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The 3-Year Cost-Effectiveness of a Nurse-Based Case Management versus Usual Care for Elderly Patients with Myocardial Infarction: Results from the KORINNA Follow-Up Study

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ABSTRACT

Objectives: To assess the 3-year cost-effectiveness of a nurse-based case management intervention in elderly patients with myocardial infarction from a societal perspective. **Methods:** The intervention consisted of one home visit and quarterly telephone calls in the first year, and semi-annual calls in the following 2 years. The primary effect measures were quality-adjusted life-years (QALYs), on the basis of the EuroQol five-dimensional questionnaire (EQ-5D-3L) and adjusted life-years from patients' self-rated health states according to the visual analogue scale (VAS-ALs). A linear regression model was used for adjusted life-years and a gamma model for costs. Estimation uncertainty was addressed by cost-effectiveness acceptability curves, which indicate the likelihood of cost-effectiveness for a given value of willingness to pay. The secondary objective was to examine EQ-5D-3L utility scores and VAS scores among survivors using linear mixed models. **Results:** Primary outcomes regarding QALY gains (+0.0295; P = 0.76) and VAS-AL gains (+0.1332; P = 0.09) in the intervention group were not significant. The overall cost difference was –€2575 (P = 0.30). The probability of cost-effectiveness of the case management at a willingness-to-pay value of €0 per QALY was 84% in the case of QALYs and 81% in the case of VAS-ALs. Secondary outcomes concerning survivors' quality of life were significantly better in the intervention group (EQ-5D-3L utilities: +0.104, P = 0.005; VAS: +8.15, P = 0.001) after 3 years. **Conclusions:** The case management was cost-neutral and led to an important and significant improvement in health status among survivors. It was associated with higher QALYs and lower costs but the differences in costs and QALYs were not statistically significant.

Keywords: case management, cost-effectiveness analysis, myocardial infarction, quality-adjusted life-years.

Introduction

Coronary heart disease (CHD) is a major cause of mortality worldwide (13.2%), with an increasing prevalence over the past decade [1]. Although recommended by the European Association of Cardiovascular Prevention and Rehabilitation [2], only 36.5% of patients with CHD participate in secondary prevention programs such as cardiac rehabilitation in Europe [3]. A different approach for secondary prevention is a nurse-based case management program, which is considered as a low-cost and effective alternative to cardiac rehabilitation [4]. In Germany, no nurse-based case management programs are at present available although only 51.6% of patients with a cardiac event receive cardiac rehabilitation [3]. In addition, elderly patients participate less frequently in cardiac rehabilitation [3] although they present more adverse health outcomes than do younger patients who have been diagnosed with CHD [5]. Several studies have shown that case management can reduce hospitalization and increase quality of life, but only a few studies have focused on patients with acute myocardial infarction (AMI) and elderly patients [4,6–8]. Moreover, studies evaluating the cost-effectiveness of case management are scarce and have not considered long-term effects and costs.

We conducted the KORINNA study ("Coronary infarction follow-up in the elderly") to analyze whether case management in elderly people with AMI can postpone unplanned readmission or death (combined end point) within 1 year of hospital discharge [9]. To analyze long-term effects, the KORINNA study was

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extended for another 2 years. The findings regarding readmissions or death have been published elsewhere [10,11] and these showed that differences between groups were significant neither after 1 year nor after 3 years. Analysis of secondary outcomes demonstrated that case management can improve blood lipid levels, functional status, and malnutrition risk after 1 year [12] and that improvements in functioning and malnutrition risk were maintained or results even advanced further after 3 years [10]. The 1-year cost-effectiveness analysis showed that case management was associated with improvements in self-rated health, but there were no significant differences in quality-adjusted life-years (QALYs) or health care costs between treatment arms [13].

Till now, no study has yet evaluated the cost-effectiveness of a case management program in elderly patients with AMI after hospital discharge. There are only three studies that performed a formal cost-effectiveness analysis for patients with CHD [14–16] and five studies that performed an analysis for patients with heart failure [17–21] estimating cost per QALY with different results.

The objective of our study was to assess the 3-year cost-effectiveness of the case management program KORINNA from a societal perspective.

Methods

The randomized controlled KORINNA trial evaluated a case management intervention by trained nurses in elderly patients with AMI.

Between September 2008 and May 2010, 340 patients were enrolled. The inclusion criteria were that patients had to be 65 years or older and had to have an acute first or recurrent AMI treated in the Central Hospital of Augsburg, which is the major hospital for the population of 830,000 in the Greater Augsburg area, southern Germany. Exclusion criteria were as follows: planned or present residence in a nursing home, severe comorbidity associated with a life expectancy of less than 1 year (e.g., terminal cancer), insufficient ability to speak German, and lack of ability because of cognitive disorders or willingness to consent.

All patients were assigned to either the intervention group or the control group on the basis of randomized blocks within strata for sex, age (65–69 years vs. 70–79 years vs. 80+ years), and number of comorbidities (none, diabetes or chronic heart failure, and both).

