Differences in trends in estimated incidence of myocardial infarction in non-diabetic and diabetic people: Monitoring Trends and Determinants on Cardiovascular Diseases (MONICA)/Cooperative Health Research in the Region of Augsburg (KORA) registry

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Abstract

Aims/hypothesis One major objective of the St Vincent Declaration was to reduce the excess risk of myocardial infarction in patients with diabetes mellitus. We estimated the trend of the incidence and relative risk of myocardial infarction in the diabetic and non-diabetic populations in southern Germany from 1985 to 2006.

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Methods Using data from the Monitoring Trends and Determinants on Cardiovascular Diseases (MONICA)/Cooperative Health Research in the Region of Augsburg (KORA) Project in southern Germany, we ascertained all fatal and non-fatal first myocardial infarctions between 1985 and 2006 ($n=14,891$, age 25–74 years). We estimated the diabetic and the non-diabetic populations using data on diabetes prevalence from surveys, and evaluated incidence of myocardial infarction in the two estimated populations. To test for time trends, we fitted Poisson regression models.

Results Of individuals with first myocardial infarction, 71% were male and 28% known to have diabetes. In the non-diabetic population, myocardial infarction incidence decreased by about 1.5% to 2.0% per year. A comparable decrease was seen in the population of diabetic women. However, in the population of diabetic men, incidence of myocardial infarction increased by about 1% per year. Over the whole study period, myocardial infarction incidence decreased by 34% and 27% in non-diabetic men and women respectively (RR 0.66, 95% CI 0.59–0.74 and 0.73, 0.62–0.87 respectively). In diabetic women, it decreased by 27% (RR 0.73, 0.61–0.88), whereas in diabetic men, it increased by 25% (RR 1.25, 1.07–1.45).

Conclusions/interpretation Our results suggest that the St Vincent goal of reducing excess cardiovascular morbidity in diabetic individuals has not been achieved and that the situation in men has actually got worse.

Keywords Diabetic and non-diabetic population · Myocardial infarction · MONICA registry · Trend

Abbreviations

KORA	Cooperative Health Research in the Region of Augsburg
MI	Myocardial infarction
MONICA	Monitoring Trends and Determinants on Cardiovascular Diseases

Introduction

In 1989, the St Vincent Declaration defined a number of major targets for the improvement of diabetes care [1]. As several studies have confirmed an increased risk of CHD and cardiovascular disease events in people with diabetes [2, 3], narrowing of the gap in cardiovascular morbidity between the diabetic and non-diabetic populations was one of the primary objectives [1]. Several studies from western Europe and the USA indicate that incidence of CHD and cardiovascular events, e.g. MI, is declining [4]. However, it is unknown whether the decline in cardiovascular events has also been observed in people with diabetes or whether the gap between the diabetic and non-diabetic populations has narrowed.

Several studies have examined the secular trends in cardiovascular mortality in people with and without diabetes [5–10], but few have been able to compare cardiovascular event rates. Analyses from Norway and the US have been based on cross-sectional surveys or hospital discharge data [11, 12]. Only one study to date has evaluated the trend of MI incidence in diabetic and non-diabetic individuals, finding favourable trends in the latter, but not in diabetic individuals [13].

In Germany from 1985 to 1994, the incidence of MI in 25- to 74-year-old diabetic individuals was found to have increased 3.7-fold in men and 5.9-fold in women, compared with non-diabetic individuals in the same age range [14]. Several efforts have been undertaken in Germany to improve diabetes treatment and thus reduce cardiovascular morbidity in diabetic individuals, but it is unknown whether MI risk in diabetic compared with non-diabetic individuals has changed. Thus, the aim of our study was to estimate time trends for the incidence of MI in diabetic and non-diabetic individuals in a region of southern Germany using a population-based registry. The study is part of an ongoing initiative in Germany, aiming to evaluate all six St Vincent objectives, i.e. (in addition to MI incidence) reduction of amputation, blindness, end-stage renal disease, stroke and worse pregnancy outcomes.

