ORIGINAL PAPER

Improving care of post-infarct patients: effects of disease management programmes and care according to international guidelines

Renee Stark · Inge Kirchberger · Matthias Hunger · Margit Heier · Reiner Leidl · Wolfgang von Scheidt · Christa Meisinger · Rolf Holle

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Abstract

Background Cardiac disease management programmes (CHD-DMPs) and secondary cardiovascular prevention guidelines aim to improve complex care of post-myocardial infarction (MI) patients. In Germany, CHD-DMPs, in addition to incorporating medical care according to guidelines (guideline-care), also ensure regular quarterly follow-up. Thus, our aim was to examine whether CHD-DMPs increase the frequency of guideline-care and whether CHD-DMPs and guideline-care improve survival over 4 years.

Methods The study included 975 post-MI patients, registered by the KORA-MI Registry (Augsburg, Germany), who completed a questionnaire in 2006. CHD-DMP enrolment was reported by physicians. Guideline-care was based on patient reports regarding medical advice (smoking, diet, or exercise) and prescribed medications (statins and platelet aggregation inhibitors plus beta-blockers or renin-angiotensin inhibitors). All-cause mortality until

R. Stark $(\boxtimes) \cdot M$. Hunger $\cdot R$. Leidl $\cdot R$. Holle Institute for Health Economics and Healthcare Management, Helmholtz Zentrum München, Neuherberg, Munich, Germany e-mail: r.stark@helmholtz-muenchen.de

I. Kirchberger · M. Heier · C. Meisinger Institute of Epidemiology II, Helmholtz Zentrum München, Neuherberg, Munich, Germany

R. Leidl

Department of Health Economics and Health Care Management, Munich School of Management, University of Munich, Munich, Germany

W. von Scheidt

Department of Internal Medicine I - Cardiology, Central Hospital of Augsburg, Augsburg, Germany

December 31, 2010 was based on municipal registration data. Cox regression analyses were adjusted for age, sex, education, years since last MI, and smoking and diabetes. *Results* Physicians reported that 495 patients were CHD-DMP participants. CHD-DMP participation increased the likelihood of receiving guideline-care (odds ratio 1.55, 95 % CI 1.20; 2.02) but did not significantly improve survival (hazard rate 0.90, 95 % CI 0.64–1.27). Guideline-care significantly improved survival (HR 0.41, 95 % CI 0.28; 0.59). Individual guideline-care components, which significantly improved survival, were beta-blockers, statins and platelet aggregation inhibitors. However, these improved survival less than guideline-care.

Conclusions This study shows that CHD-DMPs increase the likelihood of guideline care and that guideline care is the important component of CHD-DMPs for increasing survival. A relatively high percentage of usual care patients receiving guideline-care indicate high quality of care of post-MI patients. Reasons for not implementing guidelinecare should be investigated.

Keywords Disease management · Coronary disease · Secondary prevention

Introduction

Coronary heart disease (CHD) remains one of the leading causes of mortality and morbidity in industrial countries. In 2010, ischaemic heart disease accounted for 16 % of all deaths in Germany [1]. Reported age-standardized death rates for CHD in 2008 showed that the rate in Germany at 75 per 100,000 was similar to rates in the UK (69/100,000) and the USA (81/100,000), but higher than in France (29/ 100,000) and Italy (52/100,000) [2]. National and

international prevention guidelines address the treatment of risk factors such as hypertension, smoking, diabetes and hypercholesterolemia [3]. Disease management programmes (DMPs) use such evidence-based guidelines to define appropriate investigations, treatment and follow-up for CHD patients. In Germany, DMPs for CHD (CHD-DMPs) were introduced in 2003 for patients with statutory health insurance (SHI) which insured about 85 % of the population in 2012. Participation in CHD-DMP is voluntary, but patients must provide consent to be enrolled and they are excluded from the programme if follow-up requirements are not fulfilled [4, 5]. CHD-DMP guidelines regarding medical care are similar to European and American guidelines regarding the importance of medical advice about diet, exercise and smoking and the appropriate medications [3, 6]. Although guidelines provide numerous references for individual recommendations, only few studies have evaluated the effect on endpoints if most or all guideline recommendations are fulfilled [7].

