Universität Hamburg
DER FORSCHUNG | DER LEHRE | DER BILDUNG

hche | Hamburg Center for Health Economics

Measuring the relationship between costs and outcomes: the example of Acute Myocardial Infarction in German hospitals

Tom Stargardt, Jonas Schreyögg, Ivan Kondofersky

Research Paper
2012/04

Measuring the relationship between costs and outcomes: the example of Acute Myocardial Infarction in German hospitals

Tom Stargardt, Jonas Schreyögg, Ivan Kondofersky
hche Research Paper No. 2012/04
http://www.hche.eu

Abstract

In this paper, we propose a methodological approach to measure the relationship between hospital costs and health outcomes. We propose to investigate the relationship for each condition or disease area using patient-level data. We suggest to examine health outcomes as a function of costs and other patient-level variables: (1) using two-stage residual inclusion with Murphy-Topel adjustment to address costs being endogenous to health outcomes, (2) using random-effects models in both stages to correct for correlation between observation, and (3) using Cox proportional hazard models in the second stage to ensure the available information is exploited. To demonstrate its application, data on mortality following hospital treatment for acute myocardial infarction (AMI) from a large German sickness was used. Provider reimbursement was used as a proxy for treatment costs. We relied on the Ontario Acute Myocardial Infarction Mortality Prediction Rules as a disease-specific risk-adjustment instrument. 12,284 patients with a treatment for AMI in 2004-2006 were included. Results showed a reduction in hospital costs by €100 to increase the hazard of dying, i.e. mortality, by 0.43%. The negative association between costs and mortality confirms that increased resource input leads to better outcomes for treatment after AMI.

Keywords: hospital costs, acute myocardial infarction, trade-off, readmission, mortality.

Prof. Dr. Tom Stargardt

Hamburg Center for Health Economics
University of Hamburg

Esplanade 36
20354 Hamburg
Germany

Tel +49 40 428 38 - 9299
Fax +49 40 428 38 - 9498
Tom.Stargardt@wiso.uni-hamburg.de

Prof. Dr. Jonas Schreyögg

Hamburg Center for Health Economics
University of Hamburg

Esplanade 36
20354 Hamburg
Germany

Tel +49 40 42838-8041
Fax +49 40 42838-8043
jonas.schreyoegg@wiso.uni-hamburg.de

Ivan Kondofersky

Institute of Bioinformatics and Systems Biology
Helmholtz Zentrum Muenchen

Ingolstädter Landstr. 1
85764 Neuherberg
Germany

Tel +49 89 3187 3385
Fax +49 89 3187 3585
ivan.kondofersky@helmholtz-muenchen.de

1. Introduction

Rising health care expenditure has led to the implementation of numerous cost-containment measures in the inpatient sector, including the reimbursement through prospective payments systems, i.e. Diagnosis Related Groups (DRG). As a result, the pressure to contain costs has been passed from providers to physicians and caregivers by restricting the availability of resources (Yaisawarng and Burgess, 2006). Although cost-containment may be achieved by increasing the efficiency of service provision, it is likely that the pressure to contain costs may also have a (temporary) impact on treatment quality or will do so in the near future. If treatment quality is affected, however, this may reduce patient comfort or – much worse – affect medical outcomes. Therefore it is very important for policy makers as well as for decision-makers who are responsible for the allocation of scarce resources between or within hospitals to understand the potential trade-off between costs and outcomes (Mukamel and Spector, 2000).

Studies on the relationship between hospital costs and health outcomes are scarce, report conflicting results and have methodological limitations. Earlier studies were conducted at the hospital level using aggregate measures for costs and outcomes (Fleming, 1991; Carey and Burgess, 1999; Mukamel and Spector, 2000) that may have been too rough to provide useful policy implications. Other studies have focused on selected conditions to investigate the association between costs and outcomes based on patient level data (Jha et al., 2009; Chen et al., 2010; Romley et al., 2011; Stukel et al., 2012). However, the latter studies usually do not address the problem of costs being endogenous to health outcomes and did not make use of the full information available from their data.

