

Secondary Prevention in Patients with Coronary Heart Diseases: What Factors Are Associated with Health Status in Usual Primary Care?

Dominik Ose^{1*}, Justine Rochon³, Stephen M. Campbell^{1,4}, Michel Wensing^{1,2}, Jan van Lieshout², Lorenz Uhlmann³, Tobias Freund¹, Joachim Szecsenyi¹, Sabine Ludt¹

1 University Hospital of Heidelberg, Department of General Practice and Health Services, Heidelberg, Germany, **2** Radboud University Nijmegen Medical Centre, Scientific Institute for Quality of Healthcare, HB Nijmegen, The Netherlands, **3** University of Heidelberg, Institute of Medical Biometry and Informatics, Heidelberg, Germany, **4** Health Sciences – Primary Care Group, University of Manchester, Manchester, United Kingdom

Abstract

Background: For patients with coronary heart diseases a substantial part of secondary prevention is delivered in primary care. Along with the growing importance of prevention, health-related quality of life (HRQoL) is an indicator of patient-centered care that has gained increased attention. Different approaches for reorganization in primary care have been associated with improvements in HRQoL. However, these are often results of complex interventions. Evidence on aspects concerning usual primary care that actually have an impact on HRQoL remains scarce. Therefore, this observational study aimed to identify factors which are associated with HRQoL in usual primary care at practice and patient-level.

Methods: This observational study was conducted in eight European countries. We were able to match data from survey instruments for 3505 patients with coronary heart disease (CHD) in 228 practices. A multilevel analysis was performed to identify associations of EQ-5D scores at patient and practice-level.

Results: After dropping patients with missing information, our cohort consisted of 2656 patients. In this sample, 30.5% were female and the mean age was 67.5 years (SD 10.1). The final model included a total set of 14 potential explanatory variables. At practice-level no variable was associated with EQ-5D. At patient-level, lower education ($r = -0.0381$, $p < 0.0001$), female gender ($r = -0.0543$, $p < 0.0001$) and a higher number of other conditions ($r = -0.0340$, $p < 0.0001$), had a strong negative effect on HRQoL. Strong positive associations with HRQoL were found for a good medication adherence (Morisky) ($r = 0.0195$, $p < 0.0001$) and more positive evaluations of physicians' clinical behavior ($r = 0.0282$, $p = 0.002$). In terms of HRQoL no differences between single-handed and group practices exist.

Conclusion: The results of our study suggest that a better patient-physician relationship rather than organization of CHD care is associated with higher HRQoL in the primary care setting. The results may imply that interventions to improve HRQoL require a strong patient-centered approach.

Citation: Ose D, Rochon J, Campbell SM, Wensing M, van Lieshout J, et al. (2012) Secondary Prevention in Patients with Coronary Heart Diseases: What Factors Are Associated with Health Status in Usual Primary Care? PLoS ONE 7(12): e51726. doi:10.1371/journal.pone.0051726

Editor: Claudio Moretti, S.G.Battista Hospital, Italy

Received: June 27, 2012; **Accepted:** November 5, 2012; **Published:** December 26, 2012

Copyright: © 2012 Ose et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: The Bertelsmann Foundation (Gütersloh, Germany) initiated, coordinated, and funded the EPA Cardio project, in collaboration with IQ Healthcare of the Radboud University Nijmegen (The Netherlands). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: dominik.ose@med.uni-heidelberg.de

Introduction

Cardiovascular disease (CVD), and in particular coronary heart disease (CHD), are major causes of morbidity and premature death and make a substantial contribution to escalating health care costs in developed countries [1,2]. Accordingly, the treatment and prevention of CVD is a priority for health care systems; especially the modification of risk factors, e.g. hypertension, high cholesterol levels or cigarette smoking, by means of a healthy lifestyle or medication is essential [3]. These and other activities helped to reduce the death rate due to heart diseases in recent decades [4].

However, despite the availability of statins and other pharmacologic agents, e.g. aspirin or beta-blockers, the rate of improve-

ment has slowed down or stopped [5]. To address the “unmet potential for cardiovascular disease prevention” [6], various initiatives have been tried. A common remit of these endeavors, like the “2020 Impact Goals” [7] of the American Heart Association, the “Million Hearts” [8] initiative or the development of quality indicators for CVD prevention in Europe [9], is to focus more on prevention and health promotion, rather than solely on treating diagnosed disease. Such an approach requires a more intensive cross-linking between health care and community based interventions.

Primary care, as a bridge between personal health care and community health care plays a crucial role in this context. A substantial part of prevention and chronic care for CHD is

delivered in this sector [10,11]. However, concepts such as the Chronic Care Model [12], Guided Care [13], GRACE [14] (Geriatric Resources for Assessment and Care for Elders) or PACE [15] (Program of All-inclusive Care for Elderly), offer frameworks for the advancement of primary care that advocate a stronger integrated community focus.

Implementing such approaches, which have been shown to improve health care in numerous clinical studies [16–18], requires a strong patient's perspective and involvement. From the patient's perspective not merely the disease, but rather the impact of disease and treatment on daily life is important [19]. In this context "health status" characterizes the range of manifestation of diseases in a given patient, including symptoms and functional limitations. The discrepancy between actual and desired functional capacity is described as health related quality of life (HRQoL). Particularly for patients with chronic conditions, this perspective has a special meaning [20].

Along with the growing importance of prevention, HRQoL as an outcome has gained increased attention in the last years. Various studies have shown the negative impact of disease-specific conditions (e.g. heart failure, hypertension, comorbidities) and sociodemographic factors (e.g. sex, income, and ethnicity) on HRQoL for CHD patients [21,22]. On the other hand, new concepts have been associated with improvements in HRQoL [23,24].

However, these are often study results of complex interventions. Evidence on aspects concerning usual primary care that actually have an impact on HRQoL remains scarce. Especially predictors and determinants of optimum HRQoL as a guide for further development, to date are missing [22]. To fill this void, this observational study aimed to identify factors which are associated with HRQoL in usual primary care at practice and patient-level in patients with CHD. With awareness of the ongoing discussion about the future of small and single-handed practices [25,26], single and group practices were considered separately.

