Wien Klin Wochenschr (2009) 121: 623–630
DOI 10.1007/s00508-009-1238-z
Printed in Austria

Wiener klinische Wochenschrift
The Middle European Journal of Medicine

Long-term temporal trends in cardiovascular and metabolic risk factors

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Received April 23, 2009, accepted after revision July 29, 2009

Langfristige Trends bei kardiovaskulären und metabolischen Risikofaktoren

Zusammenfassung. *Ziele:* Kardiovaskuläre Risikofaktoren wie Adipositas, Bluthochdruck, erhöhte Blutfette und Blutzucker wurden in den letzten Jahren zunehmend mit dem Auftreten von Krebserkrankungen in Verbindung gebracht. Das MeCan (Metabolic Syndrome and Cancer) Projekt untersucht diese Zusammenhänge unter Verwendung österreichischer und skandinavischer Kohortendaten. Diese Daten wurden nun in der vorliegenden Studie genutzt, um langfristige Trends in den genannten Risikofaktoren zu untersuchen.

Methoden: Daten aus Gesundenuntersuchungen mit Nüchternblutabnahme im Zeitraum 1975 bis 2004 von insgesamt 239.602 Personen (Alter 25–64 Jahre) wurden für die Schätzung der Prävalenzveränderungen verwendet.

Ergebnisse: Die Prävalenz der Adipositas und der Hyperglykämie zeigte einen deutlichen Anstieg im Untersuchungszeitraum. Die Adipositas stieg dabei um einen Faktor von 1,54 (95% KI: 1,42–1,66) pro Jahrzent bei Männer und um einen Faktor von 1,48 (95% KI: 1,41–1,56) bei Frauen. Noch deutlicher war der Anstieg bei der Hyperglykämie mit einem Anstieg um das 1,62-fache (95% KI: 1,49–1,76) bei Männern und um das 1,66-fache (95% KI: 1,57–1,75) bei Frauen. Bluthochdruck sank um den Faktor 0,71 (95% KI: 0,68–0,74) bei Männern und 0,83 (95% KI: 0,79–0,86) bei Frauen. Die Prävalenz der Hyperlipidämie (gemessen durch Gesamtcholesterin und Triglyceride) stieg bis Ende der achtziger Jahre und ging anschließend zurück. Als Proxy für das Metabolische Syndrom wurde eine Kombination aus drei oder mehr dieser Risikofaktoren untersucht, diese verzeichnete einen moderaten Anstieg um das 1,15-fache (95% KI: 1,08–1,22) bei Männern und um das 1,20–fache (95% KI: 1,15–1,27) pro Dekade bei Frauen.

Schlussfolgerungen: Über die letzten drei Jahrzehnte zeigten sich sowohl in Österreich als auch in Schweden deutliche Umschichtungen in den untersuchten Risikofaktoren. Im Hinblick auf die Prävention von Herzkreislauferkrankungen aber auch Krebserkrankungen verdienen vor allem die besorgniserregenden Entwicklungen bei Übergewicht und Diabetes besondere Aufmerksamkeit.

Summary. *Objectives:* Metabolic factors such as obesity, hypertension, dyslipidemia and hyperglycemia have consistently been associated with increased risk of cardiovascular disease. There is also growing evidence that these factors are linked to cancer incidence and mortality. 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 between 1976 and 2005 were used to estimate prevalence and trends in five risk factors.

Results: Irrespective of geographic location, individual metabolic risk factors showed divergent trends across the observation period. Whereas obesity and hyperglycemia in men increased by a per decade ratio of 1.54 (95% CI: 1.42–1.66) and 1.62 (95% CI: 1.49–1.76), respectively, and in women by 1.48 (95% CI: 1.41–1.56) and 1.66 (95% CI: 1.57–1.75), 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 increased from the 1970s

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to the 1980s but declined in the succeeding decade. A combination of three or more of these risk factors increased significantly in men by a ratio of 1.15 (95% CI: 1.08-1.22) per decade and in women by 1.20 (95% CI: 1.15–1.27).

Conclusion: The study shows that individual metabolic risk factors followed divergent trends over the period of three decades even though the combination of three or more risk factors used as a proxy for the metabolic syndrome appeared to be stable over the last two of the decades. The two key components of the syndrome, namely BMI and glucose levels, increased significantly and deserve professional attention.