In this paper, we propose a methodological approach to address limitations raised by previous papers on the relationship between hospital costs and health outcomes. We suggest to examines health outcomes as a function of costs and other patient-level variables: (1) using two-stage residual inclusion with Murphy-Topel adjustment to address costs being endogenous to health outcomes, (2) using random-effects models in both stages to correct for correlation between observation, and (3) using Cox proportional hazard models at the second stage to ensure exploitation of the available information. To demonstrate its application, data on mortality following one year after index hospitalization for acute myocardial infarction (AMI) from a large German sickness was used.

The paper is structured as follows. The next section reviews the available literature on the relationship between hospital costs and health outcomes. The third section presents our proposed methodology to explore this relationship. The fourth and fifth sections describe the data used in the analysis and the estimated results, respectively. The final section discusses the implications of the results and makes suggestions for future research.

2. Previous research

Generally speaking, there have been different categories of studies that deal with the cost-outcome relationship in a broader sense. Studies either focused on the impact of outcomes on costs or vice versa in the hospital sector (Morey et al., 1992; Carey and Burgess, 1999; Yaisawarng et al., 2006; Schreyögg and Stargardt 2009) and on other providers, e.g. nursing homes (Mukamel and Spector, 2000; Weech-Maldonado et al., 2006), or investigated the impact of (in)efficiency (Deily and McKay, 2006; McKay and Deily, 2008) on outcomes. Other studies used length of stay as a proxy for resource input (Malkin et al., 2000; Picone et al., 2003).

In the following, we will focus on studies measuring the impact of costs on outcomes or vice versa in the hospital sector. From a methodological perspective, these studies have taken two different approaches:

The first is characterized by the use of aggregate measures for costs and health outcomes on the hospital level without focusing on selected conditions. Some studies have used cost functions with costs as the dependent variable, while outcome measures were used as explanatory variables in a given hospital cost function (Fleming, 1991; Morey et al 1992; Carey and Burgess, 1999). Other studies used health outcomes as the dependent variables, while hospital costs were used as one explanatory variable (Mukamel and Spector, 2000; Picone et al., 2003). Usually, mortality at the hospital level has been used as the only health outcome measure. Results varied largely. Whereas certain studies have found a positive association between hospital costs and health outcomes (Mukamel and Spector, 2000), others have concluded that low hospital costs and excellent health outcomes are not mutually exclusive (Carey and Burgess, 1999; Fleming, 1991). Finally, in most of these studies it is realized that the approach of using aggregate measures limits the ability to control for case-mix and reduces the precision of the point estimates. In addition the relationship between hospital costs and health outcomes may vary according to the conditions treated.

The second approach to measuring the hospital cost-outcome relationship emerged from the outcomes literature more recently. As opposed to the studies of the first approach, the cost-outcome relationship is investigated by concentrating on selected conditions treated in hospitals. Consequently, they use patient-level data to perform outcome-specific risk adjustment. Some studies included several conditions with AMI and congestive heart failure being among them (Jha et al., 2009; Romley et al., 2011; Stukel et al., 2012). Schreyögg & Stargardt (2010) focused on AMI only, while Chen et al., (2010) included congestive heart failure and pneumonia. However, Birkmeyer et al. (2012) focused on frequent surgical inventions while Lagu et al. (2011) investigated patients admitted with sepsis. All studies use some kind of post-hospitalization mortality-window (30 days, 90 days or one year) as outcome measures, while Romley et al., (2011) use in-hospital mortality only. Moreover, readmissions (Chen et al., 2010; Schreyögg & Stargardt, 2010; Stukel et al., 2012) and complications (Birkmeyer et al., 2012) were used as additional outcome measures. Throughout the studies risk-adjustment of outcomes was performed by including comorbidities defined by Elixhauser, Charlson or Charlson–Deyo indices (Elixhauser et al., 1998; Charlson et al. 1987; Deyo et al. 1992).

The usual model that has been used throughout the studies of the second approach allowed hospital costs, either defined through reimbursement rates or actual costs, to vary at the hospital level. Subsequently, differences in outcomes between spending quintiles or quartiles are investigated by regression analysis, usually logistic regression. Only few studies go beyond this. Lagu et al. (2011) used charges at patient-level and applied multilevel linear and logistic models. Stukel et al. (2012) developed an expenditure index for each hospital and divided hospitals in terciles according to this index. Subsequently they perform a cox-proportional hazard model considering membership to terciles as independent variable. Schreyögg & Stargardt (2010) consider patient-level costs and make use of a random effects model in combination with an IV model.