Methods

Study Sample

This analysis was conducted as part of the European Practice Assessment (EPA) - Cardio project (2006–2009). To improve cardiovascular health care in Europe, in the first stage of the project (2006–2007) instruments and methods for assessing cardiovascular risk management and prevention in primary care were developed and tested [9]. In a second stage of the EPA-Cardio project (2008–2009), a cross-sectional observational study using the EPA-Cardio instrument was conducted. A comprehensive sample of countries in North, West, South and Central Europe participated in this study (i.e. Austria, Belgium, England, Finland, France, Germany, Netherlands, Slovenia, Spain, and Switzerland) [27]. In this part of the study Spain was excluded because only data from medical records were collected and Finland due to insufficient data quality. Israel was only involved in the practice survey (Figure 1). Ethics committees of all participating countries approved the study.

For this study, general practices were recruited by the national research teams with an aim of including 36 practices in each country. Practices were randomly chosen according to the national distribution of general practices across the countries with the intention of achieving a representative country sample. In each practice, 30 patients with CHD were randomly sampled (assuming 50% response) and invited to participate. Inclusion and exclusion criteria are listed in Table 1. All general practitioners (GPs) and all

patients provided their written informed consent to participate in this study.

This article is one of two analyzing HRQoL in primary care. Within the EPA-Cardio project HRQoL was considered for patients at risk for CVD and for patients with diagnosed CHD. The complete sample comprised over 7,000 cases. Because 'patients at risk for CVD' and 'patients with diagnosed CHD' are different patient groups with different care needs and treatment plans, we decided to publish the results for both groups separately. The results for "patients at risk" were published elsewhere [28].

Study Measures

The data collection was based on the EPA-Cardio instrument. At practice-level, team members completed a questionnaire and the leading GP was interviewed using a standardized guide. These instruments contained questions to characterize the practice according to size, location or number and function of practice staff. Quality indicators (QI) that were developed during the EPA-Cardio project [9] and derived from the EPA practice-management instrument [29] were converted into questions for the practice team.

At patient-level, participants received a questionnaire including items about patient characteristics (e.g. age, gender, education and marital status) and care delivery (e.g. practice attendance, referral to exercise program). Additionally, a questionnaire on medication adherence [30], the EQ-5D and a patient satisfaction instrument (EUROPEP) were included.

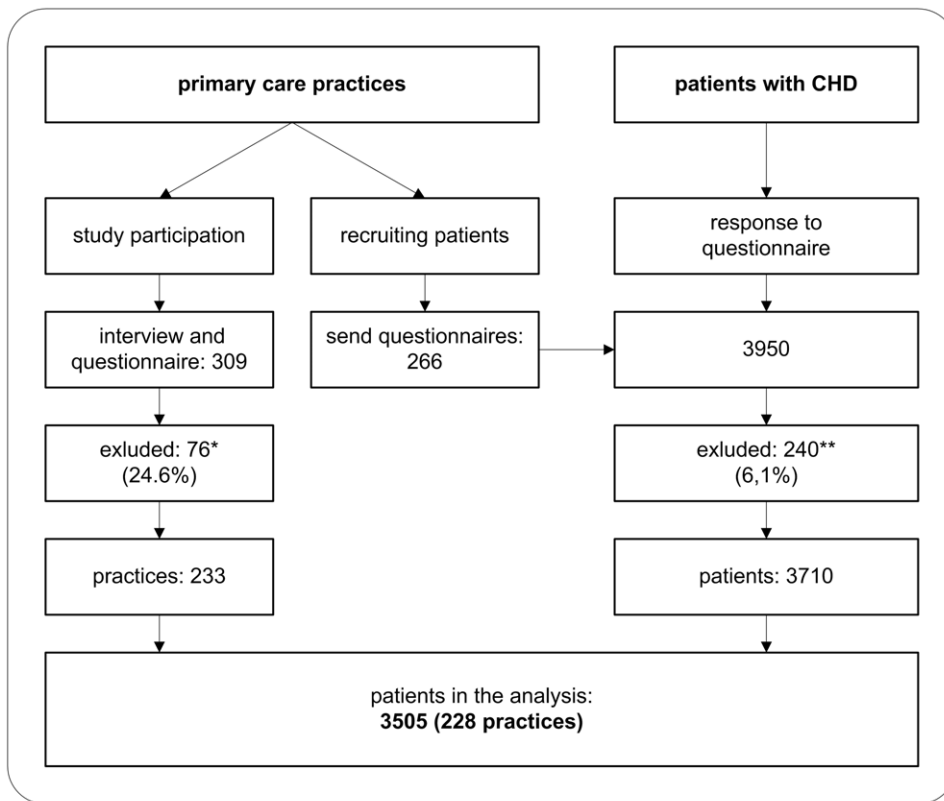
The EUROPEP (European Project on Patient Evaluation of General Practice Care) instrument is a multidimensional instrument comprising 23 questions on evaluation of specific aspects of general practice care, using a five-point answering scale. Within the two dimensions 'clinical behavior' (16 questions) and 'organization of care' (7 questions), the patients were asked questions about the clinical behavior of their general practitioner like 'Making it easy for you to tell him or her about your problems' or the organization of care like "Getting an appointment to suit you" [27].

The EQ-5D [31,32], which was used as the main outcome, is a generic instrument for describing and valuing health, and is available in more than 50 languages. The EQ-5D defines health in terms of five dimensions: mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. Each dimension is divided into three levels, indicating no problem, some or moderate problems or extreme problems. The EQ-5D score (indicating HRQoL) ranges from 0 to 1 and can be calculated by applying scores from the EQ-5D preference weights elicited from the general population. The maximum score of 1 indicates the best health state.

For this study, the EQ-5D score was calculated using the value set for the European population. The published evidence supports the validity and reliability of the EQ-5D as an outcome measure within cardiovascular diseases [33]. The minimal importance difference (MID) in health status of patients with CHD is settled within 0.03 points on the EQ-5D score [34].

Data Analysis

The main study outcome was HRQoL as measured by the EQ-5D score. This study tested a total set of 14 potential explanatory variables as predictors for HRQoL (see Table 2): 12 variables at patient-level and 2 variables on practice-level. To describe practice characteristics, as explanatory variables, we aggregated the items of the practice questionnaire and interview using the homogeneity analysis by alternating least squares (HOMALS). With this



*Finland, Spain, Israel; **Finland

Figure 1. Data flowchart.

doi:10.1371/journal.pone.0051726.g001

analysis, we identified 32 binary items with discrimination measures over 0.4 in two dimensions ‘practice quality management’ (15 items) and ‘practice CVD care’ (17 items) (Table 3). Scores were calculated by summing up the number of ‘yes’-answers resulting in a score range from zero to 15 for the practice quality-management score and from 0–17 for the CVD-care score respectively. Additionally, we grouped practices according to the full-time equivalent (FTE) of GPs in single-handed practices

(FTE≤1) and group practices (FTE>1) to appraise differences in a subgroup analysis.

