Long-term temporal trends in metabolic risk factors

Langfristige Trends bei metabolischen Risikofaktoren

Abstract

Objectives: The "metabolic syndrome" characterized by obesity, hypertension, dyslipidemia and

hyperglycemia has consistently been associated with increased risk of cardiovascular disease.

The aim of this study was to investigate long-term trends in major metabolic risk factors in three

large cohorts.

Materials and Methods: Data from 239,602 individuals aged 25-64 years participating in health

examinations from 1976 to 2005 were used to estimate prevalence and trends in risk factors.

Results: Irrespective of geographic location, single components of the metabolic syndrome

showed divergent trends across the observation period. Whereas obesity and hyperglycemia

increased by a per decade ratio of 1.54 (95%CI: 1.42-1.66) and 1.62 (95%CI: 1.49-1.76) in men

and 1.48 (95%CI: 1.41-1.56) and 1.66 (95%CI: 1.57-1.75) in women, respectively, hypertension,

decreased by 0.71 (95%CI: 0.68-0.74) in men and 0.83 (95%CI: 0.79-0.86 in women.

Dyslipidemia showed non-linear pattern. Metabolic syndrome, defined as a combination of three

of these risk factors, significantly increased by a ratio of 1.15 (95%CI: 1.08-1.22) and 1.20

(95%CI: 1.15-1.27) per decade in men and women, respectively.

Conclusion: This study showed that the single metabolic risk factors show divergent trends over

the period of three decades even if Mets appeared to be stable over the last two decades. The two

key components of the syndrome namely BMI and glucose levels, increased significantly

deserving professional attention.

Key words: metabolic syndrome, body mass index, blood pressure, blood lipids, blood sugar

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Introduction

The "metabolic syndrome" (MetS) was introduced in 1988 as a constellation of metabolic aberrations caused by overeating, sedentary life-style and other predispositions. Since its initial description, several definitions have been proposed [1, 2]. Despite differences in specific criteria among these definitions, there is wide agreement that the major characteristics of the syndrome include obesity, insulin resistance, hyperinsulinaemia, hyperglycaemia, high blood pressure, and dyslipidaemia. Presence of the MetS has consistently been associated with increased risk of cardiovascular disease, stroke and diabetes [3, 4]. There is also a growing body of literature indicating metabolic factors as risk elements for cancer incidence and mortality [5-12]. Epidemiologic evidence regarding long-term trends of single metabolic risk factors is limited. Trends of increasing BMI were consistently reported in studies covering a majority of European countries including the World Health Organisation (WHO) MONICA project [13-17] as well as the U.S. population [18-21] e.g. the NHANES surveys. More divergent results were published concerning blood pressure, cholesterol and triglycerides. The majority of studies showed a decreasing trend in blood pressure [13, 20-21], however a few studies have detected increasing trends [16-17,19]. Inconsistent trends were also observed for cholesterol [14-17,21] and triglycerides [14,19]. Smoking, not a metabolic but a major risk factor for cardiovascular and cancer disease, decreased especially in men in all western industrialized countries [14,20]. Differences in the compositions of the populations studied, limited length of observation periods and insufficient sample size may have contributed to a lack of consistent evidence in previous investigations. Based on the large sample size and an observation period covering 30 years, we aim to analyse if temporal trends in metabolic risk factors exist in different cohorts and health surveys across middle and northern Europe.

Material and Methods

The study population

The Me-Can collaborative study (Metabolic syndrome and Cancer project) was initiated in 2006, in order to create a large pooled cohort to investigate factors of the metabolic syndrome on the association with cancer risk. We used three sub-cohorts of the Me-Can collaborative study, mentioned below, from Austria and Sweden with total participants of 122,076 men and 117,526 women in the age range of 25-64 years. Whereas data from VHM&PP were used to show risk factor prevalence for Austria, VIP and Malmö provided data for Sweden. Although not necessarily representative for the whole country we merged data from Malmö and VIP in order to cover three decades of risk factor data for Sweden.