In 2012, 1.7 million patients were enrolled in CHD-DMP in Germany [4]. This corresponds to about 30 % of cardiovascular patients (own calculations based on federal statistics office data) [8, 9]. While enrolment in DMPs for type 2 diabetes has been shown to be associated with improved survival based on health insurance data, similar studies for CHD-DMP have not been performed [10, 11]. However, CHD-DMP participation of post-myocardial infarction (MI) patients has been shown to increase the frequency of medical advice regarding diet, exercise and smoking and treatment with statins and platelet aggregation inhibitors (PAI) [12]. Clin Res Cardiol (2014) 103:237-245

Because of the improved care of patients enrolled in CHD-DMP and its aim to fulfil guidelines, based on a cohort of post-MI patients, it was our objective to evaluate:

- 1. Whether enrolment in CHD-DMP improves survival?
- 2. Whether medical care which is mostly adherent to published guidelines (guideline care) is provided more frequently in CHD-DMP and whether this improves survival?
- 3. Which individual components of CHD-DMP and secondary prevention guidelines (if any) lead to increased survival?

Methods

Patients

Patients included in our study had previously had an MI and were registered in the KORA (Cooperative Health Research in the Augsburg Region) Myocardial Infarction Registry [13, 14]. As described elsewhere, included patients had filled in a postal questionnaire regarding their medical care in 2006 [12]. Physicians were then asked to report CHD-DMP enrolment status (yes/no) for all patients reporting DMP enrolment (n = 665) and 1/3 of patients denying enrolment (n = 583). Physicians reported CHD-DMP status for 1,128 patients, a response rate of 90 %. Of these, 153 patients were excluded from further analyses for various reasons as shown in Fig. 1. A total of 975 patients was included in the follow-up study. All patients provided

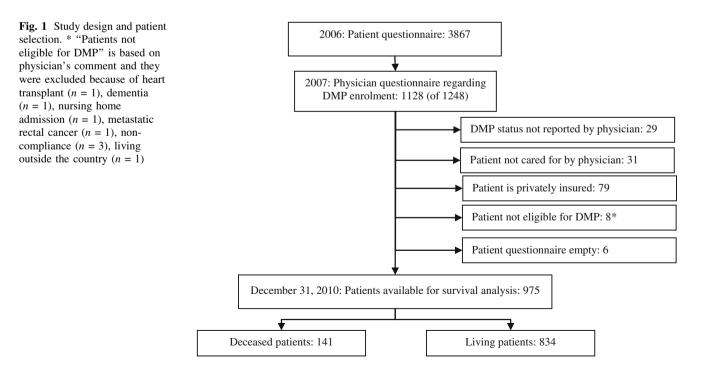


Table 1 Comparison of baseline characteristics (without imputation) of patients in 2006 according to enrolment status in the disease management programme for coronary heart disease (CHD-DMP) and guideline-care