For multivariable prediction, a series of linear models were estimated to assess the effect of variables at practice and patient-level on HRQoL; explanatory variables at country level were not examined. Because of hierarchical data structure, multilevel analysis was performed to take into account the dependence between patient outcomes (level 1) within primary care practices (level 2) and countries (level 3). The multilevel linear analysis

Table 1. Inclusion and exclusion criteria for patients with CHD.

Inclusion criteria	Exclusion criteria
Documented diagnosis, ICD 10 code: I20-I25, ICPC-2 code: K74-76	Terminal illness, cognitive disorders (e.g. dementia), psychiatric diseases (e.g. schizophrenia) and lack of language knowledge

doi:10.1371/journal.pone.0051726.t001

Table 2. Explanatory variables included in the multilevel analysis.

Variables	Categories/Scoring
Practice-level	
Quality-management score	Continuous: sum score of 'yes-answers'; range: 0–15
CVD-care score	Continuous: sum score of 'yes-answers'; range: 0–17
Patient-level	
<i>Patient characteristics</i>	
Gender	2 categories: female; male
Age	Continuous: age divided by 5
Marital status	2 categories: married/cohabitating; single/separated/divorced/widowed
Education	Years in school; 2 categories : ≤9 years; >9 years
Number of other conditions	Continuous: sum score (range: 0–11) of all patient reported symptoms or conditions including 'high blood pressure', 'high cholesterol', 'diabetes', 'angina', 'history of heart attack', 'history of PCI or bypass', 'symptoms of heart failure', 'transient ischemic attacks', 'history of stroke', 'peripheral artery disease' or 'symptoms of depression'
Body Mass Index	2 categories: up to 30; more than 30
<i>Care delivery</i>	
Being patient in practice	3 categories: up to 2 years; 3 to 7 years; more than 7 years
Practice attendance last year	3 categories: up to 3 times/year; 4 to 7 times/year; more than 7 times/year
Referral to exercise program	2 categories: Yes; No/don't Know
Medication adherence (Morisky)	Continuous sum score (4 items): 0–4 (best)
Patient satisfaction (EUROPEP)	
Clinical behavior	Continuous: (EUROPEP dimension 'clinical behavior' 16 items) mean: 1–5 (best)
Organization of care	Continuous: (EUROPEP dimension 'organization of care' 7 items) mean: 1–5 (best):

doi:10.1371/journal.pone.0051726.t002

started with a three-level null (empty) model with no predictor variables in the fixed part and only the intercepts in the random part of the model (M1). This model can be used as reference for comparing the size of contextual (practice or country) variations in EQ-5D in subsequent models. Next, two practice-level performance characteristics (practice CVD care and practice quality management) were included as fixed effects (M2). Finally, we added patient-level variables in the fixed part of the third and fourth model (M3 and M4). However, in contrast to M3 that included only relevant patient characteristics on patient-level, M4 additionally contained variables measured at patient-level but reflecting aspects of care delivery.

We first present descriptive statistics for practice-level and patient-level characteristics in the entire study sample and then subgroup analyses for single-handed and group practices. Continuous data are summarized by using means with standard deviations (SD). Categorical data are presented as frequency counts and percentages. We then report on fixed-part results of the final 3-level linear model (M4) followed by the random-part results of all four models (M1–M4). Variance partition coefficients in each level were calculated using the restricted maximum likelihood (REML) method; the corresponding intraclass correlation coefficient (ICC) at the practice and country level [35] is provided. Finally, the proportion of variance explained (EV) at each level [36] is presented for model M2–M4.

Only patients with complete data on all explanatory variables were considered in the final model and included in the analysis. The characteristics of these patients were compared with those of the patients who had to be excluded because of non-responding to the EQ-5D items or lack of information on explanatory variables.

Because this was an exploratory analysis, the significance level was set to 5% (two-sided) and no adjustment for multiple testing

was performed. All descriptive analyses were carried out by using IBM SPSS Statistics version 19 (SPSS Inc., Chicago, IL, USA). The multilevel analysis was conducted by using MLwiN 2.24 [37].

Results

Sample characteristics

For 3505 patients with CHD in 228 practices we were able to match data from survey instruments for patients and practices (Figure 1). Of the 228 participating practices, 30.7% were located in towns with more than 100,000 inhabitants and employed approximately two GP full time equivalents (FTE). Mean practice quality scores were 8.2 for CVD-care and 9.0 for quality management, respectively (Table 4).

After excluding patients with missing information, our cohort for further analysis consisted of 2656 patients (75.8% of 3505). Table 4 shows the socio-demographic characteristics as well as characteristics of care delivery of the included patients. Compared to those included, the patients excluded from further analysis were of similar mean age (68.5 years), proportion of female (36%), proportion of patients with BMI of 30 or above (23%), proportion of patients with nine or less years of education (30%), and single marital status (27%). However, those excluded had slightly fewer other conditions and lower medication adherence, and were less likely to be referred to an exercise program (41% vs. 48%). The HRQoL of the patients without missing values was similar to the HRQoL of the patients excluded from further analysis: The mean EQ-5D was 0.73 (0.22) and 0.72 (0.23), respectively.

Significant differences between single and group practices were not found for HRQoL but for some explanatory variables (Table 4). At practice-level, group practices scored higher on both practice quality dimensions and were more often located in larger towns, compared with single-handed practices. At the patient-

Table 3. Practice characteristics.