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

Introduction

Metabolic factors such as obesity, hypertension, dyslipidemia and hyperglycemia have consistently been associated with increased risk of cardiovascular disease, stroke and diabetes [1–3]. Considerable efforts have been made to combine these factors in different ways as an entity for risk prediction, with the aim of underlining the importance of the combination itself in contrast to its individual components. Since its initial description, multiple definitions have been proposed for this entity, which is denoted the metabolic syndrome [4, 5]. Beyond predicting cardiovascular disease, there is a growing body of literature linking metabolic syndrome and its individual components as risk elements for cancer incidence and mortality [6–13].

Epidemiologic evidence on long-term trends of individual metabolic risk factors is limited. Studies such as the World Health Organization (WHO) MONICA project covering the majority of European countries [14–18] and the National Health and Nutrition Examination Survey (NHANES) in the USA population [19–22] have consistently reported trends of increasing body-mass index (BMI). Published results on blood pressure, cholesterol and triglycerides have been more divergent. The majority of studies have shown a decreasing trend in blood pressure [14, 21–22], although a few studies have detected increasing trends [17–18, 20]. Inconsistent trends have also been observed for cholesterol [15–18, 22] and triglycerides [15, 20]. Smoking, not a risk factor for metabolic syndrome but a major one for cardiovascular disease and cancer, has decreased especially in men in all western industrialized countries [15, 21].

Differences in composition of the populations studied, together with limited length of observation periods and insufficient sample size, may have contributed to the lack of consistent evidence in previous investigations. The analysis reported here is based on a large sample size and an observation period covering 30 years. We aimed to investigate whether temporal trends in metabolic risk factors exist in different cohorts and health surveys across middle and northern Europe.

Materials and methods

The study population

The metabolic syndrome and cancer (Me-Can) collaborative study was initiated in 2006 to create a large pooled cohort for investigation of factors of the metabolic syndrome associated with cancer risk. In our analysis we used three sub-cohorts of the Me-Can study, one cohort from Austria and two from Sweden, with a total of 122,076 men and 117,526 women in the age range 25–64 years. Data from the Vorarlberg Health Monitor-

Table 1. Sociodemographic characteristics of the study population

Cohort	No. of participants			Mean age (SD)[a]	
	men	women	total	men	women
VHM&PP (Austria)					
1976–1985	–	–	–	–	–
1986–1995	42,263	49,094	91,357	42.6 (11.1)	42.8 (11.3)
1996–2005	23,054	21,339	44,393	40.7 (11.0)	39.8 (10.9)
Malmö (Sweden)					
1976–1985	22,241	6,750	28,991	43.7 (6.6)	46.6 (7.7)
1986–1995	–	3,774	3,774	–	54.8 (2.1)
1996–2005	–	–		–	
VIP (Sweden)					
1976–1985	–	–	–	–	–
1986–1995	12,597	14,194	26,791	45.4 (10.4)	45.5 (10.4)
1996–2005	21,921	22,375	44,296	48.8 (8.4)	48.7 (8.5)

[a] Only participants between 25 and 64 years of age were included.

ing and Prevention Program (VHM&PP) were used to show risk factor prevalence for Austria; the Västerbotten Intervention Project (VIP) and the Malmö Preventive Project (MPP) provided data for Sweden. Although not necessarily representative for the whole country, data from the MPP and the VIP were merged in order to cover three decades of risk factor data for Sweden.

The Vorarlberg Health Monitoring and Prevention Program

The VHM&PP is a population-based risk-factor surveillance program in Vorarlberg, the westernmost province in Austria [23–24]. The purpose of the program 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 letter, television, radio and newspapers to participate in a health examination up to once a year. More than two-thirds of the population of the province have participated in the program since 1985. Data from the years 1985–2005 are included in the Me-Can project and during that period the attendance rate in the VHM&PP was 66%, with roughly 176,000 persons participating.

The Västerbotten Intervention Project

The VIP is an ongoing project that aims to prevent diabetes and cardiovascular disease in residents of Västerbotten county in the north of Sweden [25]. Since 1985 all residents have been 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 average attendance rate has been 60% over the years. By the end of 2006, approximately 86,000 men and women had participated in the VIP.

