0.75	0.71	0.81	0.57
Total active leisure time	0.79	0.85	0.83	0.64
Sports participation	0.87	0.91	0.68	0.92

The criteria of Fleis⁹ suggest that ICC values between .40 and .75 represent fair to good reliability, those between .75 and .90 very good reliability, and those greater than .90 excellent reliability. According to these criteria, these four variables showed good to excellent test-retest reliability in employed/unemployed subjects, and still fair to excellent test-retest reliability in retired subjects.

For relative validity of these activity variables, Pearson product-moment correlation coefficients between the activity variables calculated from the RT3 and from the first administration of the FPACQ are provided in Table 2. Except for total active leisure time in employed/unemployed men and retired subjects and for sports participation in retired women, all correlations were significant.

Table 2. Pearson product-moment correlation coefficients between four physical activity variables calculated from the RT3 and from the first administration of the FPACQ in employed/unemployed and retired Flemish men and women (adapted from Matton et al.¹⁹)

	Employed/unemployed		Retired	
	Men (n = 32)	Women (n = 30)	Men (n = 30)	Women (n = 19)
Sedentary behaviour	0.69***	0.83***	0.78***	0.80***
Active transportation in leisure time	0.55**	0.49**	0.55**	0.52*
Total active leisure time	0.35	0.75***	0.33	0.28
Sports participation	0.77***	0.63***	0.66***	0.38

*: $P < 0.05$; **: $P < 0.01$; ***: $P < 0.001$

In addition, to determine absolute validity, paired t-tests were used to compare the magnitude of activity variables calculated from the FPACQ with those from the RT3. The following results were found for the FPACQ regarding overreporting or underreporting by participants. Sedentary behaviour was underreported by employed/unemployed women (2.91 hours/week, $P < 0.01$) and retired men (6.82 hours/week, $P < 0.001$) and women (3.70 hours/week, $P < 0.05$). Active transportation in leisure time was overreported by employed/unemployed men (1.38 hours/week, $P < 0.001$) and women (0.8 hours/week, $P < 0.01$), by retired men (1.43 hours/week, $P < 0.001$) and women (1.08 hours/week, $P < 0.05$). Total active leisure time was overreported by employed/unemployed men (4.68 hours/week, $P < 0.05$) and underreported by retired women (4.79 hours/week, $P < 0.05$). Finally, sports participation was overreported by employed/unemployed men (0.85 hours/week, $P < 0.05$) and women (0.68 hours/week, $P < 0.05$) and underreported by retired men (1.23 hours/week, $P < 0.01$).

A thorough discussion of these reliability and validity results, including a comparison with the results for other self-report physical activity questionnaires found in literature, can be found in the manuscript of Matton et al.¹⁹ However, some remarks regarding the validity results, that are interesting within the scope of this thesis, should be highlighted. First, validity results of these four physical activity variables are subject to the “quality” of the questionnaire (which is examined) but also to the limitations of the criterion measure used, which is the RT3 in the case of this study. Accelerometry-measured physical activity tends to underestimate true physical activity due to missed activities, including swimming and cycling.¹² These are activities that are part of all three activity variables reported here, especially of the active transportation in leisure time variable, which only consists of cycling and walking. Therefore, this may have caused some underestimation of the validity results. Further, except for some correlations especially found in retired people, correlations between the FPACQ and the RT3 may be considered to be supportive for the relative validity of these four variables. However, as is the case in several physical activity self-report measures,¹⁷ the FPACQ generally tends to overreport physical activity and underreport sedentary behaviour. This may especially be a problem in case these activity or sedentary behaviour variables are used to determine absolute cut-off values in order to make recommendations for physical activity or sedentary behaviour to reduce risk for certain health problems. However, this was not the aim of the current doctoral thesis, in which only associations between physical activity, sedentary behaviour and certain health outcomes were analysed.