The Vorarlberg Health Monitoring and Prevention Programme (VHM&PP)

The VHM&PP is a population-based risk factor surveillance programme in Vorarlberg, the westernmost province in Austria [22-23]. The purpose of the programme was to prevent chronic diseases, foremost cardiovascular diseases and cancer, and it was routinely performed by the Agency for Social and Preventive Medicine. All adult residents in the region were invited by written invitations, television, radio or news papers, to participate in a health examination up to once a year. Since 1985, more than two-thirds of the population of the province participated in the programme. Data from the years 1985-2005 is included in Me-Can and during these years, the attendance rate in the VHM&PP was 66% and roughly 176 000 persons participated in the programme.

The Västerbotten Intervention Project (VIP)

The Västerbotten Intervention Project (VIP) is an ongoing project aiming for prevention of diabetes and cardiovascular disease in residents of Västerbotten county in the north of Sweden [24]. Since 1985, all residents are invited for a health check-up at 40, 50 and 60 years of age, and during the first ten years of the project, residents were also invited at the age of 30. The attendance rate has been 60% on average over the years. By the end of 2006, approximately 86,000 men and women had participated in the VIP.

The Malmö Preventive Project (MPP)

Middle-aged men and women in the city of Malmö in southern Sweden, were invited to a screening programme for prevention of cardiovascular disease and alcohol abuse.[25,26] Screenings were carried out between the years 1974-1992, to which all residents within predefined birth cohorts, born between 1921-1949, were invited. The attendance rate was on average 71% over the years. A total of 33,346 men and women participated in the baseline screening, and 5722 of these men (born 1926-1938) and 387 women (born in 1931) participated in a second screening in 1981-1989. The examination at the second screening was similar to that of the first screening.

Ethical approval

The study has been approved by ethical committees of the respective countries.

Measurements

Measurements include height, weight, systolic and diastolic blood pressure, serum total cholesterol, triglycerides, and glucose levels. Anthropometric measurements were conducted in

all cohorts in a similar manner with participants wearing light indoor clothes and no shoes. Blood pressure was measured after 5-10 minutes of rest in sitting position in the VHM&PP and supine position in the VIP the MPP. Measurement was done with mercury sphygmomanometer in all cohorts. Serum measurements were performed after an overnight-fast of at least 8 hours in all individuals. Determination of glucose was done on serum in all cohorts except in MPP, where it was measured in whole blood. For determination of lipids, serum samples were used in all the cohorts. All the analysis was done using enzymatic technique.

The metabolic syndrome

To define the metabolic syndrome, we used a modified form of the National Cholesterol Education Programme Adult Treatment Panel (NCEP ATP III) [27] definition based on five commonly measured criteria: waist circumference (WC) which we replaced by BMI, blood pressure, serum triglycerides, serum high-density lipoprotein (HDL) cholesterol and fasting glucose level. In our study total cholesterol measurements were available instead of HDL-cholesterol. We used the following cut-off points: $BMI \geq 30 \text{ kg/m}^2$, hypertension defined as systolic blood pressure $\geq 140 \text{ mmHg}$ and/or diastolic blood pressure $\geq 90 \text{ mmHg}$, hypercholesterolemia as total cholesterol $\geq 6.1 \text{ mmol/l}$, hypertriglyceridaemia as triglycerides $\geq 1.69 \text{ mmol/l}$ and fasting hyperglycaemia as fasting glucose $\geq 6.1 \text{ mmol/l}$. Any combination of three of the above conditions was defined as metabolic syndrome.

Statistical analysis

Total and region specific prevalence and means of metabolic risk factors were estimated by decades separately for men and women. Trends in metabolic risk factors were assessed by sex-specific linear and logistic regression analyses adjusted for age, region, smoking status and BMI where appropriate. For the logistic regression analyses risk factors were dichotomized in normal and elevated levels according to standard guidelines as reported above. The surveys included few participants above 65 years of age. Therefore, we restricted our analysis to the age range of 25-64 years. However, to further achieve balanced participation conform to the known population age distribution in this age range we applied sampling weights for the different cohorts using data from official census for the respective countries in the respective decade [28,29]. Sampling weights were calculated for 5-year age groups, separately for sex, decade and region. Results were summarized according to decades and the following regions: Austria (VHM&PP), and Sweden (VIP, MPP). SPSS Complex Samples 16.0 (SPSS Inc. Chicago, Il 2007) was used for statistical analysis.