Quality management (15 items)
• Does the practice use a computer-supported patient file system?
• Is the computer used for creating medication prescriptions?
• Does the practice have a procedure for the management of patient information in relation to detailed examination results and the documentation of measures that were taken (e.g., blood examinations)?
• Does the practice have a procedure for the management of patient information in relation to the review of detailed examination results by the doctor (in terms of outgoing needs)?
• Do the practice doctors have direct access to medical guidelines (either on paper or electronic) in their treatment rooms?
• In general: Is practice staff allowed to contact or recall patients?
• Does the practice produce a quality report?
• Has the practice undertaken at least one clinical audit in the last 12 months?
• Did you set standards regarding this clinical audit (defined the target)?
• Did you collect data regarding this clinical audit?
• Did you evaluate the result?
• Were you able to improve the quality regarding this clinical audit topic?
• Does the practice have a critical incident register?
• Did the practice have a team meeting about quality improvement relating to CVD at least once in the last 15 months?
• Did the practice participate in cardiovascular quality improvement projects?
CVD care (17 items)
• Does the practice use case finding methods to detect patients with cardiovascular risk factors?
• Does the practice use a system for recalling patients with cardio vascular diseases?
• Does the practice use a system for recalling patients with diabetes?
• Does the practice use a system for recalling patients with hypertension?
• Does the practice use a system for recalling populations at risk for preventive care regarding cardio vascular diseases?
• Does the practice use a system for recalling populations at risk for preventive care regarding influenza?
• Does the practice have a procedure for smoking cessation (e.g. with the Minimal Intervention Strategy)?
• Does the practice participate in public health care programmes on life style (physical exercise, stop smoking)?
• Did all nurses attend \geq one training/continuing medical education event on CVD within the last 5 years?
• Did nurses take part in local/community campaigns or actions on CVD risk prevention (e.g. stop smoking campaigns, fun-runs etc)?
• Does the practice use a CVD standardized risk assessment tool?
• Is the CVD risk assessment tool integrated with the patient medical record system (e.g. so that the CVD event risk score is entered directly in to the patient's medical record)?
• Is there in general a record in the electronic or paper based patient record that the CVD standardized risk assessment tool has been offered?
• Is CVD risk advice (e.g. about modifiable risk factors such as diet and exercise) integrated with the patient medical record system?
• Do you offer regularly two or many consultations to provide advice on patient's life style?
• Does the practice have an up-to-date directory of prevention activities/organizations available locally (e.g. gyms, walking group, weight-watchers etc)?
• Did your practice participate in a project concerning cardiovascular risk management the last 2 years (apart from those mentioned above)?

doi:10.1371/journal.pone.0051726.t003

level, the percentage of patients with BMI greater or equal to 30 was higher at group practices than in single-handed practices (26% vs. 20%). Similarly, the proportion of patients with more than nine years of education was higher in group practices compared to single-handed practices (74% vs. 63%). In contrast, patients in single-handed practices were more likely to attend the practice more than seven times within one year and were also slightly more often referred to an exercise program.

Multivariable associations with HRQoL

The 3-level linear regression analysis was based on 2656 patients (level 1) nested within 228 practices (level 2) and 8 countries (level 3). There were up to 36 patients within each practice and up to 34 practices within each country. The

multilevel regression analysis showed that the HRQoL as measured by the EQ-5D score was associated with several variables, especially at the patient-level. In contrast, none of the variables at practice-level were significantly associated with the EQ-5D score (Table 5).

At the patient-level all socio-demographic characteristics were significantly associated with HRQoL except for marital status. In terms of practical impact, the regression coefficient as result of the multilevel analysis has to be interpreted carefully. In general, the value of the regression coefficient indicates a change per unit (continuous variables) or a change in contrast to a reference category (categorical variables). For example, the continuous variable "age" is in our analysis divided in 5 years units. This means, that in steps of 5 years (one unit) the EQ-5D score

Table 4. Sample description (included patients).

	Total sample	Single practice	Group practice	p-value
Practice-level				
Included practices	228	113	102	
FTE GP (SD)	2.04 (1.70)	1.00 (0.04)	3.20 (1.89)	
Practice town (>100,000 inhabitants) (%)	69 (30.7)	27 (23.9)	39 (39.4)	.0150 ^b
CVD-care score (SD)	8.24 (4.72)	6.80 (3.97)	9.79 (5.05)	<.0001 ^a
Quality-management score (SD)	9.00 (3.87)	8.05 (3.40)	10.42 (3.93)	<.0001 ^a
Patient-level				
Included patients	2656	1341	1128	
EQ-5D score (SD)	0.73 (0.22)	0.73 (0.22)	0.73 (0.22)	.6838 ^a
<i>Patient characteristics</i>				
Age (SD)	67.5 (10.1)	67.9 (10.2)	67.1 (9.9)	.0543 ^a
Gender (female) (%)	809 (30.5)	405 (30.2)	360 (31.9)	.3590 ^b
Marital status (single) (%)	623 (23.5)	305 (22.7)	279 (24.7)	.2465 ^b
Years of education (<= 9 years) (%)	841 (31.7)	491 (36.6)	289 (25.6)	<.0001 ^b
Number of other conditions (SD)	3.49 (1.79)	3.55 (1.86)	3.36 (1.70)	.0100 ^a
Body mass index (>= 30) (%)	610 (23.0)	270 (20.1)	291 (25.8)	.0008 ^b
<i>Care delivery</i>				
Being patient in practice				.0098 ^b
– up to 2 years (%)	119 (4.5)	46 (3.4)	63 (5.6)	
– 3–7 years (%)	346 (13.0)	187 (13.9)	130 (11.5)	
– more than 7 years (%)	2191 (82.5)	1108 (82.6)	935 (82.9)	
Practice attendance within 12 months				<.0001 ^b
– up to 3 times (%)	737 (27.7)	316 (23.6)	381 (33.8)	
– 4–7 times (%)	1189 (44.8)	589 (43.9)	489 (43.4)	
– more than 7 times (%)	730 (27.5)	436 (32.5)	258 (22.9)	
Referral to exercise program (yes) (%)	1273 (47.9)	660 (49.2)	529 (46.9)	.2505 ^b
Medication adherence (SD)	3.49 (0.81)	3.47 (0.85)	3.52 (0.78)	.1702 ^a
<i>Patient satisfaction (EUROPEP)</i>				
– clinical behavior (SD)	4.44 (0.66)	4.44 (0.63)	4.44 (0.70)	.8626 ^a
– organization of care (SD)	4.39 (0.68)	4.43 (0.63)	4.33 (0.74)	.0003 ^a

^a = T-Test (Single vs. Group);

^b = Chi² (Single vs. Group); CVD: Cardiovascular disease.

doi:10.1371/journal.pone.0051726.t004

decreases (negative sign) by 0.0064 (regression coefficient). For the categorical variable “gender” the regression coefficient indicates a change of -0.0543 on the EQ-5D score for “female” in contrast to “male” patients (reference category). Additionally, a higher number of other conditions (regression coefficient: -0.0340 ; 11 units), and BMI of 30 or above (regression coefficient: -0.0211) were associated with lower HRQoL.