The Malmö Preventive Project

Between 1974 and 1992 middle-aged men and women in the city of Malmö in southern Sweden were invited to a screening program, the MPP, for prevention of cardiovascular disease and alcohol abuse [26, 27]. All residents within predefined birth cohorts, born between 1921 and 1949, were invited. The average attendance rate was 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 similar screening between 1981 and 1989.

Ethical approval

The study was approved by the ethical committees of the respective countries.

Measurements

Measurements included height, weight, systolic and diastolic blood pressure, serum total cholesterol, triglycerides and glucose levels. Anthropometric measurements were made in a similar manner in all cohorts, with participants wearing light indoor clothes and no shoes. Blood pressure was measured using a mercury sphygmomanometer after 5–10 min rest in sitting position in the VHM&PP and in supine position in the VIP the MPP. Serum measurements were performed after an overnight-fast of at least 8 h in all individuals. Glucose levels were determined in serum samples in the VHM&PP and the VIP; in the MPP whole blood was used. For determination of lipids, serum samples were used in all three cohorts. Enzymatic techniques were used for all the assays.

To analyze three or more metabolic risk factors as an entity, we used a modified form of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III) [28] definition based on five commonly measured criteria: waist circumference (replaced by BMI as we lacked data on waist size), 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 ≥30, hypertension defined as systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg, hypercholesterolemia as total cholesterol >6.1 mmol/l, hypertriglyceridemia as triglycerides ≥1.69 mmol/l and fasting hyperglycemia as fasting glucose ≥6.1 mmol/l.

Statistical analysis

Total and region-specific prevalences and means of metabolic risk factors were estimated, by decades, for men and women separately. Trends in metabolic risk factors were assessed using 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 into normal and elevated levels according to standard guidelines as mentioned above. The surveys included few participants over 65 years of age, therefore we restricted our analysis to the age range 25–64 years. To achieve balanced participation conforming to the known population age distribution in this age range, we applied sampling weights for the different cohorts using data from official census records for the respective countries in the respective decade [29, 30]. Sampling weights were calculated for 5-year age groups, separately by sex, decade and region. Results were summarized according to decades and two regions: Austria (VHM&PP) and Sweden (VIP, MPP). SPSS Complex Samples 16.0 (SPSS Inc. Chicago, IL, 2007) software was used for statistical analysis.

Results

Estimated prevalences of metabolic risk factors by regions and by decades are shown for men and women separately in Tables 2 and 3 and in Fig. 1. From the first to the second decade, any combination of three elevated individual risk factors used as a proxy for metabolic syndrome increased from 10.3% to 15.8% in men and from 4.4% to 10.1% in women. There was a very slight decrease from the second to the third decade (down to 14.2% in men, 9.9% in women). Overall, prevalence of the metabolic syndrome increased per decade by a ratio of 1.15 (95% CI: 1.08–1.22) in men and 1.20 (95% CI: 1.15–1.27) in women.

The individual risk factors showed divergent trends across the three decades in both sexes (Fig. 1). The predominant trend was that obesity and impaired fasting glucose showed a strong increasing pattern, whereas blood pressure decreased 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. Risk factor trends in the

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

No. of participants	decades	obesity[a]	hyper-tension	hyper-cholester-olemia	hyper-triglyceri-demia	fasting hyper-glycemia	3 or more factors	smoking
Total								
n = 22,241	1976–1985	6.1[b]	43.0	27.1	26.2	4.7	10.3	47.9
n = 54,860	1986–1995	9.8	35.5	34.7	35.0	8.7	15.8	24.7
n = 44,975	1996–2005	14.1	33.9	25.4	30.7	13.6	14.2	19.8
	OR (95% CI)	1.54 (1.42–1.66)[c]	0.71 (0.68–0.74)	0.87 (0.83–0.91)	0.98 (0.94–1.03)	1.62 (1.49–1.76)	1.15 (1.08–1.22)	0.54 (0.52–0.57)
	P for trend	<0.001	<0.001	<0.001	0.278	<0.001	<0.001	<0.001
Austria								
–	1976–1985	–	–	–	–	–	–	–
n = 42,263	1986–1995	9.7	42.0	34.2	38.7	8.2	16.8	32.2
n = 23,054	1996–2005	14.2	40.5	24.4	34.7	12.6	16.0	25.5
Sweden								
n = 22,241	1976–1985	6.1	43.0	27.1	26.2	4.7	10.3	47.9
n = 12,597	1986–1995	9.8	28.8	34.9	30.1	9.0	13.9	17.8
n = 22,921	1996–2005	13.8	27.2	26.1	26.3	14.2	12.1	14.4