Comparison regarding CHD-DMP	Controls $(n = 480)^{a}$	CHD-DMP participants $(n = 495)^{a}$	p value*
Age (years) at postal questionnaire 2006	68.2 (10.0)	67.3 (9.2)	0.0743
Male gender (%)	79.6	77.4	0.4014
Education (% secondary general school)	67.5	71.9	0.1332
Years since last MI	9.0 (5.4) (range 0.8–21.6)	8.1 (5.0) (range 0.8–21.6)	0.0057
BMI ^b	28.1 (4.6)	28.2 (5.0)	0.9640
Reinfarction (%)	11.7	12.1	0.8265
Smoker in 2006 ^b (%)	12.7	11.5	0.5759
Diabetes (%)	34.4	32.1	0.4551
Health-related quality of life VAS ^{c,b}	66.0 (18.3)	64.8 (18.2)	0.2112
Peripheral artery disease ^b	6.5	6.4	0.9057
Revascularization ^b	71.7	76.8	0.0695
Participant in diabetes DMP (%)	19.0	24.4	0.0379
Medical care as reported in 2006			
Medical advice regarding (reported in $2006)^b$			
Diet (%)	64.1	74.8	0.0003
Exercise (%)	69.6	77.3	0.0071
Smoking ^d (%)	98.1	98.8	0.4005
Medications taken ^b			
Beta-blockers (%)	82.5	85.1	0.2709
Statins (%)	72.6	81.6	0.0008
PAI (%)	82.7	88.6	0.0092
RAI (%)	63.3	74.1	0.0003
Patients receiving guideline-care (%)	48.8	60.5	0.0003
Comparison regarding guideline-care	Controls $(n = 443)^{a}$	Guideline-care $(n = 582)^{a}$	p value*
Age (years) at postal questionnaire 2006	69.1 (10.1)	66.7 (9.1)	< 0.0001
Male gender (%)	77.9	79.0	0.6859
Education (% secondary general school)	70.4	69.2	0.6708
Years since last MI	9.6 (5.2) (range 0.8–21.6)	7.7 (5.1) (range 0.8–21.6)	< 0.0001
BMI ^b	27.7 (4.9)	28.6 (4.6)	< 0.0001
Reinfarction (%)	9.3	14.1	0.0200
Smoker in 2006 ^c (%)	11.1	13.0	0.3571
Diabetes (%)	29.6	36.3	0.0268
Health-related quality of life VAS ^{c,b}	64.3 (18.4)	66.3 (18.1)	0.1506
Peripheral artery disease ^b	6.7	6.3	0.7991
Revascularization ^b	67.6	79.9	< 0.0001
Participant in CHD-DMP (%)	44.2	56.2	0.0002
Participant in diabetes DMP (%)	16.5	26.1	0.0003
Medical care as reported in 2006			
Medical advice regarding (reported in 2006) ^b			
Diet (%)	48.3	87.5	< 0.0001
Exercise (%)	50.5	93.0	< 0.0001
Smoking ^d (%)	97.1	99.6	0.0012
Medications taken ^b			
Beta-blockers (%)	75.5	90.7	< 0.0001
	10.5	100.0	< 0.0001
Statins (%)	49.5	100.0	<0.0001

Table 1 continued

Comparison regarding guideline-care	Controls $(n = 443)^{a}$	Guideline-care $(n = 582)^{a}$	p value*
RAI (%)	57.1	78.4	< 0.0001

CHD-DMP disease management programme for coronary heart disease, DMP disease management programme, RAI renin angiotensin inhibitors, PAI platelet aggregation inhibitors

* p value is based on Wilcoxon test for continuous variables or a Chi-squared test for categorical variables

^a Values are shown as percentage or mean and standard deviation

^b Number of missing values, RAI: 11; platelet aggregation inhibitor: 13; statins: 11; beta-blocker: 11; advice exercise: 30; advice diet: 29; smoker in 2006: 1; BMI: 3; health-related quality of life, VAS: 81; guideline-care: 35; peripheral artery disease: 13; revascularization: 13

^c Regular and occasional smokers

^d Measured using visual analogue scale of Euroqol EQ-5D

^e Or patient is a non-smoker

informed consent. Data collection and follow-up questionnaires of the KORA MI Registry have been approved by the Bavarian State Ethics Committee.

Based on patient reports in the 2006 survey, the presence of the following aspects of secondary prevention guidelines (guideline care) which are included in CHD-DMP were evaluated for all patients: whether the physician had provided advice regarding diet, exercise or smoking (or patient is non-smoker) within the last year and whether the patient had taken beta-blockers, statins, agents acting on the renin-angiotensin system (ACE-inhibitors or angiotensin II antagonists labelled as RAI) or PAIs within the last week. Medications were identified on the basis of their Anatomical Therapeutic Chemical (ATC) code. Other aspects of CHD-DMP, such as coordination of care, referrals and psychological support, could not be evaluated based on our data [5]. Guideline-care was defined as being present when the patient reported receiving medical advice for at least two of three topics covering diet, exercise, or smoking and reported the intake of a PAI and a statin and either a beta-blocker or an RAI. Lack of a beta-blocker or RAI could indicate a contraindication or hypotension precluding the intake of both antihypertensives [15].