Results

Estimated prevalence of the Mets and its components divided by regions and decades are shown in Table 2 for men and Table 3 for women. Mets defined as any combination of three elevated single risk factors increased from 10.3% to 15.8% in men and from 4.4% to 10.1% in women from the first to the second decade, followed by a very slight decrease from the second to the third decade (14.2% in men, 9.9% in women). Overall, prevalence of Mets increased by a ratio of 1.15 (95% CI: 1.08-1.22) and 1.20 (95% CI: 1.15-1.27) per decade, in men and women, respectively.

The single risk factors showed divergent trends across the three decades in both sexes (Tables 2, 3). The predominant trend was that obesity and impaired fasting glucose showed a strong increasing pattern whereas blood pressure lowered over the decades in both men and women. Dyslipidemia showed a less clear pattern. The prevalence of both hypercholesterolemia and hypertriglyceridemia increased from the first to the second decade and decreased from the second to the third. For hypercholesterolemia, values were significantly lower in the most recent decade; in the case of hypertriglyceridemia changes were not significant. Prevalence of smoking declined markedly in both men and women over the three decades. Regarding risk factor trends in the subregions, the observed results are similar to the overall results, with the exception of hypertension that decreased less pronounced in the Austrian survey compared to the Swedish surveys. Trends in estimated means roughly confirmed the results of categorised risk factors. As shown in Tables 4 and 5 mean BMI and fasting glucose values for both regions increased significantly whereas diastolic blood pressure decreased and average cholesterol level remained stable. However, mean systolic blood pressure did not change significantly pointing to the possibility that the decrease in the prevalence of hypertension over the years is mainly due to control of diastolic blood pressure.

Discussion

The results of this analysis of three large-scale cohort datasets in two European countries provide further consistent evidence that metabolic risk factors followed divergent patterns across the past three decades. Whereas BMI and glucose levels increased uniformly, blood pressure and smoking decreased. Trends in blood lipids followed a non-linear pattern. Our findings concerning obesity are in agreement with all major studies performed in western industrialized countries [15-16, 30-31]. Similar obesity prevalence was reported for the European countries of the WHO MONICA project, albeit spanning a shorter time-period [15]. Whilst the magnitude of the increase of prevalence is markedly higher in the US, where the NHANES surveys showed that the age adjusted prevalence of obesity (BM≥ 30kg/m²) rose from 29.1% in 1960-62 to 49.8% in 1999-2000 among the Afro-Americans and from 12.3% to 35.7% among Caucasians in the respective years [32], the direction of the trends are similar to our findings.

Our results for glucose, blood pressure and total cholesterol were also consistent with the reports from MONICA and NHANES. It has been argued recently that the forces driving these trends operate at the population rather than the individual level because this occurs across the percentile distribution [14, 31] and this between-country evidence we present here further supports that contention. Regarding hypertension, however, the few studies performed report conflicting outcomes [16, 20, 33]. This is a risk factor that can be strongly dependent on clinical hypertension detection and treatment follow-up and we demonstrate some differences between countries and cohorts that suggest this may indeed be important. Moreover, the zero-five-end digit preference might have contributed to the increase in the likelihood of classifying individuals as hypertensive as also seen else where [34]. Additionally it is suggested that both the baseline systolic and diastolic blood pressures were significantly higher in sitting position in both volunteers and hypertensive patients as compared to supine position [35]. This could, partly, be

the case in our study where by the blood pressure values are higher in the Austrian cohorts as compared to the Swedish.

The pattern of lipid levels over time was not linear, and similarly, a previous study from Sweden showed an increase between 1985 and 1995, followed by a decline between 1995 and 2002 [15]. Prevalence of the MetS is strongly influenced by the different definitions proposed by the WHO, the NCEP or the IDF (International Diabetic Federation) [27]. Definitions overweighing glucose lead to increasing trends whereas other definitions show stable or even decreasing trends. Notably, whilst some risk factor trends are downwards and some conversely upwards, the net pattern for presence of three or more metabolic risk factors has in effect plateaued in the last decade. But the overall increasing tendency of metabolic syndrome was also observed in the NHANES surveys among US adults which also applied the ATPIII definition [19].