Baseline assessment was performed shortly before hospital discharge. In the first year, participants were interviewed quarterly; in the second and third years, participants were interviewed annually through either a computer-assisted telephone interview (CATI) or a face-to-face interview for outcome assessment. In the case of a CATI, plausibility checks were included and in the case of face-to-face interviews, double data entry was applied. Economic analyses were performed from the societal perspective. Because of a 36-month follow-up, analyses of costs and effects were performed without a discount rate as well as with a discount rate of 3% [22].

The trial was approved by the Ethics Committee of the Bavarian Chamber of Physicians (registration no. ISRCTN02893746). Further details on design and sample size calculation can be found in the study protocol, which has been published elsewhere [9]. The intervention and observation period spanned 3 years.

Comparators

The control group received usual care; that is, patients regularly visit their physician, may receive cardiac rehabilitation, or may be treated in a long-term disease management program offered by health insurance companies [23]. The intervention is described in detail elsewhere [10,11]. In brief, shortly before hospital discharge, patients received an information booklet, and a first home visit or an appointment for a telephone call was arranged. At least one home visit and quarterly telephone calls were carried out in the first year, and two telephone calls in each of the following 2 years (every 6 months), with additional visits and calls according to the patient's needs and risk level. The risk level was assessed by the study nurse during the home visits and telephone calls on the basis of compliance, social network, and the New York Heart Association Functional Classification. The risk level classification suggested by Russell et al. was used [11,24]. In a structured interview, the nurses provided counseling on the intake of medication, nutrition, physical activity, weight control, and general health behavior. During the home visits, additional measurements of vital functions (e.g., blood pressure and pulse rate) and blood glucose were performed.

Effects

In all interviews, health-related quality of life was assessed using the generic three-level EuroQol five-dimensional questionnaire (EQ-5D-3L) and the visual analogue scale (VAS). Validity and reliability of the EQ-5D-3L in patients who have suffered an AMI have been shown in several studies [25,26]. The primary effect measure in the economic evaluation was QALYs, on the basis of EQ-5D-3L health states converted into utility scores using the German time trade-off scoring algorithm [27]. QALYs were estimated for each individual as the area under the curve through linear interpolation of values for the periods between measurements [28]. When patients died during the observation period, their values were set to 0 from the day of death. It was assumed that before death, the utility function declined linearly from the observed preceding value.

To assess the sensitivity of results to different health state valuation methods, a sensitivity analysis considered life-years adjusted by patients' self-rated health states as measured by their VAS scores (VAS-ALs). To ensure comparability with utility-based QALYs, VAS scores were transformed to the 0 to 1 scale before constructing VAS-ALs.

The secondary objective was to examine EQ-5D-3L time trade-off–based utility scores and VAS scores among survivors over time.

Costs

Cost measurements were conducted from the societal perspective and data collection was not limited to disease-related services. In accordance with the study protocol [9], in the first year, medical resource use was collected quarterly and then annually in the second and third years. Indirect costs were not considered because of participants' retirement. All unit prices were reported for the year 2012 and are presented in euros. Intervention costs consisted of labor costs for study nurses to perform the case management (€31.33/h; overhead costs and wage rates of the Central Hospital of Augsburg) and travel costs (€0.30/km). The average time that nurses spent making telephone calls (19 minutes) was documented by CATI and that spent for home visits (117 minutes) by logbooks. On the basis of this information, costs per telephone call (€10) and per home visit (€57.40) were calculated.

Costs from inpatient care were calculated according to days spent in the hospital, separated in days spent in general ward and days spent in intensive care unit. Self-reported admissions were validated by the study physician using information from hospital records and discharge letters and when required readjusted and completed. For the Central Hospital of Augsburg, all hospital records were available for the 3-year period. For every participant admitted at least once to any other hospital, all hospital records and discharge letters were requested from those hospitals. Costs of all other health care components (i.e., physicians, physiotherapists, ambulatory clinic in the hospital, rehabilitation, drugs, and direct non–health care resources) were calculated from patients' self-reported resource use. Single missing values of these other costs were replaced by patients' cost data from a subsequent time frame [29,30].

Unit price calculation was primarily based on estimates published by Bock et al. [31], which provide valid and reliable information about unit prices of several medical and nonmedical resources in Germany from a societal perspective. Medication was recorded using IDOM software, a database-supported identification system [32] that logs name, units, pharmaceutical identification number, time period, package size, and price per package [33]. To estimate the cost of informal care we use the information of the existence of a care level. In Germany, the care level is declared by the long-term care insurance [34] to assess whether and to what extent patients need help in activities of daily living. If the patient is assigned to a care level and does not receive formal care, the patient gets a transfer payment. Although transfer payments are ordinarily excluded from a societal perspective, they are used here as a proxy value for informal care because it can be assumed that these patients require informal care. When patients died during the observation period, their costs were set to 0 from the day of death, and hence effects and costs were treated in the same way. Table 1 gives an overview of prices assigned to the resource quantities.

Statistical Analysis

To calculate mean QALY differences between treatment groups, we used a linear regression model controlling for stratification variables of the trial (sex, age groups, and number of comorbidities) and baseline utility [35]. The same method was applied to determine the intervention effect expressed by VAS-AL.

Table 1 – Unit prices [31].