Methods

Study population and data assessment We used data from Monitoring Trends and Determinants on Cardiovascular

diseases (MONICA)/Cooperative Health Research in the Region of Augsburg (KORA) population surveys and from the MONICA/KORA myocardial infarction registry in Augsburg, Germany, to define the diabetic and non-diabetic population background and to identify cases with fatal or non-fatal MI. Augsburg and its surrounding areas have a total population of about 600,000. The population-based Augsburg Coronary Event Registry was implemented in October 1984 as part of the WHO MONICA project [15–18]. Since 1996 the registry has been run within the framework of KORA. All cases of CHD deaths and non-fatal MI in the 25- to 74-year-old study population in Augsburg and the Augsburg and Aichach-Friedberg regions (about 400,000 inhabitants) are continuously registered [19]. Data sources for hospitalised patients include eight hospitals within the study region and two hospitals in adjacent areas. Methods of case-finding, diagnostic classification of events and data quality control have been described elsewhere [15, 17]. Up to 31 December 2000 non-fatal MI was registered on the basis of diagnostic criteria in the WHO-based MONICA protocol [15]. Since 1 January 2001 all patients with MI diagnosed according to European Society for Cardiology and American College of Cardiology criteria, including troponin measurement, have also been registered [20]. Briefly, patients surviving for at least 24 h (non-fatal MI) were interviewed while in hospital using a standardised questionnaire and further data were gathered in a concluding chart review. CHD deaths were identified through the regional health offices by checking all death certificate diagnoses giving suspected CHD as main cause of death. In addition, a written questionnaire was routinely sent to the last physician to treat the deceased person and to the coroner to establish disease history, risk factors, prior medication and circumstances of death (mean response 85%). MONICA diagnostic criteria define early CHD death as CHD deaths occurring before admission to hospital or within 24 h of hospitalisation. For this analysis, we only used the first infarction per patient.

In addition we also used data from four population-based surveys conducted in the Augsburg region between 1984 and 2001 (1984/85, 1989/90, 1994/95 and 1999/2001). The survey population was in the 25 to 74 years age range and was surveyed using cluster sampling procedures [19]. The response rate was between 68 and 79%. Diabetes was assessed by self-report of a physician's diagnosis of diabetes or by use of glucose-lowering medication. The diabetes prevalence was 3.7% to 4.6% in men and 3.5% to 3.7% in women. No significant time trend was found [21], corresponding to findings for the whole of Germany [22].

Statistical analysis The main analyses were performed separately for each sex.

We stratified the study population in three layers according to age (25–54, 55–64 and 65–74 years of age), sex and calendar year (1985–2006). The population with diabetes in each resulting stratum was estimated by obtaining the population of each stratum within the study area from the regional statistic office and multiplying this by the age- and sex-specific prevalence of diabetes, obtained from the four MONICA/KORA surveys that were carried out in 1984, 1989, 1994 and 1999/2000. As no significant time trend in diabetes prevalence was evident [21], the averaged estimate for diabetes prevalence over the four surveys was used. For men in the age groups 25 to 54, 55 to 64 and 65 to 74 years, diabetes prevalence was: 1.6% (95% CI 0.6–2.6), 7.9% (6.2–9.6) and 10.7% (10.1–11.4), respectively; for women (same age groups) it was: 1.2% (0.4–2.0), 6.7% (6.0–7.3) and 10.2% (6.6–13.7).

Stratum-specific and directly standardised incidence rates of MI (standard population: West German population 1987) were estimated for each calendar year for the total, estimated diabetic and estimated non-diabetic populations, respectively.

To test for time trends, we first fitted separate (sex-specific) Poisson regression models with incidence of MI as dependent variable for diabetic and non-diabetic individuals, using year of MI diagnosis registration (linear continuous difference from baseline year 1985) and age (three strata) as independent variables. Next, and in addition, we fitted similar common Poisson regression models to the entire population. In these models, an additional variable was included for diabetes, as well as an interaction term for diabetes and years since 1985. Finally, we evaluated differences in incidence trends between younger and older individuals (25–64 vs 65–74 years of age) by including interaction terms for age group with year difference from baseline. These analyses were again performed separately for each sex and for diabetes and non-diabetes status.

To take into account overdistribution of the dependent variable, we performed all analyses using de-scale adjustment [23]. All analyses were performed using Statistical Analysis Systems (SAS for Windows 2000, Release 9.1; SAS Institute, Cary, NC, USA).

Results

Between 1985 and 2006, 14,891 individuals with a first MI were registered. We excluded 313 individuals as their diabetes status was not known. Of the remaining 14,578 individuals with MI, 71% were men and 28% were known to have diabetes mellitus. Characteristics of individuals with MI are shown in Table 1. The majority of MIs occurred in the elderly. Mean ages at diagnosis were higher

Table 1 Description of the MI population, Augsburg, MONICA region, 1985–2006

Variables	Men		Women	
	Diabetes	No diabetes	Diabetes	No diabetes
<i>n</i>	2,635	7,694	1,497	2,752
Mean age, years (SD)	63.3 (8.2)	59.9 (9.9)	66.8 (6.7)	64.2 (8.8)
Age groups (%)				
25–54 years	15.3	28.4	6.3	14.9
55–64 years	32.7	33.2	21.7	26.1
65–74 years	52.0	38.4	71.9	59.0

in women than in men and in diabetic than in non-diabetic patients.