[a] Obesity was defined as BMI ≥ 30, hypertension as systolic blood pressure ≥140 mmHg or diastolic ≥ 90 mmHg, hypercholesterolemia > 6.1 mmol/l, hypertriglyceridemia ≥1.69 mmol/l and hyperglycemia > 6.1 mmol/l; [b] Percentages estimated using region-, decade- and sex-specific 5-year age-group sampling weights (complex samples); [c] Ratio of change per decade, estimated from logistic regression models for complex samples adjusted for age, region, smoking and BMI where appropriate.

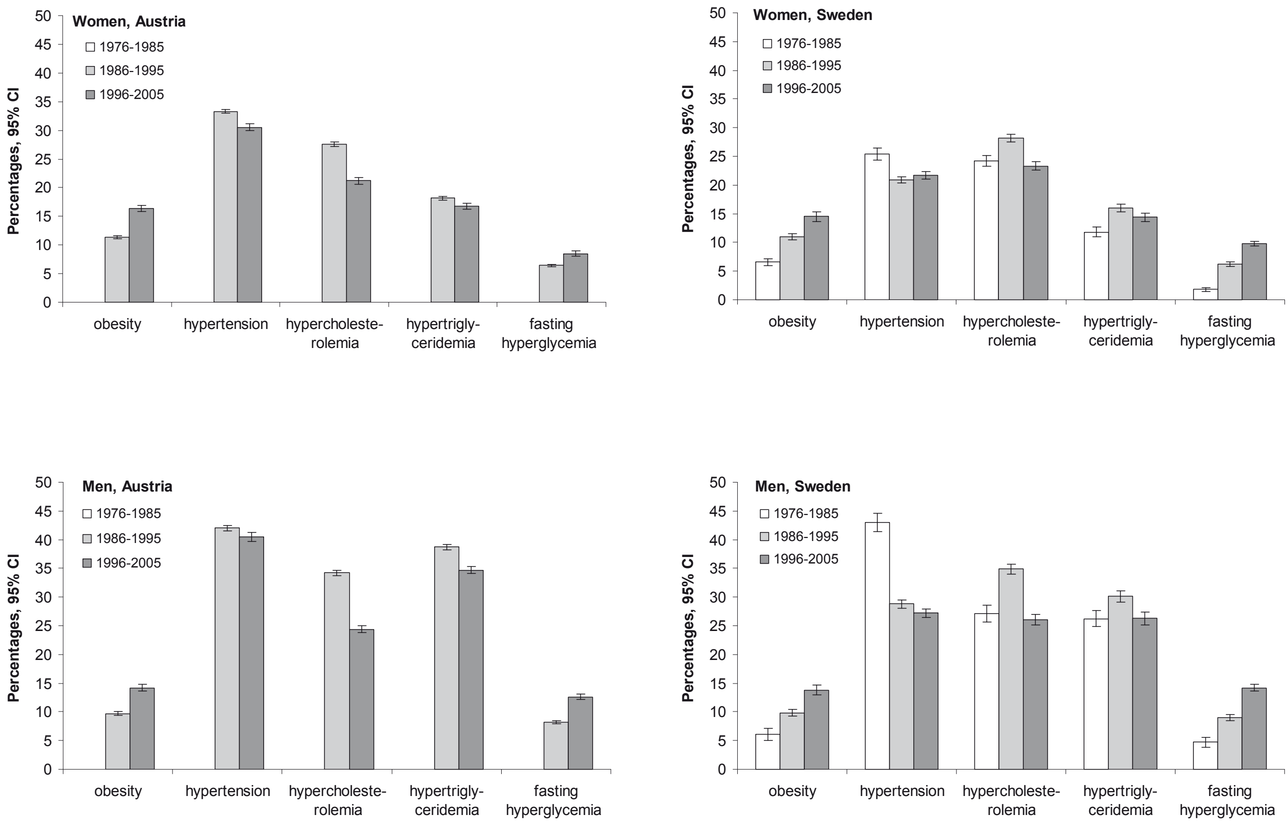

Fig. 1. Prevalence and 95% CI of obesity (BMI ≥30), hypertension (systolic blood pressure ≥140 mmHg or diastolic ≥90 mmHg), hypercholesterolemia (total cholesterol >6.1 mmol/l), hypertriglyceridemia (triglycerides ≥1.69 mmol/l) and hyperglycemia (fasting glucose >6.1 mmol/l) by decades in women and men, aged 25–64 years, Austria, Sweden

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

No. of partici-pants	decades	obesity[a]	hyper-tension	hyper-cholester-olemia	hyper-triglyceri-demia	fasting hyper-glycemia	3 or more factors	smoking
Total								
n = 6750	1976–1985	6.6[b]	25.4	24.2	11.8	1.8	4.4	39.7
n = 67,062	1986–1995	11.4	27.7	28.0	17.4	6.4	10.1	23.2
n = 43,714	1996–2005	15.6	26.5	22.6	15.7	9.3	9.9	17.9
	OR (95% CI)	1.48 (1.41–1.56)[c]	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								
–	1976–1985	–	–	–	–	–	–	–
n = 49,094	1986–1995	11.4	33.3	27.6	18.2	6.4	10.9	23.5
n = 21,339	1996–2005	16.3	30.5	21.2	16.7	8.5	10.6	18.4
Sweden								
n = 6750	1976–1985	6.6	25.4	24.2	11.8	1.8	4.4	39.7
n = 17,968	1986–1995	11.0	20.9	28.2	16.0	6.2	8.6	23.4
n = 22,375	1996–2005	14.5	21.7	23.3	14.4	9.8	8.7	17.7

[a] Obesity was defined as BMI ≥30, hypertension as systolic blood pressure ≥140 mmHg or diastolic ≥90 mmHg, hypercholesterolemia >6.1 mmol/l, hypertriglyceridemia ≥1.69 mmol/l and hyperglycemia >6.1 mmol/l; [b] Percentages estimated using region-, decade-and sex-specific 5-year age-group sampling weights (complex samples); [c] Ratio of change per decade, estimated from logistic regression models for complex samples adjusted for age, region, smoking and BMI where appropriate.

sub-regions were similar to the overall trends with the exception of hypertension, which decreased less pronouncedly in the Austrian survey than in the two Swedish surveys.