The implications of this may signal no net change in incidence of cardiovascular disease but a differing clinical presentation, whereas for cancer the implications may be quite different, especially given the strongly demonstrated association between obesity and cancer outcome in recent reports. Obesity was repeatedly shown to have positive association with overall and several site-specific malignancies including cancers of colorectum, endometrium, pancreas, kidney, gallbladder, thyroid and oesophagus [6-8]. Furthermore, obesity was shown to be associated with high prostate and breast cancer mortality [9, 10]. High glucose levels were also linked to an increased overall risk of cancer [11-12].

Our study had several strengths and potential limitations that should be considered. Major strengths are the large sample size, length of observation period and the comparable protocols between middle and northern European health surveys that were used assessing the data. Measurements were in general very similar, but there were some exceptions. Blood sample for glucose determination was serum in VHM&PP and in VIP and whole blood in MPP.

Additionally, blood pressure was measured in sitting position in VHM&PP and in supine position in VIP and MPP. These may well affect our results, however, we think to a minor extent. A further limitation of the study is the inability to examine the effect of treatment, mainly medication of high blood pressure, cholesterol and diabetes. In addition, we were unable to account for the effect of behavioural changes regarding diet, alcohol consumption or physical activity.

This study showed that the single metabolic risk factors show divergent trends over the period of three decades even if Mets appeared to be stable over the last two decades. The fact that the key components of MetS, namely BMI and glucose levels, increased significantly deserves wide spread recognition by policy makers and those concerned with health promotion and disease prevention.

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Table 1. Sociodemographic characteristics of the study population

Cohort	No	o. of particip	ants	Mean age (std.)*			
88980434360	men	women	total	men	women		
VHM&PP (A	ustria)		0000010	110000000			
76-85	-				-		
86-95	42,263	49,094	91,357	42.6 (11.1)	42.8 (11.3)		
96-05	23,054	21,339	44,393	40.7 (11.0)	39.8 (10.9)		
Malmö (Swe	eden)			- 100 V			
76-85	22,241	6,750	28,991	43.7 (6.6)	46.6 (7.7)		
86-95	(.7)	3,774	3,774		54.8 (2.1)		
96-05	-	-					
VIP (Sweder	n)						
76-85	-	-	-		-		
86-95	12,597	14,194	26,791	45.4 (10.4)	45.5 (10.4)		
96-05	21,921	22,375	44.296	48.8 (8.4)	48.7 (8.5)		

^{*} Only participants between 25 and 64 years of age were included.

Table 2. Total and region-specific prevalence of metabolic risk factors and smoking by decades in men aged 25-64 years, Austria, Sweden 1976-2005

No. of participants	decades	obesity*	hypertension	hypercholeste- rolemia	hypertrigly- ceridemia	fasting hyperglycemia	3 or more factors (modified ATP)	smoking
Total								
n=22,241	76-85	6.1 †	43.0	27.1	26.2	4.7	10.3	47.9
n=54,860	86-95	9.8	35.5	34.7	35.0	8.7	15.8	24.7
n=44,975	96-05	14.1	33.9	25.4	30.7	13.6	14.2	19.8
	OR (95% CI)	1.54 (1.42- 1.66)†† <0.001	0.71 (0.68- 0.74) <0.001	0.87 (0.83- 0.91) <0.001	0.98 (0.94- 1.03) 0.278	1.62 (1.49- 1.76) <0.001	1.15 (1.08-1.22)	0.54 (0.52- 0.57) <0.001
Austria						4,000,000,000	40000000	
· -	76-85	-	-		38.1	-	1353	7
n=42,263	86-95	9.7	42.0	34.2	38.7	8.2	16.8	32.2
n=23,054	96-05	14.2	40.5	24.4	34.7	12.6	16.0	25.5
Sweden		***************************************				1117		
n=22,241	76-85	6.1	43.0	27.1	26.2	4.7	10.3	47.9
n=12,597	86-95	9.8	28.8	34.9	30.1	9.0	13.9	17.8
n=22,921	96-05	13.8	27.2	26.1	26.3	14.2	12.1	14.4

^{*} Obesity was defined as BMI ≥30 kg/m², hypertension as sytolic blood pressure of ≥140 mmHg or diastolic ≥90 mmHg, hypercholesterolemia > 6.1 mmol/l, hypertriglyceridemia ≥1.69 mmol/l and hyperglycemia >6.1 mmol/l.