The study start of the survival analysis was defined as the date on which patients completed their survey questionnaire in 2006. CHD-DMP participation was present if the physician documented an enrolment date before or on the study start. For nine patients, the physician verified DMP enrolment but did not document the DMP start date, thus the DMP start date documented by the patient was used. Patients not enrolled in a CHD-DMP at study start were designated as controls. However, controls that were later enrolled in CHD-DMP were censored at the time point of CHD-DMP enrolment. Patients were defined as having diabetes if this was documented in the KORA MI Registry, in the patient survey, if the patient documented the intake of diabetes medications or if the patient was enrolled in a diabetes-DMP. The survival analysis examined all-cause-mortality until December 31, 2010. In order to determine whether patients were living or deceased at follow-up, the responsible municipal registration office according to the last reported address was contacted. If the patient was deceased, date and place of death were provided by the registration office, otherwise the address was either confirmed or a new address was provided and the next registration office was contacted until a definite status (living versus deceased) was determined.

Confounders used in the analysis originated either from information from the KORA MI Registry (age, sex, education, date of last MI, history of peripheral artery disease (PAD), history of revascularization such as thrombolysis, angioplasty or a coronary bypass operation) or from patient reports in the 2006 survey (smoking status, height and weight to calculate BMI). The Visual Analogue Scale of the Euroqol-5D was examined as an indicator of healthrelated quality of life (HRQoL) [16].

Statistics

There were no missing values for mortality status, CHD-DMP status, age, sex, education, time since last MI and diabetes. Missing data for other independent variables (see Table 1) were imputed, assuming data were missing at random. Single imputation was performed using Markovchain Monte-Carlo method, accounting for all variables required for the analyses and for HRQoL [17]. Reported results show imputed values unless stipulated otherwise. Baseline comparisons are two-tailed and use the Wilcoxon test for continuous variables and Chi-squared test for class variables.

The regression analyses were adjusted for the confounders: age, sex, education, smoking status in 2006, and time since last MI, diabetes diagnosis, PAD and history of revascularization. The association of guideline-care with CHD-DMP participation was evaluated using logistic **Fig. 2** Cumulative probability of death compared between CHD-DMP participants and controls over 4 years following a patient questionnaire in 2006

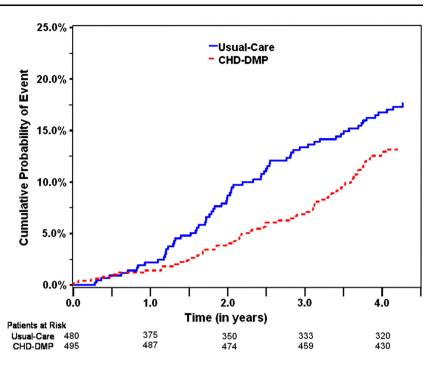


 Table 2
 Results of Cox proportional hazards models with adjustment for confounders

	Hazard ratio	Ratio limits	p value
Model 1			
CHD-DMP versus controls	0.90	0.64; 1.27	0.5521
Model 2			
Guideline-care	0.41	0.28; 0.59	< 0.0001
Model 3			
Medical advice regarding diet	0.95	0.60; 1.50	0.8162
Medical advice regarding exercise	1.18	0.74; 1.88	0.4808
Medical advice regarding smoking	1.21	0.27; 5.41	0.8039
Beta-blockers	0.62	0.42; 0.92	0.0178
Statins	0.51	0.35; 0.74	0.0004
PAIs	0.63	0.42; 0.93	0.0216
RAI	1.34	0.92; 1.96	0.1332