The relationship between the variables of care delivery and HRQoL was almost as expected. Shorter duration of being patient in practice had a negative effect on HRQoL (regression coefficients: -0.0214 for up to 2 years and -0.0250 for 3–7 years compared with more than 7 years, respectively). Patients, who were attending their practices less often, had a higher EQ-5D score compared to patients who reported to attend their practice more than 7 times within one year. All the other factors concerning care delivery, except for the organizational subscale score of the EUROPEP score (regression coefficient: -0.0032 , $p = 0.6737$), were positively associated with HRQoL. Full infor-

mation on fixed-part results from all four models can be found in Tables S1,S2,S3.

With respect to the random part of the results the null (empty) model (M1) showed a total variation in EQ-5D of 0.0405. The ICC for the country level was 0.08 and 0.06 for the practice-level. No reduction in EQ-5D variance could be observed after controlling for practice-level characteristics (M2). In contrast, including patient’s socio-demographic variables (M3) resulted in a considerable reduction of the observed variance. Further reduction of the variance in EQ-5D was reached by adding variables of care delivery (M4) (Table 6). The final model explained the variance at the country level to 31.4%, at the practice-level to 62.1% and at the patient-level to 19.6% (Figure 2).

Single-handed and group practices

The results of the final model were similar when single-handed practices and group practices were considered separately. However, for patients in single-handed practices ‘single marital status’ had a statistically significant negative effect on the EQ-5D score,

Table 5. Fixed part results of the random intercept model with overall EQ-5D score as dependent variable (2656 patients within 228 GPs within 8 countries), including all variables on patient and practice-level.

	Total sample*			Single practices**			Group practices***		
	coeff.	(SE)	p-value	coeff.	(SE)	p-value	coeff.	(SE)	p-value
Intercept	0.7047	(0.0467)	<.0001	0.8296	(0.0640)	<.0001	0.6009	(0.0667)	<.0001
Practice-level									
CVD-care score	−0.0017	(0.0017)	.3185	−0.0032	(0.0024)	.1786	−0.0011	(0.0025)	.6517
Quality-management score	0.0021	(0.0018)	.2231	0.0028	(0.0025)	.2759	0.0011	(0.0025)	.6697
Patient-level									
<i>Patient characteristics</i>									
Age (5-years unit)	−0.0064	(0.0019)	.0008	−0.0101	(0.0027)	.0001	−0.0036	(0.0030)	.2374
Gender (female)	−0.0543	(0.0083)	<.0001	−0.0439	(0.0118)	.0002	−0.0662	(0.0125)	<.0001
Marital status (single)	−0.0142	(0.0088)	.1074	−0.0294	(0.0127)	.0205	−0.0037	(0.0133)	.7808
Years of education (<= 9 years in school)	−0.0381	(0.0083)	<.0001	−0.0471	(0.0112)	<.0001	−0.0296	(0.0137)	.0304
Number of other conditions	−0.0340	(0.0022)	<.0001	−0.0367	(0.0030)	<.0001	−0.0319	(0.0035)	<.0001
Body mass index (>= 30)	−0.0211	(0.0086)	.0145	−0.0127	(0.0127)	.3165	−0.0279	(0.0130)	.0314
<i>Care delivery</i>									
Being patient in practice			.0473			.0320			.5838
– up to 2 years	−0.0214	(0.0176)		−0.0394	(0.0280)		−0.0256	(0.0248)	
– 3–7 years	−0.0250	(0.0110)		−0.0352	(0.0150)		−0.0041	(0.0181)	
– more than 7 years	Reference			Reference			Reference		
Practice attendance within 12 months			<.0001			<.0001			<.0001
– up to 3 times	0.1210	(0.0109)		0.0940	(0.0156)		0.1566	(0.0165)	
– 4–7 times	0.0801	(0.0091)		0.0731	(0.0126)		0.0910	(0.0146)	
– more than 7 times	Reference			Reference			Reference		
Referral to exercise program (yes)	0.0240	(0.0075)	.0013	0.0135	(0.0107)	.2047	0.0394	(0.0115)	.0006
Medication adherence	0.0195	(0.0045)	<.0001	0.0179	(0.0062)	.0039	0.0180	(0.0072)	.0117
<i>Patient satisfaction (EUROPEP)</i>									
– clinical behavior	0.0282	(0.0076)	.0002	0.0335	(0.0114)	.0034	0.0324	(0.0111)	.0035
– organization of care	−0.0032	(0.0075)	.6737	−0.0142	(0.0116)	.2194	0.0007	(0.0109)	.9523

coeff.: regression coefficient, SE: standard error, CVD: Cardiovascular disease.

*2656 patients, 228 practices, 8 countries.

**1341 patients, 113 practices, 8 countries.

***1128 patients, 102 practices, 8 countries.

doi:10.1371/journal.pone.0051726.t005

whereas a negative but statistically non-significant association was observed between BMI and HRQoL and ‘referral to exercise program’ and HRQoL. In group practices, a non-significant association with HRQoL was observed for patient’s age and the time of being patient in practice.

The random-part analysis for group and single-handed practices (Table 6) revealed a greater importance of patient characteristics in single-handed practice compared to group practices. Including of ‘patient characteristics’ in the multilevel model resulted at the practice-level in an increase explained variance to 67%. However, in group practices the explained variance increased only to 28%. In contrast, including variables of ‘care delivery’ explained more variance in group practices (28% to 69%) compared to single-handed practices (67% to 69%).

Discussion

The aim of this observational study was to identify factors which are associated with HRQoL in usual primary care at practice and patient-level. Relating to the practice-level, neither the score of the

dimension ‘quality-management’ nor the score ‘practice CVD-care’ were associated with HRQoL in our analysis. However, the level of these scores was quite low. On average, only 60% of the quality-management items (mean 9.0; range 0–15) and 48% of CVD-care items (mean 8.2; range 0–17) respectively, were implemented. Moreover, the standard deviations indicated that there were large differences between practices. These differences could also be seen when comparing single-handed and group practices. Group practices scored significant higher on quality indicators compared to single-handed practices. However, the EQ-5D scores in both groups were similar. The subgroup analysis revealed that the measured aspects of practice organization had no significant impact on HRQoL. This lack of association between practice characteristics and HRQoL was not expected, as aspects of good practice organization have been shown to improve quality of care in previous studies [38–40]. On the other hand, our findings do not exclude a positive or negative impact of practice organization on HRQoL over time due to the cross-sectional study design.