Units	Unit Price (in 2012 euros)
Direct health care	
Physicians	
General practitioner	20.22/contact
Internist	64.65/contact
Orthopedist	25.27/contact
Neurologist	45.58/contact
Ophthalmologist	35.09/contact
Otolaryngologist	27.55/contact
Gynecologist	30.53/contact
Dermatologist	19.10/contact
Urologist	24.97/contact
Other	43.97/contact
Physiotherapist	16.62/contact
Ambulatory clinic in the hospital	40.31/contact
Inpatient care/hospital/general ward	589.32/d
Inpatient care/hospital/intensive care unit	1357.65/d
Inpatient rehabilitation	122.09/d
Outpatient rehabilitation	48.29/d
Drugs	
Direct non–health care	
Outpatient nursing service	30.00/h
Paid household help	10.20/h
Informal care (care level)	
None	0/mo
1	235.00/mo
2	440.00/mo
3	700.00/mo

To analyze EQ-5D-3L utility and VAS data over time, linear mixed models with the stratification variables as fixed effects and an additional random intercept were fitted. Mixed models based on full maximum likelihood estimation have been shown to be an effective method to account for dropout when estimating longitudinal change [36]. Resource use data and corresponding cost data were presented as mean values with SD. To analyze costs, a generalized gamma regression model with log-link was used to account for the skewed distribution of the data [37]. From the gamma model, adjusted mean differences in costs between intervention and control groups were estimated using the method of recycled predictions. This method creates an identical covariate structure for each treatment group by first assuming that all individuals are cases and predicting costs and then assuming that all individuals are controls and predicting costs [38,39]. Calculating the difference in the mean predictions for all individuals between these two scenarios then yields an estimate of the adjusted marginal difference in costs between intervention and control groups. A 95% confidence interval (CI) for the adjusted cost difference was estimated from 1000 bootstrap replications using the percentile method.

We performed a cost-effectiveness analysis, in which incremental cost-effectiveness ratios (ICERs) were calculated only in the case of a positive ICER, meaning that case management is neither dominant nor dominated [40].

Estimation uncertainty was addressed by bootstrapping ($n = 1000$) incremental cost and effect estimates and plotting them on the cost-effectiveness plane (CE plane) to generate the joint density of incremental costs and incremental effects [41,42]. The proportion of the joint density located within the southeast quadrant of the CE plane suggests the likelihood of dominance of case management and the joint density in the northwest quadrant of being dominated [41]. From the resulting bootstrap distribution, we also calculated cost-effectiveness acceptability curves, which indicate the likelihood that the intervention is cost-effective for a given value of willingness to pay (WTP).

The primary cost-effectiveness analysis excluded patients who withdrew consent or were lost to follow-up during the 3-year study period. In a sensitivity analysis, we applied a missing value imputation approach to include data from all randomized patients. To impute missing values for an individual who dropped out before measurement time point t, we first fitted a logistic model to predict survival of the participant at t. Explanatory variables were the stratification variables (i.e., sex, age in groups, and number of comorbidities), treatment assignment, and the one-period-lagged health status (EQ-5D-3L utility or VAS) [43]. From the resulting predicted distribution, a Bernoulli random number was drawn, reflecting whether the participant was assumed to have died. In the case of death, the cost and utility from time point t were set to 0. Otherwise, a second imputation model with the same covariates as the logistic model was fitted on the subsample of all participants still living at time point t to predict values for cost and utility. For the imputation of utilities, this second model used the predictive mean matching method to ensure that imputed data are actually observable EQ-5D-3L (or VAS) values [44]. The model for cost used the "regression method" applied to log-transformed values to account for the skewness of the underlying data. The aforementioned two steps were then repeated for all subsequent time points until the 36-month measurement. To avoid missing lagged values in the following cycles, the imputed values from the preceding cycle were used [43]. Overall, this imputation model is based on the assumption that the missing observations are missing at random given the observed data, especially given sex, age, number of comorbidities, treatment arm, and health status before dropout.

To account for the uncertainty associated with imputed values, we bootstrapped the whole imputation and estimation process. Therefore, the full data set including missing values was first bootstrapped and then the imputation process was applied in each bootstrap sample [45].

All analyses were performed with SAS version 9.2 (SAS Institute, Inc., Cary, NC).

Results

From the 340 patients randomized, 11 patients were retrospectively excluded in coordination with the study's advisory board because of death or withdrawal of consent before hospital discharge. Thus, our analysis included 329 patients (Fig. 1). Within the first 3 months, 4 participants in the control group and 13 participants in the intervention group died, of whom 10 had no contact with the study nurse between hospital discharge and death. Within the next 9 months, 9 participants in the control group and 5 participants in the intervention group died. Within the next 24 months, 19 participants in the control group and 11 participants in the intervention group died. Characteristics of both randomized patients and patients without withdrawals at baseline are presented in Table 2.