All models are controlled for the confounders sex, age, education, and years since last MI, smoking in 2006, diabetes in 2006, peripheral vascular disease and revascularization. Imputed variables were used for this model

CHD-DMP disease management programme for coronary heart disease

regression. Survival analyses were performed using Cox proportional hazards regression. As mentioned above, patients who were enrolled in CHD-DMP after the starting point of the study (completion of the questionnaire) were censored to the time point of CHD-DMP enrolment in the Cox proportional hazards regression. All analyses were

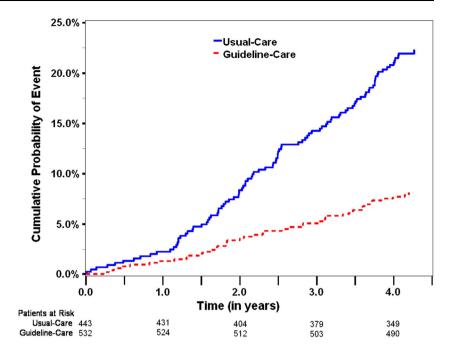
performed using SAS 9.2, and variables with a p value <0.05 were considered significant.

Results

Baseline characteristics

Of 1,128 patients whose CHD-DMP participation was verified, 153 patients were excluded for reasons shown in Fig. 1, leaving 975 patients included in this study. These subjects had an average age of 67.8 (range 34.4-87.9), 78 % were male and 33 % had diabetes. Physicians reported that 495 patients were participating in CHD-DMP at study start in 2006, while 480 were not enrolled at that time and thus were designated as controls. However, 94 controls were enrolled in CHD-DMP after study start until the end of 2007. CHD-DMP participants had been enrolled in the programme for a median of 0.9 years (range 0-2.8 years). Baseline patient characteristics according to CHD-DMP enrolment are shown in Table 1. Demographic variables were similar between the groups, but the last MI of CHD-DMP participants was more recent than that of controls. According to physician reports, 19 % of controls and 24 % of CHD-DMP participants were enrolled in the DMP for type 2 diabetes at start of study. Comparison of CHD-DMP participants and controls regarding their selfreported medical care in 2006 (Table 1) revealed that CHD-DMP participants more frequently reported receiving medical advice regarding diet and exercise. They also reported the intake of statins, RAI and PAIs more frequently. Guideline-care was more frequently reported by

Fig. 3 Cumulative probability of death compared between patients receiving guidelinecare and usual care over 4 years following a patient questionnaire in 2006



CHD-DMP participants. Overall 55 % of patients in our sample received guideline-care. As also shown in Table 1, patients receiving guideline-care were younger (66.7 versus 69.1 years), their last MI was more recent (7.7 versus 9.6 years), a higher proportion had a re-infarction (14.1 versus 9.3 %), they had a higher BMI (28.6 versus 27.7), and more frequently had diabetes (36.3 versus 29.6 %) and more frequently had a revascularization.

Multivariate analysis of factors associated with receiving guideline-care showed that enrolment in CHD-DMP (odds ratio (OR) 1.54, 95 % CI 1.19–2.01), having diabetes (OR 1.48, 95 % CI 1.12–1.97), fewer years since the last MI (OR 0.94, 95 % CI 0.92–0.97) and revascularization (OR 1.45, 95 % CI 1.06–1.99) increased the likelihood of receiving guideline-care.

Evaluation of survival revealed that 141 patients had died until the end of 2010 (see Fig. 1). Comparison of mortality between CHD-DMP participants and controls is shown in Fig. 2 and indicates some difference between the groups. The unadjusted survival analysis showed that CHD-DMP participation reduced mortality risk by about 25 % (hazard ratio (HR) 0.73, 95 % CI 0.52–1.03). Adjusting for confounders showed an HR of 0.90 (see Table 2). The unadjusted survival analysis of patients receiving guideline-care showed that all-cause-mortality was reduced by 66 % (HR 0.34, 95 % CI 0.24–0.49). Adjusting for confounders resulted in an HR of 0.41 (see Table 2). Further adjustment for BMI (which was significantly different between the groups) and HRQoL resulted in a HR of 0.44 (95 % CI 0.30–0.64) (Fig. 3).