Results of the studies that focused on selected conditions again diverge and reveal that the cost-outcome relationship may vary according to the condition investigated. For instance, Chen et al. (2010) found a positive association between costs and health outcomes for congestive heart failure, but found a negative association for pneumonia. In contrast, using a different sample, Romley et al. (2011) found a positive association between costs and outcomes for pneumonia. For AMI three studies found a positive association between costs and outcomes measured as in-hospital or post-hospitalization mortality (Romley et al. 2011;

Stukel et al. 2012; Schreyögg & Stargardt 2010) while one study did not find any association (Jha et al. 2009). Although a focus on selected conditions indeed represents a progress compared to earlier studies of the first approach, most of these studies have certain methodological limitations which may explain divergent results. Some of these studies acknowledge that endogeneity bias may limit the results since costs were endogenous to health outcomes. Moreover, the available studies do not make use of the full information available in their regression models, since outcomes are usually aggregated and then included as binary variable; hospital spending is grouped into categories. Schreyögg & Stargardt (2010) are the only authors that addressed these limitations.

Our proposed model to investigate the relationship between costs and outcomes goes beyond the model used by Schreyögg & Stargardt (2010) in several ways. At first, we put more emphasis on the use of variables that adjust for structural characteristics of the hospitals, i.e. the treating hospital's quality in the specialty area. Second, we include the distance between the patient's residence and the hospital that treated the patient as a proxy for time to care. This improves risk-adjustment as timely access to health care may influence costs and outcomes for AMI (Shen and Hsia, 2011). Third, we allow for different functional forms for costs in the outcome equations. Fourth, using the Nelson-Aalen-Breslow estimate to approximate the baseline hazard, we were able to predict mortality depending on costs.

3. Methods

3.1 Data and setting

Since it is very likely that the cost-outcome relationship varies by condition and even by hospital and in order to present our proposed methodological approach we used hospital treatment for AMI in Germany as an example. AMI has several important advantages when it comes to investigating the relationship between costs and outcomes. First, because AMI requires immediate medical attention, patient selection between hospitals is less relevant than for other conditions. Second, the incidence of AMI is high, and it is the leading cause of death in the elderly, resulting in a substantial number of hospital cases. Third, hospitals that provide higher-quality care can achieve substantially improved outcomes, e.g. lower mortality rates (Landrum et al., 2004; McClellan and Staiger, 2000; Shen, 2002).

Patients with an admission for AMI (ICD-10: I21) between 1st January 2004 and 31st December 2006 insured at the Techniker Krankenkasse, a German sickness fund that operated nationwide with more than 5.8 million insured in 2005 (8.2% of German residents with public health insurance), were followed up after treatment for one year. To ensure incident cases of

AMI, patients had not to be admitted with AMI or have been coded AMI as an in-hospital complication in the previous year. Data on costs of initial AMI hospital treatment to the sickness fund, co-morbidities, age, and gender was collected. In addition, data on mortality until one year after AMI was collected. To control for hospital characteristics and the treating hospital's quality, the sickness fund's data was matched to data from the hospital quality reports 2006 from the German Institute for Quality and Patient Safety (BQS).

Patients were excluded if admitted and discharged on the same day or if costs were below €100, as we assumed that these patients were potentially misclassified. We also excluded patients whose treating hospital could not be identified due to issues of data protection. To exclude hospitals with insufficient AMI capabilities, patients treated in hospitals with less than 10 AMI patients from all sickness funds in 2006 were excluded from our dataset. To guarantee a minimum number of observations per hospital, we also excluded hospitals with less than 5 AMI patients in our dataset.

3.2 Measurement of costs and outcomes

For the purpose of this study, we used hospital reimbursement rates for index hospitalization with AMI as a proxy for treatment costs. Similar to other DRG-systems the German DRG system is based on a modular bottom-up cost-accounting approach (Finkler et al., 2006). DRG costs weights are recalculated on an annual basis based on information from the national cost data study maintained by InEK (Institute for the Calculation of Hospital Reimbursement). The approximately 300 hospitals regularly participating in this study are required to use a standardized cost-accounting approach that allows costs to be separated according to diagnostic services, laboratory, drugs, ward costs, and overhead costs (Schreyögg et al., 2006). Thus, all hospitals have to allocate costs for each condition in the same way. For instance, it is explicitly defined how costs of cardiologists and electrophysiologists have to be allocated to patients with AMI or other conditions and how costs have to be re-allocated between different departments involved in the treatment of a given patient.