Effects

Table 3 presents the results of the primary analysis together with the corresponding sensitivity analyses. The adjusted mean QALY difference between the intervention and control groups during the 3-year period was 0.0295 ($P = 0.2968$; CI –0.1579 to 0.2169). The adjusted mean difference in VAS-ALs was 0.1332 ($P = 0.0912$; CI –0.0215 to 0.2878). The goodness of fit of our regression models in terms of R^2 was 0.35 (QALYs) and 0.34 (VAS-ALs). Applying a discount rate of 3% did not alter results. The analyses based on a multiple imputation approach reduced the differences for either measure of effectiveness.

Table 4 presents the secondary analyses and shows utilities (EQ-5D index) and VAS scores among survivors in the two

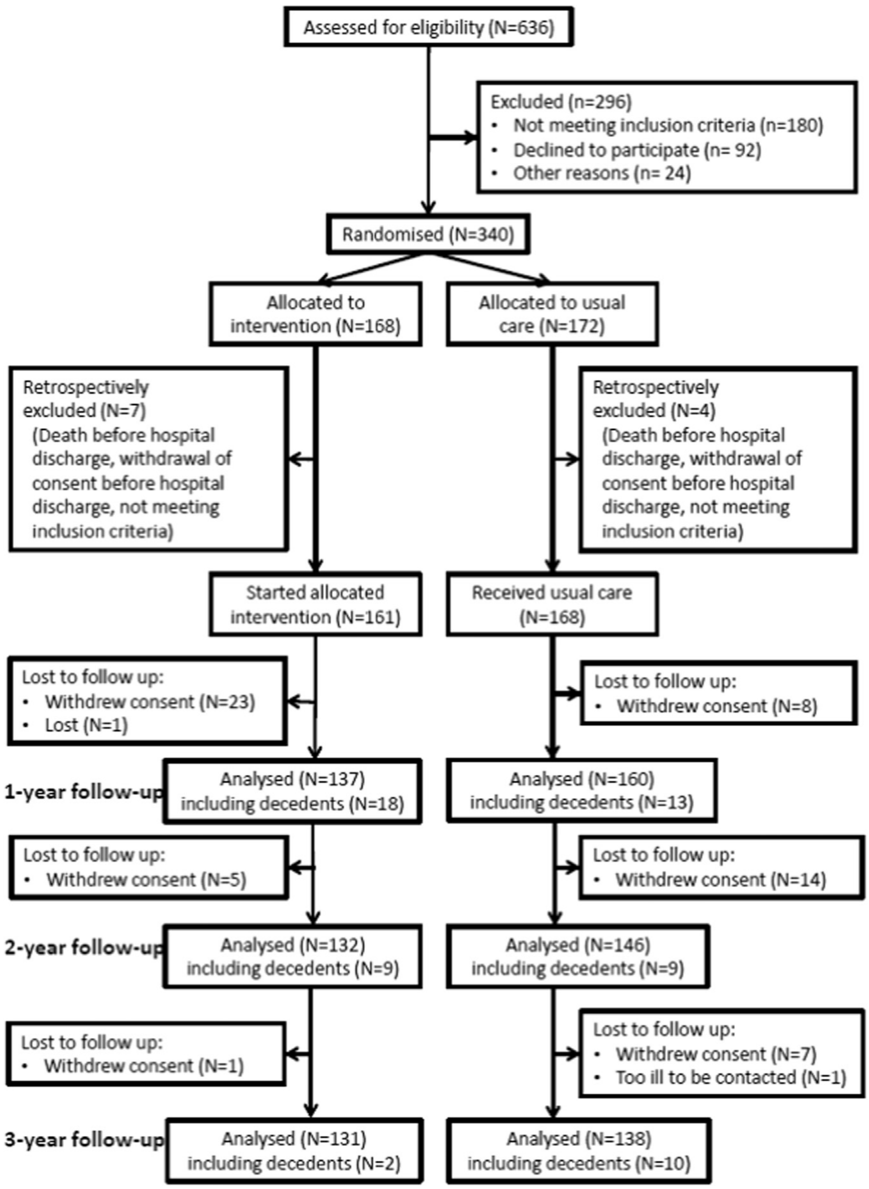

Fig. 1 – Consort flow chart

Table 2 – Patient baseline characteristics.

Patient baseline characteristics	Randomized patients(n = 329)		Patients without withdrawals(n = 269)	
	Intervention (n = 161)	Control (n = 168)	Intervention (n = 131)	Control (n = 138)
Age (y), mean ± SD	75.2 ± 6.0	75.6 ± 5.9	74.8 ± 5.8	75.6 ± 6.1
Sex, % females	37.3	38.7	35.1	38.4
No comorbidity (neither diabetes nor CHF) (%)	54.7	51.2	53.4	51.5
One comorbidity (diabetes or CHF) (%)	32.9	33.3	35.1	32.6
Two comorbidities (diabetes and CHF) (%)	12.4	15.5	11.5	15.9
Living alone (%)	27.9	26.8	24.4	28.3
NYHA I (%)	46.0	41.7	48.1	42.0
NYHA II (%)	24.8	31.6	22.9	29.7
NYHA III (%)	24.8	22.6	24.4	23.9
NYHA IV (%)	2.5	2.4	2.3	2.2
VAS, mean ± SD	58.9 ± 20.7	57.8 ± 20.1	59.5 ± 20.2	58.3 ± 20.2
EQ-5D index*, mean ± SD	0.74 ± 0.32	0.73 ± 0.31	0.74 ± 0.31	0.74 ± 0.31