Incidence of myocardial infarction and relative risks Figure 1 shows the standardised incidence rates for each year. There were brief oscillations, in particular in men. Over the whole study period, MI incidence declined in non-diabetic men and women, as well as in diabetic women; in diabetic men, MI incidence increased. In women, the RR of MI in the diabetic compared with the non-diabetic population (expressed as comparative incidence figures from direct standardisation) ranged from 5.11 (95% CI 3.41–7.67) in 2003 to 11.46 (7.82–16.81) in 2001, with no significant trend during the study period. In men, RR was between 3.71 (2.71–5.09) in 1987 and 8.86 (6.90–11.37) in 2000, increasing significantly during the observation period ($p<0.001$).

Trend results from the Poisson regression are given in Table 2. Models 1a and 1b present RRs in the diabetic and the non-diabetic populations. In the latter, we found an estimated decrease of MI of about 1.5% to 2.0% per year. In diabetic women, there was a comparable decrease. In diabetic men, by contrast, the incidence of MI increased by about 1% per year. The interaction between diabetes and calendar year trend was significant in men, as can be seen in Model 2 ($p<0.001$) (Table 2).

The increase of MI in diabetic men was particularly marked in the age groups up to 64 years, but not in 65 to 74-year-old individuals, with RRs per age group as follows: 25–54 years: RR 1.02, 95% CI 1.01–1.04; 55–64 years: RR 1.02, 1.01–1.03; 65–74 years: RR 1.00, 0.99–1.01; however, the interaction between incidence trend and age was not quite significant ($p=0.06$).

Over the whole study period, the incidence of MI decreased by 34% and 27% in non-diabetic men and women (RR 0.66, 0.59–0.74 and 0.73, 0.62–0.87), respectively. In diabetic women, it decreased by 27% (RR 0.73, 0.61–0.88), whereas in diabetic men it increased by 25% (RR 1.25, 1.07–1.45).

Fig. 1 Age-standardised incidence of MI in diabetic (top rows) and non-diabetic (bottom rows) participants, MONICA/KORA Augsburg 1985–2006, in (a) men and (b) women. Values were standardised to the German standard population

Discussion

Study findings and implications Our study is part of an evaluation of how well the St Vincent objectives have been met in Germany. In southern Germany, between 1985 and 2006, we found a significant decrease in the incidence of MI in non-diabetic men and women. In diabetic women, the incidence of MI also decreased significantly, whereas in diabetic men it increased significantly. Correspondingly, the RR for MI in the diabetic compared with the non-diabetic population remained stable in women, but increased in men. Thus, despite national programmes designed to improve

diabetes care, e.g. disease management programmes, the reduction of excess cardiovascular morbidity in diabetic individuals as a declared main objective in the St Vincent declaration [1] has not been achieved. This applies in particular for diabetic men, in whom RR for MI was actually higher, especially in the younger and middle-aged age groups.

Speculating on the possible reasons, it is possible that trends in the prevalence of MI risk factors, e.g. obesity, or trends in healthcare for cardiovascular diseases were different for diabetic vs non-diabetic men. However, we were unable to find any such explanations in the Augsburg populations. Overall, the prevalence of obesity increased, whereas hypertension and dyslipidaemia tended to decrease [24]. The use of glucose-lowering, as well as antihypertensive and lipid-lowering agents increased in diabetic men and women [25]. Moreover, other changes in diagnostic or therapeutic strategies that possibly affect men and women differently may also have occurred. As diabetes mellitus is more frequent in women than men, the interaction between diabetes mellitus and CHD in men may have received less attention during the study period, but our analysis found no evidence for this in the study region.

Comparison with other studies Whereas a number of studies have evaluated the trend of cardiovascular mortality rates in diabetic and non-diabetic individuals [7, 9, 10], only a few have looked at event rates. In Norway, the percentage of diabetic and non-diabetic individuals with a history of MI did not change between 1984 and 1997; however, the results were based on self-reports from two cross-sectional surveys [12]. In the USA, a sharp increase in the number of diabetic patients hospitalised for MI was observed between 1988 and 2002, but the study was based on hospital discharge data and MI incidence in the diabetic and non-diabetic populations was not analysed [11]. Only one study has analysed the trend of MI incidence [13]. In contrast to our study, it found that the incidence of first MI decreased only in non-diabetic men, with a decline in the incidence of first MI seen neither in non-diabetic women, nor in diabetic men or women. Thus this Swedish study also showed a worsening in diabetic men as compared with diabetic women. Compared with Germany, the RRs for MI in diabetic compared with non-diabetic individuals were much higher in Sweden (RR approx. 8 and 15 for men and women, respectively) [13]. The authors of this study also failed to find an explanation for their findings. They speculate that diabetes as such may have a strong influence and is an independent risk factor for cardiovascular diseases, and that a residual risk remains despite improvements of other risk factors due to preventive interventions. However, this would not explain the differences between men and women. Interestingly, another Swedish study, which evaluated the trend of excess mortality rates ascribed