Trends in estimated means roughly confirmed the results of categorized risk factors. Mean BMI and fasting glucose values for both regions increased significantly, whereas diastolic blood pressure decreased and average cholesterol level remained stable (Tables 4, 5). However, mean systolic blood pressure did not change significantly, pointing to the possibility that the decrease in prevalence of hypertension over the years was mainly due to control of diastolic 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 have followed divergent patterns across the past three decades (1976–2005). Whereas BMI and glucose levels increased uniformly, blood pressure and smoking decreased. Trends in blood lipids followed a non-linear pattern. Our findings on obesity are in agreement with all major studies in western industrialized countries [16–17, 31–32]. Similar obesity prevalence was reported for the European countries of the WHO MONICA project, albeit spanning a shorter time-period [16]. Although the magnitude of the increase in obesity is markedly higher in the USA, where the NHANES surveys showed that the age-adjusted prevalence of obesity (BMI ≥30) 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 white Americans in the same period [33], the direction of the trends is similar in our findings.

Our results for glucose, blood pressure and total cholesterol are also consistent with the reports from MONICA and NHANES. It has been argued recently that the forces driving these trends operate at the population level rather than the individual level, because the trends occur across the percentile distribution [15, 32]; the inter-country evidence we present here further supports that contention. For hypertension, however, the few studies performed report conflicting outcomes [17, 21, 34]. This is a risk factor that can be strongly dependent on clinical 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 an increased likelihood of classifying individuals as hypertensive, as also seen elsewhere [35]. In addition, it has been suggested that both systolic and diastolic blood pressures at baseline are significantly higher in sitting position than in supine position in both volunteers and hypertensive patients [36]. This could partly be the case in our study, where the blood pressure values were higher in the Austrian cohorts than in the Swedish ones.