Note. CHF: NYHA III and NYHA IV.
CHF, chronic heart failure; EQ-5D, EuroQol five-dimensional questionnaire; NYHA, New York Heart Association; VAS, visual analogue scale.
* EQ-5D index is based on German population tariff and time trade-off scoring [27].

treatment arms over time. In the intervention group, utility scores from the EQ-5D-3L were significantly higher at month 3 (+0.078) and month 6 (+0.052) than at baseline. Scores, however, returned toward baseline levels at 12 months and were lower than baseline scores in the second and third years, although statistically not significant. In the control group, utility scores did not change during the first year, but there was a significant decrease in utility scores in the second (–0.068) and third years (–0.142). In the third year, the intervention group had a significantly higher utility score than the control group (+0.104; P = 0.0054).

VAS values showed significant improvements between baseline and all subsequent measurement time points in the intervention group and no significant changes from baseline in the control group. In the third year, the intervention group had a significantly higher VAS value than the control group (+8.15; P = 0.0010), and VAS values in the intervention group were significantly higher over all time points.

Resource Use and Costs

Table 5 presents an overview of unadjusted mean resource use over the course of time and mean costs during the 3-year period per patient. On average, patients received 1.2 home visits and 5.6 telephone interviews in the intervention group, resulting in intervention costs of €166 per participant. About 90% of patients received no benefits from the German long-term care insurance, 7% were assigned to care level 1, 3% to care level 2, and none to care level 3. Resource use within 3 years was stable with the exception of inpatient care, rehabilitation, and paid household help. Inpatient care decreased over time. In the first year, patients in the intervention group spent on average 8.7 days in hospital and those in the control group spent 11.71 days. These numbers decreased to 3.55 days for the intervention group and 4.93 days for the control group in the third year. Case management was associated with lower costs in all health care resource categories with the exception of paid household work. The largest difference between groups was found for inpatient care, in which patients

Table 3 – Effectiveness in QALYs and VAS-ALs adjusted for sex, age, number of comorbidities (diabetes and CHF), and baseline values for health states; cost differences adjusted for sex, age, and number of comorbidities (diabetes and CHF).

	Difference (P value), IG-CG			
	Primary analysis (n = 269)		Sensitivity analysis (n = 329)	
	Without discounting	Discount rate = 3%	Multiple imputation without discounting	Multiple imputation discount rate = 3%
QALYs	0.0295 (0.7568) CI: –0.1579 to 0.2169	0.0268 (0.7714) CI: –0.1544 to 0.2079	0.0023 (0.984) CI: –0.1847 to 0.1843	0.0010 (0.996) CI: –0.1799 to 0.1771
Sensitivity analysis				
VAS-ALs	0.1332 (0.0912) CI: –0.0215 to 0.2878	0.1288 (0.0913) CI: –0.0208 to 0.2783	0.1158 (0.124) CI: –0.0400 to 0.2653	0.1124 (0.122) CI: –0.0380 to 0.2567
Costs	–2575 (0.2968) CI: –8158 to 2386	–2509 (0.2986) CI: –7950 to 2339	–3401 (0.176) CI: –8304 to 1922	–3290 (0.182) CI: –8057 to 1884

CHF, chronic heart failure; CI, confidence interval; IG-CG, intervention group-control group; QALY, quality-adjusted life-year (using the EQ-5D index based on German population tariff and time trade-off scoring [27]; VAS, visual analogue scale; VAS-AL, VAS-adjusted life-year using patients' EQ-VAS score (self-rated health).
Complete case, sample including decedents.

Table 4 – Secondary analyses: effectiveness in quality of life for survivors only, adjusted for sex, age, number of comorbidities (none, diabetes or CHF, both).

	Mean change in the respective month compared with baseline (P value)		
	Intervention	Control	Difference in mean change between intervention and control group (P value)
EQ-5D index based on German population tariff and time trade-off [27]			
Month 3	(n = 130) 0.078 (0.0019)	(n = 161) 0.018 (0.4324)	0.060 (0.0757)
Month 6	(n = 127) 0.052 (0.0401)	(n = 153) 0.033 (0.1490)	0.019 (0.5868)
Month 9	(n = 123) 0.012 (0.6325)	(n = 152) 0.006 (0.7800)	0.006 (0.8656)
Month 12	(n = 119) –0.005 (0.8617)	(n = 147) –0.012 (0.6012)	0.008 (0.8228)
Month 24	(n = 105) –0.020 (0.4519)	(n = 124) –0.068 (0.0061)	0.048 (0.1883)
Month 36	(n = 102) –0.038 (0.1613)	(n = 106) –0.142 (<0.0001)	0.104 (0.0054)
Patients' VAS score, self-rated health			
Month 3	(n = 130) 7.98 (<0.0001)	(n = 161) 2.36 (0.1251)	5.61 (0.0145)
Month 6	(n = 127) 10.83 (<0.0001)	(n = 153) 2.83 (0.0615)	8.00 (0.0004)
Month 9	(n = 123) 11.84 (<0.0001)	(n = 152) 1.97 (0.1940)	9.88 (<0.0001)
Month 12	(n = 119) 10.11 (<0.0001)	(n = 147) 0.90 (0.5591)	9.21 (<0.0001)
Month 24	(n = 105) 8.28 (<0.0001)	(n = 124) 0.87 (0.5976)	7.42 (0.0021)
Month 36	(n = 102) 8.13 (<0.0001)	(n = 106) –0.03 (0.9886)	8.15 (0.0010)