Table 6. Random part of all three random intercept models with overall EQ-5D score as dependent variable (2656 individuals within 228 GPs within 8 countries).

	All practices			Single-handed practice			Group practice		
	VC	(SE)	EV	VC	(SE)	EV	VC	(SE)	EV
Model 1: Null model									
Countries	0.0038	(0.0020)		0.0034	(0.0020)		0.0047	(0.0028)	
Practices	0.0029	(0.0006)		0.0036	(0.0010)		0.0020	(0.0009)	
Patients (plus random)	0.0405	(0.0012)		0.0411	(0.0017)		0.0428	(0.0019)	
Model 2: Practice-level covariates added									
Countries	0.0037	(0.0020)	2.90%	0.0032	(0.0019)	5.62%	0.0044	(0.0026)	6.01%
Practices	0.0029	(0.0006)	0.34%	0.0034	(0.0010)	3.93%	0.0021	(0.0009)	NA
Patients (plus random)	0.0405	(0.0012)	0.00%	0.0411	(0.0017)	NA	0.0428	(0.0019)	0.05%
Model 3: Patient characteristics added									
Countries	0.0033	(0.0017)	13.19%	0.0023	(0.0013)	32.25%	0.0039	(0.0223)	16.74%
Practices	0.0014	(0.0004)	52.07%	0.0012	(0.0006)	67.42%	0.0014	(0.0007)	27.92%
Patients (plus random)	0.0347	(0.0010)	14.36%	0.0342	(0.0014)	16.70%	0.0369	(0.0016)	13.83%
Model 4: Care delivery added									
Countries	0.0026	(0.0014)	31.40%	0.0016	(0.0010)	52.37%	0.0018	(0.0011)	61.37%
Practices	0.0011	(0.0004)	62.07%	0.0011	(0.0005)	69.38%	0.0006	(0.0005)	69.04%
Patients (plus random)	0.0326	(0.0009)	19.55%	0.0327	(0.0013)	20.35%	0.0335	(0.0015)	21.66%

VC: Variance component, SE: standard error, EV: explained variance, NA: not available.
doi:10.1371/journal.pone.0051726.t006

At patient-level, lower education, female gender and a higher number of other conditions, had the strongest negative impact on HRQoL. Whereas the negative impact of lower education, female gender and individual conditions (e.g. hypertension) is well known [22,41,42], the association between the number of conditions and

HRQoL has not been explicitly demonstrated in patients with CHD. To date, the correlation between HRQoL and the number of conditions was mainly known for other diseases, like diabetes [43].

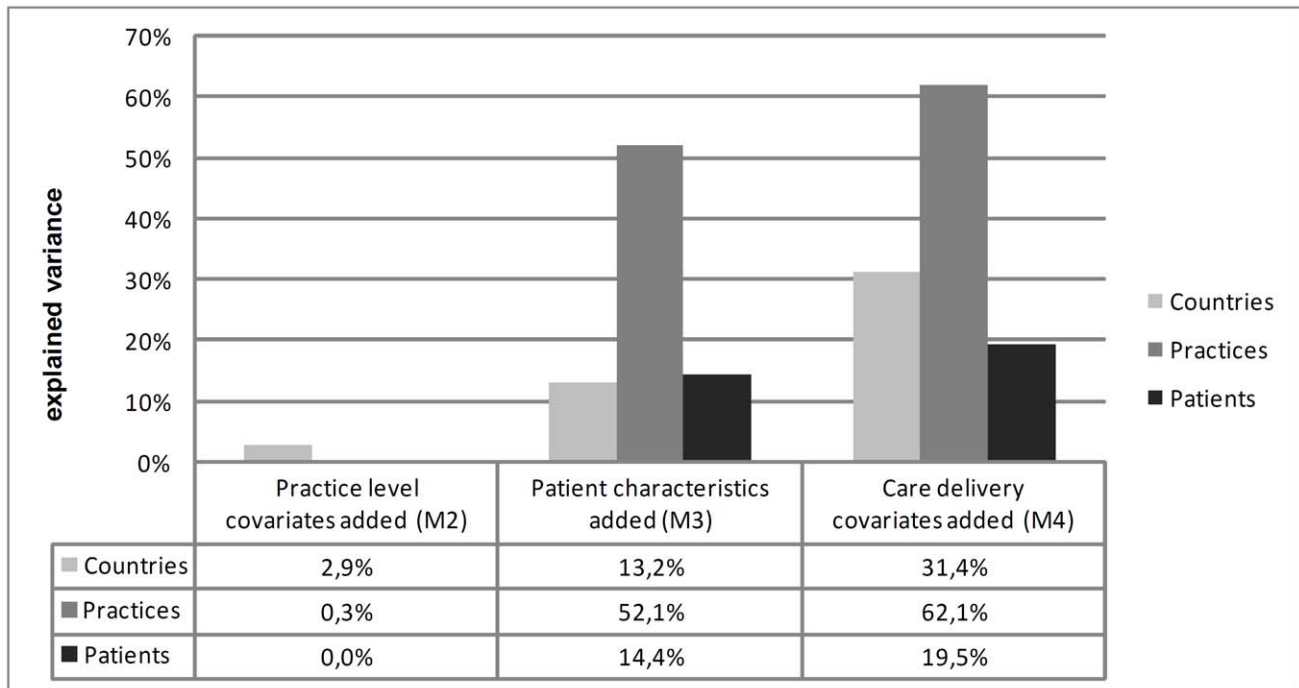


Figure 2. Proportion of variance in overall EQ-5D score explained at each level.
doi:10.1371/journal.pone.0051726.g002

The strongest positive association with HRQoL was found in our study for good medication adherence (Morisky) and a higher score in the EUROPEP dimension ‘clinical behavior’ (indicating a good patient-doctor relationship). As good medication adherence is (among other aspects) influenced by interaction between patients and treating physicians [44,45], both variables underline the importance of patient-doctor relationship on HRQoL. Previous research has shown that patient-physician relationship can be linked to improved health outcomes [46].