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 [16].

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

cohort	decades[b]	BMI	systolic blood pressure, mmHg	diastolic blood pressure, mmHg	total cholesterol, mmol/l	triglycerides, mmol/l	fasting glucose, mmol/l
Total							
n = 22,241	1976–1985	24.5 (24.4–24.7)[a]	128.4 (127.7–129.0)	85.0 (84.7–85.5)	5.6 (5.5–5.6)	1.5 (1.4–1.5)[c]	5.1 (5.0–5.2)
n = 54,860	1986–1995	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	1996–2005	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[b]	0.011	<0.001	<0.001	0.24	<0.001
Austria							
–	1976–1985	–	–	–	–	–	–
n = 42,263	1986–1995	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	1996–2005	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							
n = 22,241	1976–1985	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	1986–1995	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	1996–2005	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)

[a] Means (95% CI) estimated using region-, decade- and sex-specific 5-year age-group sampling weights (complex samples); [b] Effect of decade (*P* for trend) was tested in linear regression analyses for complex samples adjusted for age, region, smoking and BMI where appropriate. In case of non-linear pattern (lipids), *P*-values were given comparing 3rd versus 1st decade; [c] Triglycerides were log-transformed, means thus obtained represent geometric means.

Prevalence of the metabolic syndrome is strongly influenced by the differing definitions proposed by the WHO, the NCEP and the International Diabetic Federation [28]. Definitions that overweight glucose lead to increasing trends, whereas other definitions show stable or even decreasing trends. Notably, although some risk factor trends were downwards and some conversely upwards, the net pattern for presence of three or more metabolic risk factors reached a plateau in the last decade of our analysis. Nevertheless, the overall increasing tendency towards metabolic syndrome was similarly observed in the NHANES surveys in the USA, where the ATP III definition was also used [20].

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 the colorectum, endometrium, pancreas, kidney, gallbladder, thyroid and esophagus [7–9]. Furthermore, obesity was shown to be associated with high mortality in prostate and breast cancers [10, 11]. High glucose levels were also linked to an increased overall risk of cancer [12–13].

Our study had several strengths and potential limitations that should be considered. Major strengths were the large sample size, length of observation period and the comparable protocols for the middle and northern European health surveys that were used in assessing the data.

The lack of data for waist circumference and HDL cholesterol limited us from drawing conclusions about temporal trends in metabolic syndrome according to its most recent definition [2].

In general, measurements were very similar in the three cohorts, but there were some exceptions. Glucose was determined in serum samples in the VHM&PP and VIP and in whole blood in the MPP; in addition, blood pressure was measured in the sitting position in the VHM&PP and in supine position in the VIP and MPP. These differences may well affect our results, although we think it would be to a minor extent. A further limitation of the study was the inability to examine the effect of treatment, mainly of high blood pressure, cholesterol and diabetes. The database itself does not have treatment information; however, prescribing patterns are available in part for the study regions and periods. The EuroMedStat group recently showed that statin utilization in treatment of hypercholesterolemia is higher in Sweden than in Austria [37]; however, given the similar trends for blood lipids in the two regions, this suggests that there are other, population-level, factors involved. In addition, we were unable to account for the effect of behavioral changes on diet, alcohol consumption and physical activity.

This study showed that trends for individual metabolic risk factors diverged over a period of three decades, 1976–2005, even though a combination of three or more of the factors appeared to be stable over the last two of the decades. Key components of the metabolic

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

cohort	decades[b]	BMI, kg/sqm	systolic blood pressure, mmHg	diastolic blood pressure, mmHg	total cholesterol, mmol/l	triglycerides, mmol/l	fasting glucose, mmol/l
Total							
n = 6750	1976–1985	23.4 (23.2–23.5)[a]	121.2 (120.7–121.7)	80.6 (80.3–80.9)	5.5 (5.5–5.5)	1.1 (1.1–1.1)[c]	4.8 (4.7–4.8)
n = 67,062	1986–1995	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	1996–2005	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[b]	0.512	<0.001	<0.001	0.288	<0.001
Austria							
–	1976–1985	–	–	–	–	–	–
n = 49,094	1986–1995	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	1996–2005	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 = 6750	1976–1985	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	1986–1995	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	1996–2005	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)

[a] Means (95% CI) estimated using region-, decade- and sex-specific 5-year age-group sampling weights (complex samples); [b] Effect of decade (*P* for trend) was tested in linear regression analyses for complex samples adjusted for age, region, smoking and BMI where appropriate. In case of non-linear pattern (lipids), *P*-values were given comparing 3rd versus 1st decade; [c] Triglycerides were log-transformed, means thus obtained represent geometric means.

syndrome, namely BMI and glucose levels, increased significantly and require widespread recognition by policy makers and those concerned with promotion of health and prevention of disease.