CHF, chronic heart failure; EQ-5D, EuroQol five-dimensional questionnaire; VAS, visual analogue scale.

in the control group had on average €3170 higher costs than those in the intervention group. The adjusted overall cost difference (Table 3) from the gamma model was estimated at –€2576 (CI –8158 to 2386). Applying a discount rate of 3%, the difference remained stable at –€2509 (CI –7950 to 2339). The analysis with multiple imputations led to an undiscounted and discounted difference of –€3401 (CI –8304 to 1922) and –€3290 (CI –8057 to 1884), respectively. Mean costs per day survived showed no difference between groups (€34.66 in the intervention group and €34.03 in the control group).

Cost-Effectiveness

Because costs were lower (–€2576; P = 0.2968) and QALYs were higher (+0.0295; P = 0.7568) in the intervention group and differences remained stable after applying a discount rate of 3%, no ICER was calculated [40]. The corresponding CE plane (Fig. 2A) plots differences in mean total costs on the vertical axis and differences in mean QALYs on the horizontal axis for each of the 1000 bootstrap resamples. Fifty-three percent of the bootstrap observations were located in the southeast quadrant of the CE plane.

The sensitivity analysis using VAS-ALs also showed that case management was associated with higher effects (0.1332; P = 0.0912) and lower costs (–€2576; P = 0.2968) and 78% of bootstrap samples were located in the southeast quadrant (Fig. 2B).

The resulting cost-effectiveness acceptability curve is a decreasing function and so it does not asymptote to 1 (Fig. 3A). This means that 84% of the density involves cost saving (cut point of the y-axis), but only 62% of the density involves health gains (asymptote) and 38% involves health losses. As a consequence, the probability of acceptable cost-effectiveness of the case management was 84% at a WTP of €0 per QALY. The probability in the case of applying the method of self-rating was 81% at a WTP of €0 per VAS-AL, increasing to 95% at a WTP of €24,290 per VAS-AL (Fig. 3B). Discounting did not alter probabilities at a WTP of €0, and probability of 95% was reached at a WTP of €26,690 per VAS-AL.

After applying a multiple imputation approach, the probability of acceptable cost-effectiveness at a WTP of €0 per QALY and per VAS-AL, respectively, was 91% and was not influenced by discounting; at a WTP of €8400 per VAS-AL and €8640 with discounting, respectively, the probability was 95%.

Discussion

This study compared the costs and effects of a case management intervention by trained nurses in elderly patients suffering from AMI with usual care over a time horizon of 3 years. The primary effect measure in the economic evaluation was QALYs constructed using population-based EQ-5D-3L utilities, which ensures comparability with other studies. To assess the sensitivity of results to different health state valuation methods, we also constructed VAS-ALs [46]. Both methods indicated QALY gains, whether or not discounting. Within the first year, results varied depending on health state valuation methods: applying the QALY concept, case management indicated QALY losses; using VAS-AL, case management indicated QALY gains [13]. The reason behind this could be that the case management, as a complex intervention, improved domains within the first year that are not fully reflected in the EQ-5D-3L, or the sensitivity of the EQ-5D-3L was not sufficient to detect improvements. In the intervention group, 10 participants died in the first 3 months after discharge before having any contact with the study nurse and so their early deaths should be regarded as random because the intervention is unlikely to be the reason for it. In the further course of the study, the number of decedents was balanced and it increased in the control group in the third year. The combination of early deaths in the intervention group and the delayed positive effect on EQ-5D utilities led to QALY losses within the first year. Moreover, it brought about insignificance of QALY gains and led to QALY losses in 38%, respectively, after the third year.

The secondary outcomes in terms of both EQ-5D-3L utilities and VAS scores among survivors showed a significantly higher health state in the intervention group after 3 years. The positive effect on

Table 5 – Mean resource use per patient (in number of contacts unless stated otherwise) over different years and raw unadjusted mean costs over 3 y in euros (calculated from unit prices from 2012).