^{††} Ratio of change per decade, estimated from logistic regression models for complex samples adjusted for age, region, smoking and body-mass-index where appropriate.

Table 3. Total and region-specific prevalence of metabolic risk factors and smoking by decades in women aged 25-64 years, Austria, Sweden 1976-2005

No. of participants	decades	obesity*	hypertension	hypercholeste- rolemia	hypertrigly- ceridemia	fasting hyperglycemia	3 or more factors (modified ATP)	smoking
Total								
n=6,750	76-85	6.6 †	25.4	24.2	11.8	1.8	4.4	39.7
n=67,062	86-95	11.4	27.7	28.0	17.4	6.4	10.1	23.2
n=43,714	96-05	15.6	26.5	22.6	15.7	9.3	9.9	17.9
101000000000000000000000000000000000000	OR (95% CI)	1.48 (1.41- 1.56)††	0.83 (0.79-0- 86)	0.82 (0.80-0.86)	0.99 (0.94- 1.03)	1.66 (1.57- 1.75)	1.20 (1.15-1.27)	0.61 (0.59-0.63)
	p for trend	< 0.001	< 0.001	< 0.001	0.439	< 0.001	< 0.001	< 0.001
Austria								
-	76-85	127	-		121		2	-
n=49,094	86-95	11.4	33.3	27.6	18.2	6.4	10.9	23.5
n=21,339	96-05	16.3	30.5	21.2	16.7	8.5	10.6	18.4
Sweden		131-2311-23	***************************************				***************************************	
n=6,750	76-85	6.6	25.4	24.2	11.8	1.8	4.4	39.7
n=17,968	86-95	11.0	20.9	28.2	16.0	6.2	8.6	23.4
n=22,375	96-05	14.5	21.7	23.3	14.4	9.8	8.7	17.7

^{*} Obesity was defined as BMI ≥30 kg/m², hypertension as sytolic blood pressure of ≥140 mmHg or diastolic ≥90 mmHg, hypercholesterolemia > 6.1 mmol/l, hypertriglyceridemia ≥1.69 mmol/l and hyperglycemia >6.1 mmol/l.

[†]Percentages estimated using region-, decade-, and sex-specific 5-year age-group sampling weights (complex samples).

^{††} Ratio of change per decade, estimated from logistic regression models for complex samples adjusted for age, region, smoking and body-mass-index where appropriate.

Table 4. Total and region-specific means (95% CI) of metabolic risk factors by decades in men aged 25-64 years, Austria, Sweden 1976-2005

cohort	decades†	BMI, kg/sqm	systolic blood pressure, mmHg	diastolic blood pressure, mmHg	total cholesterol, mmol/l	triglycerides, mmol/l	fasting glucose, mmol/l
Total							
n=22,241	76-85	24.5 (24.4-24.7)*	128.4 (127.7-129.0)	85.0 (84.7-85.5)	5.6 (5.5-5.6)	1.5 (1.4-1.5)††	5.1 (5.0-5.2)
n=54,860	86-95	25.6 (25.5-25.6)	129.7 (129.5-129.9)	81.1 (81.0-81.2)	5.7 (5.7-5.7)	1.7 (1.7-1.7)	5.1 (5.1-5.1)
n=44,975	96-05	26.2 (26.1-26.3)	129.9 (129.6-130.1)	80.6 (80.4-80-8)	5.5 (5.5-5.5)	1.6 (1.6-1.6)	5.4 (5.4-5.4)
	p for trend	<0.001†	0,011	< 0.001	< 0.001	0.24	< 0.001
Austria							
1070	76-85			+	21		-
n=42,263	86-95	25.5 (25.4-25.5)	131.4 (131.2-131.6)	82.5 (82.4-82.6)	5.7 (5.7-5.7)	1.8 (1.8-1.8)	4.8 (4.8-4.8)
n=23,054	96-05	26.0 (26.0-26.1)	132.2 (131.9-132.5)	82.2 (82.0-82.3)	5.6 (5.6-5.6)	1.7 (1.7-1.7)	5.3 (5.2-5.3)
Sweden			- 2 2			* *	
n=22,241	76-85	24.5 (24.4-24.7)	128.4 (127.5-128-2)	85.1 (84.7-85.5)	5.6 (5.5-5.6)	1.5 (1.4-1.5)	5.1 (5.0-5.2)
n=12,597	86-95	25.7 (25.6-25-7)	127.8 (127.5-128.2)	79.7 (79.5-80.0)	5.7 (5.7-5.7)	1.5 (1.5-1.6)	5.3 (5.3-5.4)
n=22,921	96-05	26.3 (26.2-26.4)	127.5 (127.1-127.9)	79.1 (78.8-79.3)	5.4 (5.4-5.5)	1.5 (1.4-1.5)	5.5 (5.5-5.6)