Although the FPACQ questionnaire was found to be reasonably valid in adults, the use of objective physical activity measures could be encouraged. The reason for this is that in general, objective physical activity measures are characterized by lower measurement error, which may yield more valid results. This is even more the case when comparing effects on metabolic syndrome risk between physical activity and physical fitness or other characteristics measured objectively. However, some objective measurement techniques also may have limitations. In contrast to overestimates of physical activity with self-reports, accelerometry-measured physical activity tends to underestimate true physical activity due to missed activities.¹² Furthermore, accelerometers may underreport high intensity activities and overreport low intensity activities,³⁰ whereas self-report physical activity questionnaires are known to do the opposite, as they overreport high intensity activities and underreport low intensity activities.²⁶

Ideally, in future studies objective measurement techniques, showing low measurement error, should be used. Within the present study design, no large-scale use of these objective measurement techniques was made, because of the larger financial and time investment and the increased burden of participants involved in most of these techniques.

2.2.2. Mental health

Regarding mental health, data of five different self-report mental health questionnaires were used within the scope of this doctoral thesis, more specifically the GHQ-12, SCL-90-R, MOSSSS, PSS and UCL.^{4, 6, 11, 28, 29} Within the frame of the theme 1 and theme 2 studies of the Flemish Policy Research Centre, the existing paper-and-pencil versions were converted into computerized versions, as computerized administration of questionnaires may render important advantages compared to paper-and-pencil administration. As mentioned above, in chapter 2.1.1. of this doctoral thesis, these advantages are discussed and the test-retest reliability, equivalence and respondent preference of the computerized versus paper-and-pencil versions were examined.

Regarding validity, a validated Dutch version of the GHQ-12, SCL-90-R and UCL was used. Validity results of the Dutch versions of these three questionnaires are presented extensively in their respective manuals.^{1, 18, 28} The MOSSSS and the PSS were adopted from the original English questionnaires. The MOSSSS is also used in the “Health Interview Survey, Belgium”, which is a large-scale survey on several health topics executed by the Scientific Institute of Public Health every three or four years in a representative sample of the Belgian population. In the current doctoral thesis, the Dutch version of this questionnaire, which was translated by the Scientific Institute of Public Health, was used. The translation of the Perceived Stress Scale (PSS) was executed using a translate/back-translate protocol executed by the author of this thesis and an independent native English speaker who immigrated in Belgium and speaks Dutch every day. However, so far, no validation studies have been made on the Dutch version of the MOSSSS and the PSS, as opposed to the UCL and the Dutch version of the GHQ-12 and the SCL-90-R. Although the original English versions of the MOSSSS and the PSS are found to be valid,^{4, 29} further validation studies on the Dutch version should be executed in the Flemish population.

2.2.3. Metabolic syndrome risk

A cross-sectional comparison of the continuous metabolic syndrome risk score with the IDF metabolic syndrome definition³² provided promising results. However, prospective validation should be executed, examining the predictive power of this continuous risk score for relevant clinical outcomes, including incident diabetes and cardiovascular disease. Furthermore, its predictive power for these relevant clinical outcomes should be compared with that of existing internationally recognised binary definitions, such as the IDF definition.³² Such prospective validation studies are needed to determine true validity of this new risk score and (advanced) utility compared to that of existing definitions. Moreover, studies in other ethnic groups should be conducted to examine whether factor structure of the metabolic syndrome is different compared to European populations, and therefore whether different risk scores should be used in different populations. Clearly, validation studies should also be conducted in these (ethnically) different populations.

In a 9 year follow-up, Hillier et al.¹³ revealed that in nondiabetic adults, age-adjusted risk for incident diabetes and cardiovascular disease increased progressively for every 1-standard deviation increase in their recently developed continuous metabolic syndrome risk score ($P < .05$), which was based on waist circumference, triglycerides, glucose and systolic blood pressure.

2.3. Causality

A limitation of the four association studies presented in this thesis was the cross-sectional design. This type of design implies that all measurements were executed at the same moment in time. Therefore, cause-and-effect relationships cannot be taken for granted. In case of the metabolic syndrome-related studies, subjects with cardiovascular disease and diabetes were excluded in an attempt to (at least) partially eliminate the possibility of causality in the direction opposite of what was hypothesized, as cardiovascular disease and diabetes are two important metabolic syndrome risk health outcomes that may influence health-related lifestyle, physical fitness and mental health.