Category	Intervention				Control			
	Resource use, mean ± SD			Costs (€), mean ± SD (3 y, N = 131)	Resource use, mean ± SD			Costs (€), mean ± SD (3 y, N = 138)
	Year 1 (N = 137)	Year 2 (N = 132)	Year 3 (N = 131)		Year 1 (N = 160)	Year 2 (N = 146)	Year 3 (N = 138)	
Physicians	17.23 ± 12.38	20.65 ± 17.79	20.78 ± 20.50	1,328 ± 1,139	21.68 ± 15.83	21.94 ± 15.60	20.83 ± 16.60	1,543 ± 1,138
Physiotherapist	3.59 ± 8.36	3.92 ± 10.42	3.02 ± 9.74	145 ± 319	5.35 ± 13.05	6.13 ± 13.44	5.43 ± 13.65	279 ± 604
Ambulatory clinic in the hospital	0.85 ± 2.73	0.91 ± 3.00	1.14 ± 3.49	90 ± 206	1.35 ± 6.08	0.81 ± 2.75	1.40 ± 3.79	117 ± 264
Inpatient care (d)	8.70 ± 17.18	5.21 ± 13.68	3.55 ± 8.89	10,747 ± 16,689	11.71 ± 25.29	6.19 ± 14.18	4.93 ± 11.71	13,916 ± 22,240
Rehabilitation (d)	11.32 ± 11.84	0.78 ± 3.92	0.90 ± 5.63	1,529 ± 1,704	12.43 ± 12.50	1.36 ± 5.28	0.59 ± 3.50	1,674 ± 1,831
Drugs (no. of medications)	6.97 ± 2.45	6.93 ± 2.67	6.81 ± 2.88	2,833 ± 2,324	7.4 ± 2.38	7.37 ± 2.55	7.35 ± 2.60	3,131 ± 2,177
Intervention program				166 ± 83				
Sum of direct health care costs(including intervention)				16,837 ± 17,768				20,660 ± 23,285
Outpatient nursing service (h)	3.66 ± 16.09	2.39 ± 15.00	3.23 ± 17.57	240 ± 1,169	5.72 ± 21.66	10.90 ± 70.08	7.60 ± 30.91	502 ± 2,135
Paid household help (h)	37.96 ± 193.12	90.36 ± 852.39	64.70 ± 577.00	1,632 ± 14,844	13.25 ± 62.58	25.16 ± 98.46	13.00 ± 51.00	482 ± 1,637
Informal care				110 ± 500				363 ± 1,391
Sum of direct non–health care costs				1,982 ± 14,927				1,347 ± 3,303
Sum of total costs				18,819 ± 23,256				22,008 ± 24,166

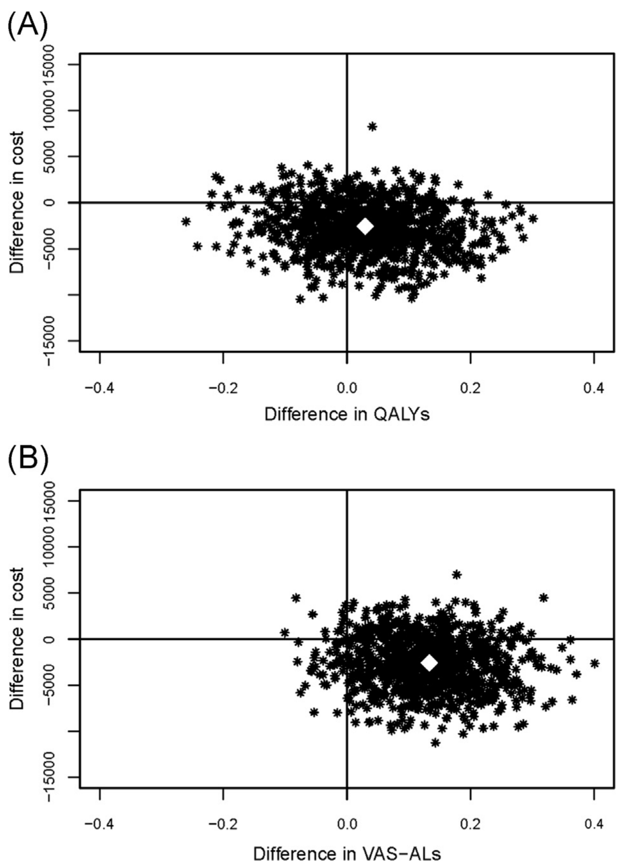

Fig 2 – Cost-effectiveness planes; a: Costs and QALYs; b: Sensitivity analysis of Costs and VAS-ALs; QALY, quality-adjusted life year using the EQ-5D Index based on German population tariff and time trade-off scoring (27); VAS-AL, quality-adjusted life year using patients' EQ VAS score (self-rated health)

EQ-5D-3L utilities (0.104) can be regarded as important because the minimally important difference for patients with AMI was 0.089 [47]. Compared with the results of the 1-year follow-up, the positive effect increased and became significant regarding EQ-5D utilities and maintained regarding VAS scores, respectively, after 3 years. This could indicate that, as also found in another study [48], VAS scores are more sensitive in heart patients and thus revealed improvements, which are not covered by EQ-5D utilities in early stages but later on. In the 1-year follow-up, we assumed that VAS scores could reflect only an adaption process rather than a better health but this could not be confirmed. Regardless of VAS scores, EQ-5D utilities became significant only in the long run. In contrast, significant intervention effects could be shown within the first year for functional status and for malnutrition risk, which maintained after the 3-year follow-up intervention [10,12]. It is conceivable that improvements in functional status were subsequently translated into higher utility scores.