Particularly, good communication between doctors and patients could lead to better physical health by identifying the diagnosis, finding an appropriate treatment plan or strengthening self-management in chronic care. Additionally, positive effects on psychosocial outcomes can be a result of patient-centered communication from which patients feel recognized, validated, worthy, reassured, and comforted [46]. In secondary prevention and chronic care, a good patient-physician relationship is the basis of a multifaceted regimen, which involves long-term management of risk factors, support of medication adherence and lifestyle interventions, like obesity or physical activity counseling [47–50]. From this point of view, potential for improvements in HRQoL particularly exist in strengthening the patient-doctor relationship.

Strengths and limitations

The EPA cardio study is one of the largest international studies on the management of cardiovascular prevention in European primary care. We used multilevel modeling to account for the hierarchical data structure and to identify predictors of HRQoL adjusting for all other variables. Hierarchical models combine information across units to produce accurate and well calibrated prediction of outcomes. This analytic approach has been found to be very relevant in health services research as patients’ data were similarly clustered at more than one level. We used validated measures and collected morbidity data from medical records in contrast to self-reported morbidity indicators that could lead to misclassifications.

Nevertheless, in some countries it was difficult to enroll 36 practices as intended. In the multivariable analyses, the total number of cases decreased due to missing data, as we conducted a complete case analysis. The EQ-5D instrument showed a ceiling

effect with 30% of people scoring the highest value. As also reported in other studies, EQ-5D may be less sensitive to describe mild severity health levels. However, the EQ-5D instrument is reported to have a better discrimination capacity for socio-demographic and morbidity indicators that were focused in our study. Because of the observational design of our study, the correlations found cannot be used to attest causal associations.

Conclusion

The results of our study may suggest that the patient-physician relationship rather than the organization of CVD care and aspects of quality management is an important predictor of health status in usual primary care. This is also reflected in the finding, that no differences between single-handed and group practices concerning HRQoL exist. For further development, the results may imply that interventions to improve HRQoL require a strong patient-centered approach. That the majority of patients, as shown by our results, have a long-term relationship to their primary care practice, is a good basis for further developments in this field.

Supporting Information

Table S1 Fixed part results of the random intercept models fitted to the total sample.

(DOCX)

Table S2 Fixed part results of the random intercept models fitted to subsample of single-handed practices.

(DOCX)

Table S3 Fixed part results of the random intercept models fitted to subsample of group practices.

(DOCX)

Author Contributions

Conceived and designed the experiments: JS MW SMC JvL SL. Analyzed the data: DO TF LU JR. Wrote the paper: DO JR SL. Critically reviewed the manuscript for important intellectual content: DO JR SMC MW JvL LU TF JS SL. Approved the final version submitted for publication: DO JR SMC MW JvL LU TF JS SL.

References

- Mensah GA, Brown DW (2007) An overview of cardiovascular disease burden in the United States. *Health Aff (Millwood)* 26: 38–48.
- Leal J, Luengo-Fernandez R, Gray A, Petersen S, Rayner M (2006) Economic burden of cardiovascular diseases in the enlarged European Union. *Eur Heart J* 27: 1610–1619.
- Yusuf S, Reddy S, Ounpuu S, Anand S (2001) Global burden of cardiovascular diseases - Part II: Variations in cardiovascular disease by specific ethnic groups and geographic regions and prevention strategies. *Circulation* 104: 2855–2864.
- Rosamond W, Flegal KM, Furie K, Go A, Greenlund K, et al. (2008) Heart disease and stroke statistics—2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 117: e25–146.
- Brown JR, O’Connor GT (2010) Coronary heart disease and prevention in the United States. *N Engl J Med* 362: 2150–2153.
- van Dam RM, Willett WC (2009) Unmet potential for cardiovascular disease prevention in the United States. *Circulation* 120: 1171–1173.
- Lloyd-Jones DM, Hong YL, Labarthe D, Mozaffarian D, Appel LJ, et al. (2010) Defining and Setting National Goals for Cardiovascular Health Promotion and Disease Reduction The American Heart Association’s Strategic Impact Goal Through 2020 and Beyond. *Circulation* 121: 586–613.
- Frieden TR, Berwick DM (2011) The “Million Hearts” initiative—preventing heart attacks and strokes. *N Engl J Med* 365: e27.
- Campbell SM, Ludt S, Van Lieshout J, Boffin N, Wensing M, et al. (2008) Quality indicators for the prevention and management of cardiovascular disease in primary care in nine European countries. *Eur J Cardiovasc Prev Rehabil* 15: 509–515.
- Graham I, Atar D, Borch-Johnsen K, Boysen G, Burell G, et al. (2007) European guidelines on cardiovascular disease prevention in clinical practice: executive summary: Fourth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 28: 2375–2414.
- van Lieshout J, Wensing M, Campbell SM, Grol R (2009) Primary care strength linked to prevention programs for cardiovascular disease. *Am J Manag Care* 15: 255–262.
- Bodenheimer T, Wagner EH, Grumbach K (2002) Improving primary care for patients with chronic illness. *JAMA* 288: 1775–1779.
- Boyd CM, Boulton C, Shadmi E, Leff B, Brager R, et al. (2007) Guided care for multimorbid older adults. *Gerontologist* 47: 697–704.
- Counsell SR, Callahan CM, Clark DO, Tu W, Buttar AB, et al. (2007) Geriatric care management for low-income seniors: a randomized controlled trial. *JAMA* 298: 2623–2633.
- Friedman SM, Steinwachs DM, Rathouz PJ, Burton LC, Mukamel DB (2005) Characteristics predicting nursing home admission in the program of all-inclusive care for elderly people. *Gerontologist* 45: 157–166.
- Boyd CM, Reider L, Frey K, Scharfstein D, Leff B, et al. (2010) The effects of guided care on the perceived quality of health care for multi-morbid older persons: 18-month outcomes from a cluster-randomized controlled trial. *J Gen Intern Med* 25: 235–242.
- Bielaszka-DuVernay C (2011) The ‘GRACE’ model: in-home assessments lead to better care for dual eligibles. *Health Aff (Millwood)* 30: 431–434.
- Nadash P (2004) Two models of managed long-term care: comparing PACE with a Medicaid-only plan. *Gerontologist* 44: 644–654.
- Redelmeier DA, Rozin P, Kahneman D (1993) Understanding patients’ decisions. Cognitive and emotional perspectives. *JAMA* 270: 72–76.
- Rumsfeld JS (2002) Health status and clinical practice: when will they meet? *Circulation* 106: 5–7.