Table 2 Results of Poisson models: relative risks for MI, Augsburg MONICA region, 1984–2006

Variables	Relative risk for MI (95% CI)	
	Men	Women
Model 1a (diabetic)		
Calendar year	1.01 (1.00–1.02)*	0.99 (0.98–0.99)*
Age (years) ^a		
55–64	1.73 (1.52–1.98)*	2.17 (1.71–2.79)*
65–74	3.05 (2.70–3.47)*	5.48 (4.41–6.90)*
Model 1b (non-diabetic)		
Calendar year	0.98 (0.98–0.99)*	0.99 (0.98–0.99)*
Age (years) ^a		
55–64	4.97 (4.58–5.40)*	6.61 (5.64–7.76)*
65–74	9.07 (8.37–9.83)*	18.00 (15.65–20.79)*
Model 2		
Calendar year	0.98 (0.97–0.99)*	0.99 (0.98–0.99)*
Diabetes mellitus	3.30 (2.74–3.95)*	6.38 (5.36–7.58)*
Age (years) ^a		
55–64	4.36 (3.94–4.82)*	5.76 (4.95–6.72)*
65–74	7.80 (7.07–8.61)*	15.19 (13.24–17.49)*
Diabetes × calendar year	1.03 (1.01–1.04)*	1.00 (0.99–1.01)

^a Baseline: 25–54 years* $p < 0.05$

to diabetes, found the trend to be more advantageous in women than in men. The authors suggest that this might be explained by the greater willingness of women to follow their doctors' advice or by the fact that diabetic women smoke less than male counterparts [26].

Study limitations A number of limitations have to be considered. First, the results of our study are dependent on the estimates of the number of diabetic individuals in the background population and are based on the assumption that diabetes prevalence remained stable over time. There is evidence that this assumption is valid, since no significant change in diabetes prevalence was found in repeat surveys [21] or in other German surveys [22]. However, participation in these surveys decreased with diabetic individuals more likely to be non-participants [27]. Furthermore, a number of individuals are likely to have undiagnosed diabetes [27]. It is possible that the prevalence of undiagnosed diabetes decreased during the study period, due to higher disease awareness and diabetes screening. However, we have no data to suggest that these phenomena, if present, would explain the different trends in men and women. Nevertheless, we cannot rule out the possibility of bias.

Second, we did not include clinical variables, because in individuals with fatal MI (39% of all MIs), these data are based on the patients' medical history and documentation of their routine clinical care.

Third, the definition of MI changed in 2000, since troponin measurement was included in the criteria list. This might have led to an inclusion of 'milder' MI cases [28] and such cases might be unevenly distributed in diabetic and non-diabetic individuals, or in men and women. However, when for 2001 to 2004 only MI cases with creatinine kinase of >300 U/l (an indicator for MI severity) were included, the diabetes prevalence was not significantly lower (27% vs 29%), with no relevant difference between men and women (data not shown). In patients who died before reaching the hospital, the new definition is not applicable. Thus, there is no evidence that the changed definition could have affected diabetic or non-diabetic individuals or men and women in a substantially different way; the RRs therefore should be unbiased.

Fourth, in diabetic and non-diabetic men, the time trend was not linear (significant test on non-linearity, data not shown). Over short time periods, the increases and decreases were within the statistical uncertainties. We consider these non-linearities to be due to brief oscillations and not to structural deviations from an increase (non-diabetic men) or decrease (diabetic men) of the incidence course over time.

Fifth and last, we limited our analysis to individuals between 25 and 74 years of age, although many patients with MI and a large proportion of patients with diabetes are above this upper limit. However, the population-based surveys used as data source were limited to this age group and we preferred to use the region-specific estimates of diabetes prevalence from these well established KORA surveys.

Conclusions With regard to the objectives of the St Vincent Declaration, we found a decrease in incidence of first MI in the estimated populations of non-diabetic men, non-diabetic women and diabetic women. However, in the estimated population of diabetic men, especially in younger age groups, incidence was increased. Thus, our results suggest that the St Vincent goal of reducing excess cardiovascular morbidity in diabetic individuals has not been achieved and that the situation in men has actually become worse.

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Duality of interest The authors declare that there is no duality of interest associated with this manuscript.

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