Survival analysis of the individual components of the CHD-DMP shows that the intake of beta-blockers, statins

and PAIs were the components of the CHD-DMP programme and of guideline-care, which were independently associated with increased survival (see Table 2). However, the risk reduction of the individual medications was less than the combined therapy of guideline-care.

Discussion

CHD-DMPs were introduced to improve medical care of patients with coronary heart disease. Our study examined a sample of patients with a previous MI. We found that CHD-DMP participants more frequently reported appropriate medical care and were more likely to receive guideline-care. However, CHD-DMP participation did not significantly improve survival. We found that 60 % of CHD-DMP participants and almost 50 % of controls were receiving guideline-care and guideline-care significantly improved survival. Examination of the individual CHD-DMP components showed that beta-blockers, statins and platelet aggregation inhibitors significantly improved survival but the individual effect was lower than the combination in guideline-care.

In CHD-DMP, regulations define appropriate therapies, follow-up and clinical parameters which are documented by physicians and submitted for evaluation. The submitted data is used to provide individual feedback to physicians regarding their performance and to evaluate intermediate outcomes of CHD-DMP participants. Improvements in individual healthcare processes associated with DMPs have been shown for CHD and diabetes [12, 18, 19]. However, changes in complex care, such as guideline-care, have not been previously evaluated. Some trials of secondary prevention of CHD have evaluated the achievement of single treatment goals, but not the use of combined treatments [20, 21]. Our analyses show that post-MI patients who are enrolled in CHD-DMP or who are perceived to have an increased risk, patients with diabetes or a recent MI, are more likely to receive guideline-care. However, cardiovascular mortality risk for post-MI patients persists at 5 % per year after the first MI and at 10 % per year after the second MI for many years (independent of age and sex) if patients do not receive effective preventative treatment [22].

CHD-DMP enrolment did not significantly improve survival in our study. This may have been due to an inadequate sample size, especially considering that we only observed a 10 % difference in hazard ratio. However, no previous studies of a similar CHD-DMP intervention were available on which to base a sample size calculation. Furthermore, revascularization has improved prognosis after an acute myocardial infarction in the last years [23]. Examining the effect of CHD-DMP enrolment in the subgroup of patients who had a revascularization in the past and whose last myocardial infarction was at most 8 years prior to study start (n = 451), shows that CHD-DMP does have a significant effect on mortality (HR 0.50, 95 % CI 0.27–0.93) when adjusting for age, sex, education, smoking and PAD. This effect becomes not significant but indicates a trend (HR 0.58, 95 % CI 0.31-1.10) if further adjustment for guideline-care is made. Studies using SHI data have shown an association between increased survival and diabetes-DMP for Germany [10, 11]. These studies found significant differences in survival ranging from 3.1 to 6.6 %. They had a large number of patients available for analysis but also lacked randomisation and were not population-based. The observed improvement in survival associated with guideline-care has not been previously shown. Since our study was not randomised, selection bias must be considered. A review of ten studies of secondary prevention programmes for CHD (randomised clinical trials) published until the year 2000, found no survival advantage (summary risk ratio 0.91, 95 % CI 0.79-1.04) but did show a risk reduction for hospitalisations of 0.84 (95 % CI 0.79–0.94) [24]. However, the reviewed studies only assessed diet and exercise interventions. Newer secondary prevention programmes in CHD patients have shown improved blood pressure and cholesterol control and a reduction in patients requiring hospitalisation but have not reported survival [21, 25]. Trials evaluating outcomes with respect to whether therapy is consistent with guidelines often evaluate whether guidelines are fulfilled on discharge from hospital [7, 26, 27]. One of these studies showed a 1-year survival advantage for patients after an acute MI treated with aspirin, an ACE-inhibitor and a statin added to beta-blockers, but the patients were not randomised [7].