21. Bell RJ, Rivera-Woll L, Davison SL, Topliss DJ, Donath S, et al. (2007) Well-being, health-related quality of life and cardiovascular disease risk profile in women with subclinical thyroid disease - a community-based study. *Clin Endocrinol (Oxf)* 66: 548–556.
22. Xie J, Wu EQ, Zheng ZJ, Sullivan PW, Zhan L, et al. (2008) Patient-reported health status in coronary heart disease in the United States: age, sex, racial, and ethnic differences. *Circulation* 118: 491–497.
23. Koertge J, Weidner G, Elliott-Eller M, Scherwitz L, Merritt-Worden TA, et al. (2003) Improvement in medical risk factors and quality of life in women and men with coronary artery disease in the Multicenter Lifestyle Demonstration Project. *Am J Cardiol* 91: 1316–1322.
24. Wang W, Chair SY, Thompson DR, Twinn SF (2012) Effects of home-based rehabilitation on health-related quality of life and psychological status in Chinese patients recovering from acute myocardial infarction. *Heart Lung* 41: 15–25.
25. Friedberg MW, Safran DG, Coltin KL, Dresser M, Schneider EC (2009) Readiness for the Patient-Centered Medical Home: structural capabilities of Massachusetts primary care practices. *J Gen Intern Med* 24: 162–169.
26. Takach M, Gauthier A, Sims-Kastelein K, Kaya N, Fund C (2010) Strengthening Primary and Chronic Care: State Innovations to Transform and Link Small Practices: Commonwealth Fund.
27. Wensing M, Mainz J, Grol R (2000) A standardised instrument for patient evaluations of general practice care in Europe. *Eur J Gen Pract* 6: 82–87.
28. Ludt S, Wensing M, Szecsenyi J, van Lieshout J, Rochon J, et al. (2011) Predictors of health-related quality of life in patients at risk for cardiovascular disease in European primary care. *PLoS One* 6: e29334.
29. Engels Y, Dautzenberg M, Campbell S, Broge B, Boffin N, et al. (2006) Testing a European set of indicators for the evaluation of the management of primary care practices. *Fam Pract* 23: 137–147.
30. Morisky DE, Green LW, Levine DM (1986) Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 24: 67–74.
31. Greiner W, Weijnen T, Nieuwenhuizen M, Oppe S, Badia X, et al. (2003) A single European currency for EQ-5D health states. Results from a six-country study. *Eur J Health Econ* 4: 222–231.
32. Williams A (1990) EuroQol—a new facility for the measurement of health-related quality of life. *Health Policy* 16: 199–208.
33. Dyer MT, Goldsmith KA, Sharples LS, Buxton MJ (2010) A review of health utilities using the EQ-5D in studies of cardiovascular disease. *Health Qual Life Outcomes* 8: 13.
34. Garster NC, Palta M, Sweitzer NK, Kaplan RM, Fryback DG (2009) Measuring health-related quality of life in population-based studies of coronary heart disease: comparing six generic indexes and a disease-specific proxy score. *Qual Life Res* 18: 1239–1247.
35. Davis P, Scott A (1995) The effect of interviewer variance on domain comparisons. *Survey Methodology* 21: 99–106.
36. Raudenbusch S, Bryk A (2002) Hierarchical linear models: Applications and data analysis methods (2nd ed). Thousand Oaks, CA: Sage.
37. Rasbash J, Brown W, Healy M, Cameron B, Charlton C (2011) *Mlwin* version 2.24.
38. Vargas RB, Mangione CM, Asch S, Keeseey J, Rosen M, et al. (2007) Can a chronic care model collaborative reduce heart disease risk in patients with diabetes? *J Gen Intern Med* 22: 215–222.
39. Friedberg MW, Coltin KL, Safran DG, Dresser M, Zaslavsky AM, et al. (2009) Associations between structural capabilities of primary care practices and performance on selected quality measures. *Ann Intern Med* 151: 456–463.
40. Tsai AC, Morton SC, Mangione CM, Keeler EB (2005) A meta-analysis of interventions to improve care for chronic illnesses. *Am J Manag Care* 11: 478–488.
41. Parker RM, Williams MV, Weiss BD, Baker DW, Davis TC, et al. (1999) Health literacy - Report of the Council on Scientific Affairs. *JAMA* 281: 552–557.
42. Ford ES, Mokdad AH, Li C, McGuire LC, Strine TW, et al. (2008) Gender differences in coronary heart disease and health-related quality of life: findings from 10 states from the 2004 behavioral risk factor surveillance system. *J Womens Health (Larchmt)* 17: 757–768.
43. Ose D, Wensing M, Szecsenyi J, Joos S, Hermann K, et al. (2009) Impact of primary care-based disease management on the health-related quality of life in patients with type 2 diabetes and comorbidity. *Diabetes Care* 32: 1594–1596.
44. Piette JD, Heisler M, Krein S, Kerr EA (2005) The role of patient-physician trust in moderating medication nonadherence due to cost pressures. *Arch Intern Med* 165: 1749–1755.
45. Wroth TH, Pathman DE (2006) Primary medication adherence in a rural population: The role of the patient-physician relationship and satisfaction with care. *Journal of the American Board of Family Medicine* 19: 478–486.
46. Street RL, Makoul G, Arora NK, Epstein RM (2009) How does communication heal? Pathways linking clinician-patient communication to health outcomes. *Patient Educ Couns* 74: 295–301.
47. Simons-Morton DG, Blair SN, King AC, Morgan TM, Applegate WB, et al. (2001) Effects of physical activity counseling in primary care - The activity counseling trial: A randomized controlled trial. *Jama-Journal of the American Medical Association* 286: 677–687.
48. Byrne M, Walsh J, Murphy AW (2005) Secondary prevention of coronary heart disease: Patient beliefs and health-related behaviour. *J Psychosom Res* 58: 403–415.
49. Eriksson MK, Hagberg L, Lindholm L, Malmgren-Olsson EB, Osterlind J, et al. (2010) Quality of Life and Cost-effectiveness of a 3-Year Trial of Lifestyle Intervention in Primary Health Care. *Arch Intern Med* 170: 1470–1479.
50. Wadden TA, Volger S, Sarwer DB, Vetter ML, Tsai AG, et al. (2011) A Two-Year Randomized Trial of Obesity Treatment in Primary Care Practice. *N Engl J Med* 365: 1969–1979.