Intervention and longitudinal (prospective) studies should be conducted to confirm causality of the associations found in our studies. Studies using a prospective design to examine the research questions of study four, five and six are scarce. In a *longitudinal study*, subjects would be measured at (at least) two different moments in time, more specifically at baseline and at follow-up (e.g. five years later). Baseline measurements would include 1) a medical examination/measurement of metabolic syndrome risk factors, 2) measurement of all predictors which are hypothesized to influence the outcome variable, and 3) measurement of all variables which are hypothesized to confound the association between predictors and the outcome variable. Follow-up measurements would (at least) include measurement of the outcome variable. For example, in case of the metabolic syndrome risk related hypotheses examined in the present thesis using a cross-sectional design, predictors could include physical activity, sedentary behaviour, aerobic fitness, muscular strength or measures of distress (i.e. perceived stress, anxiety, depression, sleeping problems). Confounding variables could include age, height, education level, smoking status and dietary intake. The metabolic syndrome risk factors could be re-examined at follow-up. Based on the baseline medical examination, subjects with the metabolic syndrome, cardiovascular disease or diabetes (including medication use) at baseline could be excluded from analyses. Using multiple linear regression models and other statistical techniques, the association between baseline values for the predictor variables and follow-up value for the continuous metabolic syndrome risk score could be examined, adjusting for age, height, education level, smoking status, dietary intake, duration of follow-up, and baseline metabolic syndrome risk score.

Intervention studies might be interesting to examine whether certain types of physical activity or fitness programs are more efficacious than others in lowering metabolic syndrome risk, or whether certain types of (sports) activities may provide increased benefits in primary or secondary prevention of stress-related mental health problems, based on the suggested theories concerning social support and coping. For example, to examine whether resistance training might provide benefits in lowering metabolic syndrome risk, which are additional to benefits from aerobic training in women, the following intervention study could be executed. Participants are subjected to a baseline assessment including 1) a medical examination/measurement of all metabolic syndrome risk factors, 2) measurement of maximal muscular strength and aerobic fitness, 3) measurement of confounding variables age, height, education level, smoking status, dietary intake and physical activity pattern. Women, who were not involved in an exercise program during the past year, who are free

from diabetes and cardiovascular disease and who do not take any medications for diabetes or cardiovascular disease could be included in the study. Subjects are divided into two groups, more specifically an endurance training group and a combined training group. The endurance training group is only subjected to an endurance training program whereas the combined training group is subjected to the training program of the endurance training group, supplemented by a resistance training program. Subjects are randomly designated to one of both groups, and analyses are adjusted for baseline differences between both groups regarding aerobic fitness, muscular strength and confounding variables. Furthermore, during training period, subjects are instructed not to change their normal daily physical activity or dietary pattern. When the training period is finalized, post-training versus baseline changes for the metabolic syndrome risk score/individual metabolic syndrome risk factors are examined for both groups, and compared between both groups.

2.4. Other limitations and recommendations for further research

In study four and six, only physical activity of moderate to vigorous intensity was included in analyses, based on the current physical activity recommendations.³³ However, activities of lower intensity may also be associated with a decrease in metabolic syndrome risk. A prospective study in middle-aged men and women without metabolic syndrome at baseline, measuring physical activity energy expenditure, and therefore including activities of all intensities performed in everyday life, suggested that an increase in energy expenditure, necessary to move from the lowest to the second lowest energy expenditure quartile, which can be achieved by e.g. 1 hour of brisk walking, was associated with a significantly lower metabolic syndrome risk.⁷ This result suggests that also lower intensity activities might play an important role in lowering metabolic syndrome risk. Further large-scale longitudinal studies are needed to determine whether a specific threshold of physical activity level exists.

Finally, more multivariate studies should be conducted, simultaneously investigating the association and relative contribution of several possible characteristics or determinants of metabolic syndrome risk, and preferably showing a longitudinal design. In this context, international studies, applying similar measurement techniques could provide unique opportunities for meta-analyses. Such studies provide valuable information for effective prevention strategies aiming to attack the metabolic syndrome epidemic.