Hospital reimbursement for AMI in Germany uses multiple DRGs and supplementary fees to differentiate according to type of treatment, e.g. AMI including bare-metal stent with severe complications. To determine the reimbursement for each case the cost weights for each treated case was multiplied by the base rate of each hospital. At the time of the study, the German DRG system was still being implemented. Thus the base rate of each hospital was mainly driven by the hospitals' historical cost per relative weight (2004: base rate driven to

100% by historical cost, 2005: base rate driven at least to 80% by historical costs, and 2006: base rate driven at least to 60% by historical cost). Thus, a hospital with high staffing ratios would have had a base rate well above the federal average between 2004 and 2006. To sum up, provider reimbursement through DRGs at the time of the study reflected a) the intensity of treatment through classification in disease according to the performed procedures reflected by the cost weights and b) the overall level of resources consumed in a facility through the base rate depending on the hospital's historical costs. To avoid extreme values for treatment costs, we truncated provider reimbursement at €50,000.

Mortality due to AMI during follow-up was used as outcome measure. For each AMI patient, we selected the index hospitalization during which a primary diagnosis of AMI was made. Mortality was assessed for up to one year after discharge from the index hospitalization.

3.3 Covariates for patient characteristics and patient co-morbidities

The literature contains various proposals for risk scores that make use of secondary diagnoses and/or prescription data to predict mortality. The Charlson Comorbidity Index, which consists of 19 comorbidity groups, for example, provides a taxonomy for comorbidities to predict 1-year mortality after an inpatient stay (Charlson et al., 1987), while the Elixhauser Score, which consists of 30 comorbidity groups, was originally defined to predict hospital costs, length of stay and in-hospital mortality based on ICD codes. While these two comprehensive risk adjustment instruments have a broader spectrum of use, disease-specific risk adjustment instrument ought to be preferred. This is because disease-specific risk adjustment instruments are usually much more clinically sensible to the condition analysed and usually have more predictive power (Tu et al., 2001).

For AMI, the Ontario Acute Myocardial Infarction Mortality Prediction Rules were specifically developed to predict risk-adjusted 30-day and one-year mortality after AMI from administrative data after hospital discharge (Tu et al., 2001). The original ICD-9 codes have been adapted to the Canadian ICD-10 version (Vermeulen et al., 2007). As a slightly different version of ICD-10, German ICD-10, is used in Germany, we made minor adjustments. We defined a variable for shock (R57), congestive heart failure (I50), cancer (all ICD codes starting with C), pulmonary edema (J18.2, J81), acute renal failure (N17, N19, R34), chronic renal failure (I12, I13, N18, T82.4, Z99.2), cerebrovascular disease (G45, I60-69), cardiac dysrhythmia (I46.0, I46.9, I47, I48, I49, R00.1), and diabetes with complications (E10.0-E10.8, E11.0-E11.8, E13.0-E13.8, E14.0-14.8). In addition, covariates were formed for diabetes without

complications (E10.9, E11.9, E13.9, E14.9) and ischemic heart disease (I25). The covariates have been used before to explain variation in costs by other studies on AMI (Evans et al., 2007; Schreyögg et al., 2010). We also controlled for age, gender, disposable income per inhabitant in the postal code area of the patient as a proxy for income. To measure time to care, we calculated the distance between the 3-digit postal code of the patient's residence and the hospital using Google Maps.

3.4 Covariates for the treating hospital's structural quality and for structural characteristics of the hospital

Because it is generally acknowledged that there are certain hospital characteristics, especially if related to the hospital's specialization for the condition analysed, exerting influence on outcomes and expenditure, we also controlled for hospital level variables. As a proxy for labour intensity we included the number of nurses in full time equivalents. In previous studies, costs (and outcomes) were found to be correlated with hospital size and teaching status (Flood et al., 1984; Schreyögg et al., 2011). Therefore we also included the number of beds as a proxy for hospital size and information on the teaching status as a proxy for general resource capabilities. To control for the overall treatment quality of the hospital in treating AMI, we also included the total number of AMIs treated by the hospital (from the hospital quality reports 2006) and a variable that indicated whether the hospital had a special department or a specialisation in cardiovascular diseases. These two variables reflect the impact of hospital experience in treating AMI (Hughes et al., 1987) on outcomes as well as the impact of potential economies of scale on costs.