^{*}Means (95% CI) estimated using region-, decade-, and sex-specific 5-year age-group sampling weights (complex samples).

[†] Effect of decade (p for trend) was tested in linear regression analyses for complex samples adjusted for age, region, smoking and body-mass-index where appropriate. In case of non linear pattern (lipids) p-values were given comparing 3rd versus 1st decade.

^{††} Triglycerides were log-transformed, means thus obtained represent geometric means.

Table 5. Total and region-specific means (95% CI) of metabolic risk factors by decades in women aged 25-64 years, Austria, Sweden 1976-2005

cohort	decades†	BMI, kg/sqm	systolic blood pressure, mmHg	diastolic blood pressure, mmHg	total cholesterol, mmol/l	triglycerides, mmol/l	fasting glucose, mmol/l
Total							
n=6,750	76-85	23.4 (23.2-23.5)*	121.2 (120.7-121.7)	80.6 (80.3-80.9)	5.5 (5.5-5.5)	1.1 (1.1-1.1) ††	4.8 (4.7-4.8)
n=67,062	86-95	24.7 (24.6-24.7)	125.1 (124.9-125.3)	78.3 (78.2-78.4)	5.5 (5.5-5.5)	1.3 (1.2-1.3)	5.0 (5.0-5.0)
n=43,714	96-05	25.3 (25.2-25.4)	125.0 (124.7-125.3)	77.4 (77.2-77-6)	5.4 (5.4-5.4)	1.2 (1.2-1.2)	5.2 (56.2-5.3)
	p for trend	<0.001†	0.512	< 0.001	< 0.001	0.288	< 0.001
Austria		7.0					
	76-85	*		•			
n=49,094	86-95	24.4 (24.4-24.5)	127.1 (126.9-127.3)	80.0 (79.8-80.1)	5.5 (5.5-5.5)	1.3 (1.3-1.3)	4.7 (4.7-4.7)
n=21,339	96-05	25.1 (25.0-25.2)	126.6 (126.2-126.9)	79.0 (78.8-79.2)	5.4 (5.4-5.5)	1.2 (1.2-1.2)	5.0 (5.0-5.1)
Sweden							
n=6,750	76-85	23.4 (23.2-23.5)	121.2 (120.7-121.7)	80.6 (80.3-80.9)	5.5 (5.5-5.5)	1,1 (1,1-1,1)	4.8 (4.7-4.8)
n=17,968	86-95	24.8 (24.7-24.9)	122.5 (122.2-122.8)	76.5 (76.3-76.7)	5.5 (5.5-5.5)	1.2 (1.2-1.2)	5.2 (5.2-5.2)
n=22,375	96-05	25.4 (25.3-25.6)	123.0 (122.6-123.4)	75.6 (75.3-75.9)	5.4 (5.3-5.4)	1.2 (1.2-1.2)	5.4 (5.4-5.4)

^{*}Means (95% CI) estimated using region-, decade-, and sex-specific 5-year age-group sampling weights (complex samples).

[†] Effect of decade (p for trend) was tested in linear regression analyses for complex samples adjusted for age, region, smoking and body-mass-index where appropriate. In case of non linear pattern (lipids) p-values were given comparing 3rd versus 1st decade.

^{††} Triglycerides were log-transformed, means thus obtained represent geometric means.