Conflict of Interest
The authors declare that there is no conflict of interest.

Funding Sources
Our research was supported by the World Cancer Research Fund International (to P.S.) and grant no. OENB-12737 the Austrian National Bank (to H.U.).

References

1. Ford ES (2005) Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: a summary of the evidence. Diabetes Care 28: 1769–1778
2. Lorenzo C, Williams K, Hunt KJ, Haffner SM (2007) The National Cholesterol Education Program – Adult Treatment Panel III, International Diabetes Federation, and World Health Organization definitions of the metabolic syndrome as predictors of incident cardiovascular disease and diabetes. Diabetes Care 30: 8–13
3. Bergovec M, Reiner Z, Miličić D, Vražić H (2008) Differences in risk factors for coronary heart disease in patients from continental and Mediterranean regions of Croatia. Wien Klin Wochenschr 120: 684–692
4. Daskalopoulou SS, Athyros VG, Kolovou GD, Anagnostopoulou KK, Mikhailidis DP (2006) Definitions of metabolic syndrome: Where are we now? Curr Vasc Pharmacol 4: 185–197
5. Li C, Ford ES (2006) Definition of the metabolic syndrome: What's new and what predicts risk? Metab Syndr Relat Disord 4: 237–251
6. Cowey S, Hardy RW (2006) The metabolic syndrome: a high-risk state for cancer? Am J Pathol 169: 1505–1522
7. Lukanova A, Björ O, Kaaks R, Lenner P, Lindahl B, Hallmans G, et al (2006) Body mass index and cancer: results from the Northern Sweden Health and Disease Cohort. Int J Cancer 118: 458–466
8. Rapp K, Schroeder J, Klenk J, Stoehr S, Ulmer H, Concin H, et al (2005) Obesity and incidence of cancer: a large cohort study of over 145,000 adults in Austria. Br J Cancer 93: 1062–1067
9. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M (2008) Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 371 (9612): 569–578
10. MacInnis, RJ, English DR (2006) Body size and composition and prostate cancer risk: systematic review and meta-regression analysis. Cancer Causes Control 17: 989–1003
11. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 348: 1625–1638
12. Manjer J, Kaaks R, Riboli E, Berglund G (2001) Risk of breast cancer in relation to anthropometry, blood pressure, blood lipids and glucose metabolism: a prospective study within the Malmö Preventive Project. Eur J Cancer Prev 10: 33–42
13. Rapp K, Schroeder J, Klenk J, Ulmer H, Concin H, Diem G, et al (2006) Fasting blood glucose and cancer risk in a cohort of more than 140,000 adults in Austria. Diabetologia 49: 945–952
14. Tunstall-Pedoe H, Connaghan J, Woodward M, Tolonen H, Kuulasmaa K (2006) Pattern of declining blood pressure across replicate population surveys of the WHO MONICA project, mid-1980s to mid-1990s, and the role of medication. BMJ 332 (7542): 629–635
15. Berg CM, Lissner L, Aires N, Lappas G, Toren K, Wilhelmsen L, et al (2005) Trends in blood lipid levels, blood pres-