3.5 Empirical Model

We hypothesized that health outcomes are a function of resource input, patient characteristics, co-morbidities, and hospital characteristics that reflect the treating hospital's quality:

$$Outcome_i = f \text{ (resource input, co-morbidities, treating hospital's quality)}$$

In addition to the treatment setting, the use of resources for the treatment of AMI also depends on the expected health outcomes, e.g. expected mortality. We assume that a physician who expects above average mortality, i.e. due to high severity of disease, will most likely use resource inputs above average. For example, the physician might then decide on a longer period of ICU care or order additional therapeutic or diagnostic procedures to be

performed. Since it can be assumed that perfect control for co-morbidities is impossible, a strong correlation between expected health outcomes and actual health outcomes, e.g. expected mortality and actual mortality, may exist. Therefore, the relationship between health outcomes and resource input may work in both ways. In our model, costs are thus assumed to be endogenous to health outcomes, i.e. that costs are correlated with the error term in the models for health outcomes. Consequently, we used a two stage estimation method that required the use of instrumental variables.

Model Costs:	$E(Y_I \mid X_I, \varepsilon_I)$
Model Health Outcomes:	$E(Y_{II} \mid X_{II}, \varepsilon_{II}, E(Y_I \mid X_{II}, \varepsilon_I))$

To decide on the correct specification in the first stage, we employed the Modified Park test (Manning and Mullahy, 2001; Park, 1966). It resulted in a coefficient of 1.34 indicating that either Poisson or Gamma distributions are most appropriate. Given that the independent variable is continuous and there is a large difference in the variance and the mean, we choose a gamma distribution for our data. When deciding on the link function, Pregibon's Link test (Pregibon, 1980) produced a rejection for a log-link function (t-value: -11.48). This is most likely due to the truncation of costs at €50,000 that may have introduced a natural dependence between the residuals and the model fit. Alternative link functions such as the identity or the inverse link, however, yielded t-values even greater than 100. This indicated that the log-link function performs, by far, best.

Because of the violation of the assumption of independence of observations if patients were treated in the same hospital, we employed multilevel modelling. Random intercepts were assumed to follow a normal distribution. As an overall goodness of fit, we tested the correlation between predicted values and residuals (Pearson's Correlation test). It resulted in a correlation of 0.0317 (95% CI calculated by Fisher transformation: 0.0140; 0.0493) that is smaller than 0.05, suggesting that overall model fit is acceptable.

To fully utilize the information from our data, we used a Cox proportional hazard model to model our health outcome (time to death) in the second stage. To assess the validity of the proportional hazards assumption, we plotted scaled Schoenfeld residuals against event time. In addition, according to a test suggested by Grambsch and Therneau (1994), we regressed scaled Schoenfeld residuals on event time for each covariate and tested for zero slope. To allow for predictions on mortality, we used the Nelson-Aalen-Breslow estimate (Nelson, 1972) to approximate the survival curve while at the same time controlling for ties in the data. We

predicted mortality depending on costs at 30 days, 90 days, and 365 days. To do so, we set each covariate to the mean.

As in the case of our first stage model, likelihood ratio test suggested that multilevel modelling significantly improved model fit (p<0.0001). If compared to using mean squared prediction error (MSE), the Frailty Cox proportional hazard model had a 7.04% higher precision than the model without random intercepts. We thus model:

$$Y_{\mathrm{I}} = \alpha_1 X_I + \alpha_2 Z_I + \varepsilon_I$$
$$Y_{\mathrm{II}} = \beta_I X_{II} + \beta_2 Z_{II} + \varepsilon_{II}$$

Y_I is a vector of costs at the patient level, while Y_{II} represents a vector of the health outcomes, measured in time to death. X_I and X_{II} are two vectors of covariates at the patient level that include variables that measure severity, known to be associated with costs and health outcomes. In contrast to X_I, X_{II} contains the residuals which were computed in the first stage. Vectors Z_I and Z_{II} represent covariates at the hospital level that are known predictors of hospital costs and health outcome. Z_I also contains two instruments that are strongly correlated with Y_I, but not with Y_{II}. Vectors α_1, α_2, $ß_1$, and $ß_2$ represent vectors of parameter estimates. Vectors ε_I and ε_{II} are the error terms for the cost model and the model for our health outcomes, mortality, respectively.