Direct costs were mainly driven by hospitalization and were lower in the intervention group (–€3189). Only costs of paid household work were higher in the intervention group (€1.150) but, at baseline, a difference already existed in the use of paid household help (13.5% in the intervention group vs. 8% in the control group). All cost differences were not significant. Similar cost differences already emerged within the first year. There were lower direct costs at an altitude of €1.072 and higher costs of paid household work (€388). It became obvious that cost differences increased linearly. In case of differences continuing in this way, it can be assumed that differences would become significant in a longer follow-up. Economic evaluations almost always are piggy-back analyses that are embedded in clinical trials. Therefore, low power is a common problem in economic evaluation because sample size calculation is oriented toward clinical main outcome rather than to detect differences in costs or QALYs [49]. Because of high variance of cost data, very large differences or study samples are needed to achieve significant results.

Nevertheless, the results could also be affected concerning the lower costs in the intervention group because costs were set to 0 from the day of death. For that reason, we analyzed the mean costs per day survived, which showed no difference (€34.66 in the intervention group and €34.03 in the control group) although costs during the last year of life usually are higher than those for nonterminal years [50].

A limitation of our study was the single-center design, which restricts generalization to other population characteristics and health care structures. Furthermore, 92 of the 636 patients assessed for eligibility declined to participate before randomization and 60 withdrew consent after randomization. Patients refusing participation (n = 92) were, on average, 2 years younger than the participants but did not differ with respect to sex and comorbidities. If there were additional systematic differences, the external validity of our findings may be affected. As 60 patients withdrew consent, we applied a missing value imputation approach by including subjects who withdrew consent or were lost to follow-up during the 3-year study period. The resulting estimation of probability of

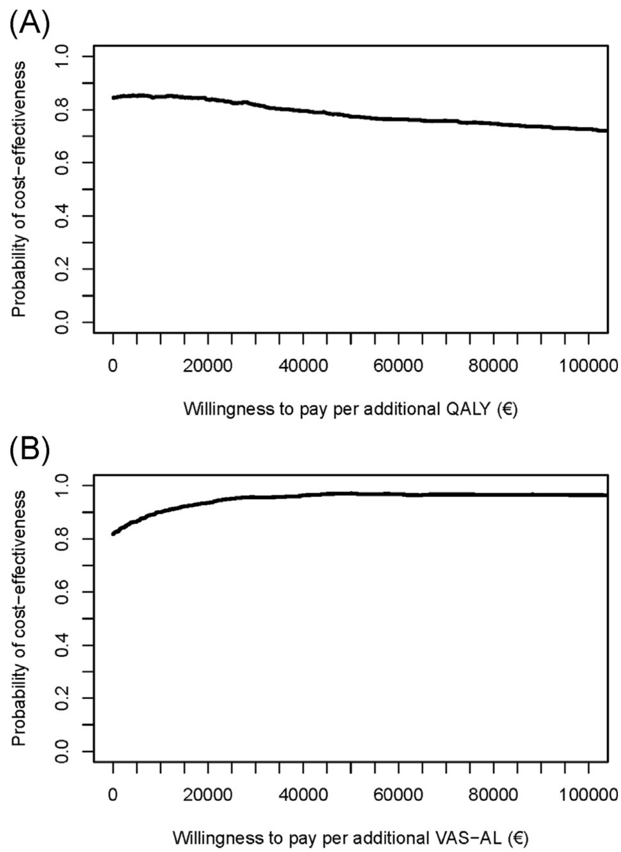

Fig. 3 – Cost-effectiveness acceptability curves (CEAC); a: CEAC QALY; b: Sensitivity analysis of CEAC VAS-ALs; QALY, quality-adjusted life year using the EQ-5D Index based on German population tariff and time trade-off scoring (27); VAS-AL, quality-adjusted life year using patients' EQ VAS score (self-rated health)

cost-effectiveness of the case management remained stable and so our results can be considered to be robust with respect to attrition.

Strengths of the study include its randomized design, the inclusion of different valuation perspectives with regard to quality-of-life impacts, and thorough cost collection. For the last one, all hospital admissions were validated to reduce recall bias. Resource use was not limited to disease-related services but broadly defined, thus taking into account that case management is a complex intervention. Moreover, the follow-up period of 3 years is suited to detect long-term cost-effectiveness of case management programs in elderly people with AMI.

To our knowledge, no cost-effectiveness study has yet been conducted to evaluate a case management program in elderly patients with AMI after hospital discharge. Several nurse-led intervention programs focused on patients younger than 65 years or were tailored to patients with heart failure so that the generalization to higher age groups or to patients discharged after an acute cardiac event cannot be ensured. For patients with CHD, there is only one study on cost-effectiveness with a follow-up period of 4 years [14] and two studies covering a period of 1 year [15,16]. In the 4-year follow-up study, Raftery et al. [14] observed no differences in costs but differences in QALYs (+0.124 QALYs; ICER €1590/QALY). They also reported nonsignificantly lower costs for hospital admissions in the intervention group. Compared with the KORINNA study, the intervention took place in clinics, the study participants were almost 9 years younger, and only cardiac-related resource use data were collected and so estimated total costs are not comparable with our study.

Conclusions

The case management KORINNA was cost-neutral and led to an important and significant improvement in health status among survivors. It was associated with higher QALYs and lower costs within a time horizon of 3 years but the differences in costs and QALYs were not statistically significant.

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