sure, alcohol and smoking habits from 1985 to 2002: results from INTERGENE and GOT-MONICA. Eur J Cardiovasc Prev Rehabil 12: 115–125
16. Evans A, Tolonen H, Hense HW, Ferrario M, Sans S, Kuulasmaa K (2001) Trends in coronary risk factors in the WHO MONICA project. Int J Epidemiol 30 [Suppl 1]: 35–40
17. Basterra-Gortari FJ, Bes-Rastrollo M, Seguí-Gómez M, Forga L, Martínez JA, Martínez-González MA (2007) Trends in obesity, diabetes mellitus, hypertension and hypercholesterolemia in Spain (1997–2003). Med Clin (Barc) 129: 405–408
18. Serra-Majem L, Pastor-Ferrer MC, Castell C, Ribas-Barba L, Román-Viñas B, Ribera LF, et al (2007) Trends in blood lipids and fat soluble vitamins in Catalonia, Spain (1992–2003). Public Health Nutr 10: 1379–1388
19. Ford ES, Giles WH, Dietz WH (2002) Prevalence of metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. JAMA 287: 356–359
20. Ford ES, Giles WH, Mokdad AH (2004) Increasing prevalence of metabolic syndrome among US adults. Diabetic Care 27: 2444–2449
21. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al (2005) Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA 293: 1868–1874
22. Goff DC, Howard G, Russell GB, Labarthe DR, et al (2001) Birth cohort evidence of population influences on blood pressure in the United States. Ann Epidemiol 11: 271–279
23. Ulmer H, Kelleher C, Diem G, Concin H (2003) Long-term tracking of cardiovascular risk factors among men and women in a large population-based health system: the Vorarlberg Health Monitoring & Promotion Programme. Eur Heart J 24: 1004–1013
24. Ulmer H, Kelleher C, Diem G, Concin H, Ruttmann E (2004) Estimation of seasonal variations in risk factor profiles and mortality from coronary heart disease. Wien Klin Wochenschr 116: 662–668
25. Lindahl B, Weinehall L, Asplund K, Hallmans G (1999) Screening for impaired glucose tolerance. Results from a population-based study in 21,057 individuals. Diabetes Care 22: 1988–1992
26. Berglund G, Eriksson KF, Israelsson B, Kjellström T, Lindgärde F, Mattiasson I, et al (1996) Cardiovascular risk groups and mortality in an urban Swedish male population: the Malmo Preventive Project. J Intern Med 239: 489–497
27. Berglund G, Nilsson P, Eriksson KF, Nilsson JA, Hedblad B, Kristenson H, et al (2000) Long-term outcome of the Malmo preventive project: mortality and cardiovascular morbidity. J Intern Med 247: 19–29
28. Grundy SM, Brewer HB Jr, Cleeman JI, Smith SC Jr, Lenfant C (2004) Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association conference on scientific issues related to definition. Circulation 109: 433–438
29. Statistik Austria-Statistiken www.statistik.at/. Accessed 2009.01.10
30. Statistics Sweden. www.scb.se/default____2154.asp. Accessed 2009.01.10
31. Ulmer H, Diem G, Bischof HP, Ruttmann E, Concin H (2001) Recent trends and sociodemographic distribution of cardiovascular risk factors: results from two population surveys in the Austrian WHO CINDI demonstration area. Wien Klin Wochenschr 113: 573–579
32. Ulmer H, Kelleher CC, Fitz-Simon N, Diem G, Concin H (2007) Secular trends in cardiovascular risk factors: an age-period cohort analysis of 698,954 health examinations in 181,350 Austrian men and women. J Intern Med 261: 566–576
33. Okosun IS, Chandra KM, Boev A, Boltri JM, Choi ST, Parish DC, et al (2004) Abdominal adiposity in U.S. adults: prevalence and trends, 1960–2000. Prev Med 39: 197–206
34. Park HS, Kim SM, Lee JS, Lee J, Han JH, Yoon DK, et al (2007) Prevalence and trends of metabolic syndrome in Korea: Korean National Health and Nutrition Survey 1998–2001. Diabetes Obes Metab 9: 50–58
35. Broad J, Wells S, Marshall R, Jackson R (2007) Zero end-digit preference in recorded blood pressure and its impact on classification of patients for pharmacologic management in primary care – PREDICT-CVD-6. Br J Gen Pract 57: 897–903
36. Malhotra S, Malhotra AS, Pandhi P (2000) Supine versus sitting blood pressure in healthy volunteers and hypertensive patients before and after calcium antagonist treatment. Indian J Physiol Allied Sci 54: 27–33
37. Walley T, Folino-Gallo P, Stephens P, Van Ganse E (2005) Trends in prescribing and utilization of statins and other lipid lowering drugs across Europe 1997–2003. Br J Clin Pharmacol 60: 543–551