This gives the following log likelihood functions, with G(ξ) being the covariance matrix of the randomly distributed random effect vector $ß_2$ and D(ψ) being the covariance matrix of the randomly distributed random effect vector α_2. Notation details include the display of the linear predictors $\eta_I = \alpha_1 * X_I + \alpha_2 * Z_I$ and $\eta_{II} = ß_1 * X_{II} + ß_2 * Z_{II}$.

$$l_{\mathrm{I}}(\alpha_1, \alpha_2, \xi) = l(\alpha_1, \alpha_2) - \frac{1}{2}\alpha_2{}' G(\xi)^{-1}\alpha_2$$
$$l_{\mathrm{II}}(\beta_1, \beta_2, \psi) = \sum_{i=1}^{n} \delta_i \left(\eta_{Ii} - \log\left(\sum_{j=R(t_i)} \exp\left(\eta_{IIj}\right)\right) - \frac{1}{2}\beta_2{}' D(\psi)^{-1}\beta_2\right)$$

Because of the non-linearity of the second-stage estimation, we subsequently used two stage residual inclusion instead of the more common two stage least square approach. Actual costs and residuals from the first-stage regression were employed in the second-stage (Terza et al., 2008). The method requires the use of instrumental variables, i.e. variables that are highly correlated with the endogenous variable (costs), but not with unobserved determinants of the main outcome variable (time to death). We believe that average costs in federal state, as a

proxy for the historically driven cost structure of the hospital by state regulation, and price per square meter in the hospital's county meet these criteria. To make sure weak correlation is unlikely to be a source of bias, *F*-statistics for both instruments were obtained (Bound, Jaeger, and Baker 1995; Staiger and Stock 1997).

To adjust standard errors of the second-stage regression for including estimated residuals from the first stage, Murphy-Topel Adjustment was employed (Murphy and Topel, 1985; Greene, 2002). This involves the derivation of first and second order derivatives of the log likelihood function of a gamma mixed model (Fahrmeir and Tutz, 2001), as well as the first and second order derivatives of the log partial likelihood function of a cox frailty model (Cox 1975):