The individual components of the CHD-DMP and guideline-care which were associated with improved survival only correspond to a subset of guideline-care. We found improved survival associated with statins, betablockers and antiplatelet agents. Statins have been shown to improve survival even for patients with a low risk of vascular disease [28]. Also blood pressure-reducing drugs (including beta-blockers and RAIs) have been shown to proportionally reduce cardiovascular disease regardless of pre-treatment blood pressure [29]. The use of aspirin is also recommended in secondary prevention, reducing the incidence of serious vascular events [30]. Although medical advice for diet and exercise were individually not associated with survival, this may indicate that their effect is not independent of drug treatment in secondary prevention or may reflect the difficulty of translating medical advice into changes in patient behaviour. Special patient education programmes regarding diet or exercise are not part of the CHD-DMP. However, given an exact protocol, the importance and independent effect of diet in cardiovascular mortality has been recently shown [31]. Thus numerous studies show the importance of the individual components of guideline-care, but guideline-care shows the importance of the combination of the individual components-the additive effect of these components-since this leads to a higher risk reduction than associated with any single component.

Our study has several methodological limitations. Since patients are not randomised regarding either DMP participation or guideline-care, treatment choices may reflect selection bias [32]. Although a randomised trial protocol was available, DMPs were politically legislated before these studies were performed [33]. CHD-DMP enrolment was also not consistent during the study since 20 % of controls were enrolled in CHD-DMP shortly after the study start date. However, censoring controls who enrolled in CHD-DMP after study start to the time point of CHD-DMP enrolment attempted to control for their change in status in the survival analysis. This also illustrates the difficulty of excluding treatment spill-over effects in medical practices with both types of patients, especially since physicians in DMP must participate in additional medical education. Of the 97 controls enrolled in CHD-DMP after the study start date, 65 % already reported receiving guideline-care in 2006. Furthermore, both CHD-DMP enrolment, guidelinecare and its components (diet, exercise and medications) were not evaluated during the follow-up period. Thus patients may have changed their status, but this is not accounted for in the analysis which would be compatible with an intention to treat analysis. Selection bias may also determine which patients receive guideline-care since the care of patients with other severe comorbidities (e.g. cancer), will not focus on secondary prevention of CHD. The failure to receive guideline-care may also indicate a poor health status. For example, patients may not receive PAIs if they are receiving oral anticoagulants such as for atrial fibrillation. Overall cardiovascular risk of patients in 2006 cannot be established from our data, however the risk of patients in CHD-DMP may be higher since their last MI was more recent. Adjustments for HRQoL attempted to account for unknown differences in health status. Lack of recent laboratory and clinical measurements (e.g. blood pressure, LDL-cholesterol) and patient-reported medication intake are further study limitations. Thus, it is unknown whether factors such as lipid levels or hypertension are being adequately controlled or if all medications were reported by patients. Also important confounders such as heart failure, left ventricular ejection fraction, heart rate and renal failure were not available for analysis, which also limits the explanatory power of the results [34, 35].

The advantage of our study is that individual processes and complex aspects of CHD care could be evaluated in a population-based study. The association of this care with survival was analysed adjusting for socio-demographic variables not available in health insurance data. The control group and the starting point of the study were exactly defined. Furthermore, we evaluated how well the therapy of these high risk post-MI patients complied with German CHD-DMP and international guidelines and showed that guideline-care improved survival, a result which is not restricted only to Germany. Since enrolment in CHD-DMP was significantly associated with receiving guideline-care, it is possible that the DMP has increased awareness of the guidelines and adherence to them and has also improved the care of patients not enrolled in CHD-DMP.

Conclusions

This is the first population-based study to show that CHD-DMP increases the likelihood of receiving guideline-care in post-MI patients. Although CHD-DMP improved survival only insignificantly, adherence to guideline-care significantly improved survival. Our results indicate that larger studies are required to evaluate the effect of CHD-DMP on survival but that randomised controlled trials are actually required to evaluate the effect of CHD-DMPs and guideline-care on survival.

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Conflict of interest The authors declare that they have no conflict of interest.

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