3. Practical implications

Based on the findings of the studies described in this thesis, some implications will be formulated. However, as regards the association studies, they were all cross-sectionally designed to investigate whether certain associations exist in rather large population-based samples. Therefore, the implications formulated based on these four studies should be interpreted with caution. Moreover, the results should induce further longitudinal and intervention studies, resulting in more specific implications.

First of all, the computerized versions of five mental health questionnaire were found to be reliable psychological health measurement instruments that can be used as a practical alternative for the traditional versions in a general population of adults. Since computerized assessment is associated with several important advantages, not only for the clinician, but also for the responder and the researcher, these results should encourage further computerization and reliability and equivalence testing of (mental health) questionnaires, certainly when considering that in the future, computer usage will be common in all age categories, including seniors.⁵ The Flemish Physical Activity Computerized Questionnaire (FPACQ) is an example of a reliable and reasonably valid computerized questionnaire, measuring different dimensions of physical activity in adolescents²¹ and adults.¹⁹ Internet applications of these questionnaires will probably render supplemental advantages.

Based on several arguments, the use of a continuous metabolic syndrome risk score should be encouraged, certainly for research purposes. First of all, our results and the results of others¹³ prove that these (comparable) continuous risk scores can serve as a valid alternative for the existing binary definitions. Furthermore, because of its continuous character, no information is lost, as there is using the binary definitions. Moreover, a more realistic weight is given to the individual risk factors. Based on these strengths, the continuous risk score enables us to find more valid results. Therefore, it would be interesting if more future studies would apply a continuous metabolic syndrome risk score.

As sports activities may provide a stronger social network, and may have a beneficial influence on peoples' self-esteem and self efficacy, they could provide important primary and secondary prevention tools for stress, and associated depression and anxiety, based on the mechanisms of social support and coping. In the United States, stress-related disorders cost

the nation more than \$42 billion per year. Furthermore, \$150 billion of revenue is lost to stress annually in lost productivity, absenteeism, poor decision-making, stress-related mental illness, and substance abuse.¹⁶ As medication usage may also be considered as an economic cost, sports participation should be considered as an important alternative. Anti-depressive drugs and especially benzodiazepine drugs should be mentioned here. Benzodiazepine drugs are often prescribed for anxiety symptoms, sleeping problems and stress. These drugs are often used chronically, and therefore have become a major concern for policy makers. This is particularly the case for Belgium, where elevated levels of chronic use have repeatedly been observed.²⁰ The “Health Interview Survey, Belgium”, executed by the Scientific Institute of Public Health in 2004, recently presented results on the use of these drugs in the Flemish region of Belgium.³ About 3.8% and 3.2% of Flemish respondents reported that they had been using anti-depressive drugs or benzodiazepine drugs respectively during the past 24 hours. In their discussion on the figures on medication use, they presented the use of benzodiazepine drugs as one of the three most urgent problems that should be tackled, by stating that “Without any doubt, there is a medicalisation of social problems (stress at work, familial and matrimonial problems,...) that maybe should better be solved in a different way.”.

Reducing time spent in sedentary behaviour should become part of future physical activity recommendations aiming to reduce metabolic syndrome risk and its comorbidities, as this type of behavioural change might provide benign effects additional to those of increased physical activity. This might provide unique opportunities for reducing risk in the general population, showing high levels of sedentary behaviour besides low levels of physical activity, and for clinical groups (e.g. obese individuals) showing resistance to physical activity programs. In recommending certain types of physical activity, exercise resulting in higher aerobic fitness is probably effective. However, based on our results, women might additionally benefit from resistance training, resulting in higher muscular strength. Resistance training might also provide a unique tool for certain populations, including obese individuals, as they might not be very enthusiastic about aerobic exercise. Although the results of our last study suggest that the effect of physical activity is primarily an indirect effect, mediated by aerobic fitness and muscular strength, these results should be interpreted with caution and further research should be executed, examining whether low-intensity physical activities, not resulting in higher aerobic fitness or muscular strength, also provide protective effects regarding metabolic syndrome risk.

4. References

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