$$MT = V_2 + V_2(CV_1C' - RV_1C' - CV_1R')V_2$$

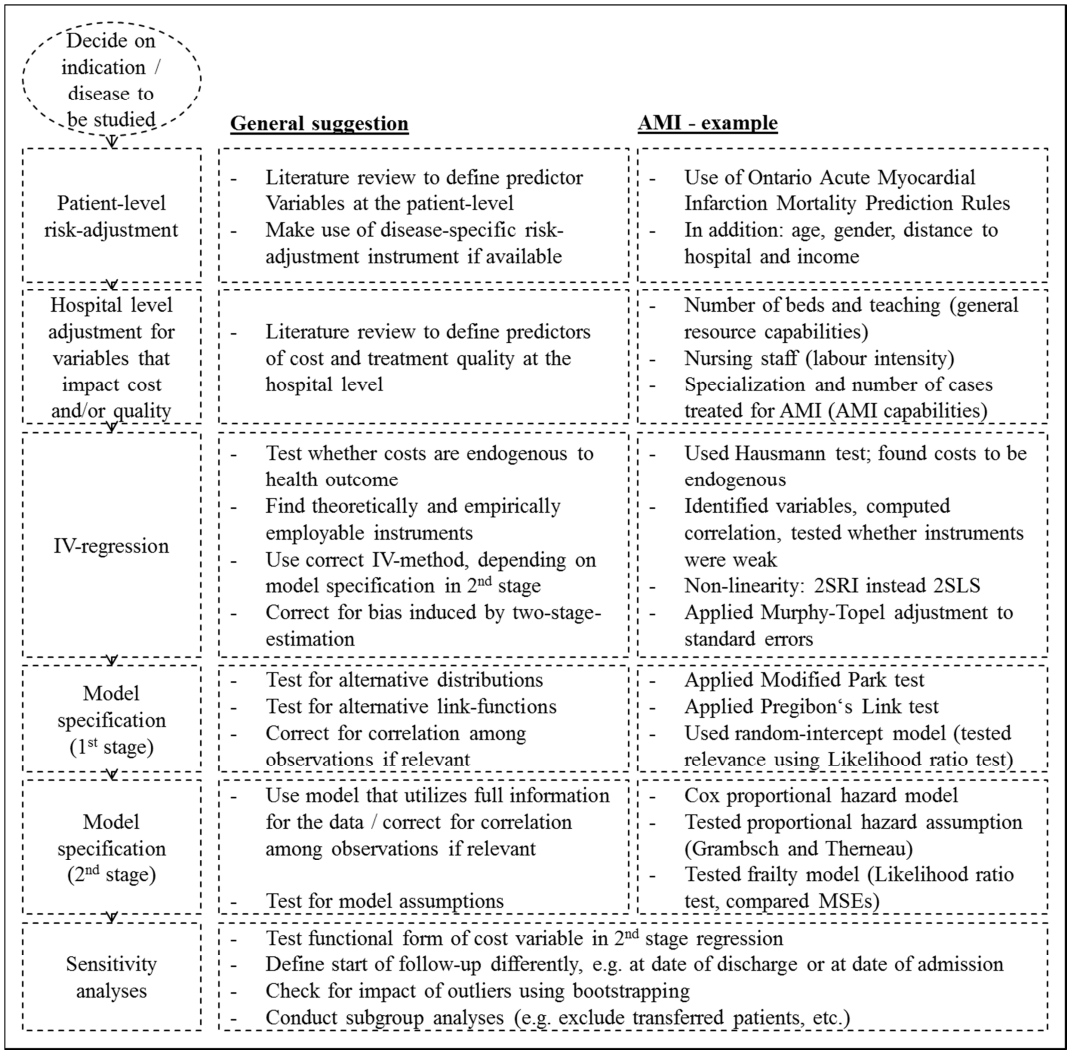
V_1 is the covariance matrix of the 1st stage regression that is derived using the inverse second order derivative of the log likelihood function l_I (see F_1 in the appendix). V_2 is the covariance matrix of the 2nd stage regression that is derived using the inverse second order derivative of the log likelihood function l_2 (see F_2 in the appendix). R is the matrix of the first order derivative of the log likelihood function l_{II} by the parameters of the 2nd stage regression (see s_2 in the appendix) multiplied by the first order derivative of the log likelihood function l_1 of the 1st stage regression by the parameters of the 1st stage (see s_1 in appendix). C is a matrix of the first order derivative of the log likelihood function l_{II} by the parameters of the second stage (see s_2 in the appendix) multiplied by the first order derivative of the log likelihood function l_{II} by the parameters of the 1st stage (see s_{21} in the appendix). A summary of our general proposed methodological approach and our implementation in the case of AMI is given in Figure 1.

3.6 Sensitivity analysis

We ran multiple sensitivity analyses. At first, we tested whether functional form impacted results. In the base model, we included costs in its linear form into the second stage regression thereby assuming a log-linear relationship between outcomes and costs. We therefore tested different functional forms by also including squared costs (and squared residuals) in the second stage regression. Second, we tested whether the introduction of the DRG system throughout the study period resulted in changes in the trade-off between costs and quality by regressing for 2004, 2005, and 2006 separately. Third, we excluded the 2,074 patients that had been transferred during their initial hospital stay. Fourth, as starting follow-up at discharge

while including hospital mortality may have led to a different time at risk for our outcomes depending on length of stay, we reran the models following-up for 365 days from admission. Fifth, we extended our observation period for 2 years instead of 1 year in the base model. Finally, we applied bootstrapping based on 1000 randomly drawn samples from our data. This allowed us to produce an estimate of the standard error of all coefficients in our model. Thus we were able to compute bootstrapped p-values to determine the significance of covariates. A summary of estimating standard errors via bootstrapping is presented by Efron and Tibshirani (1994).

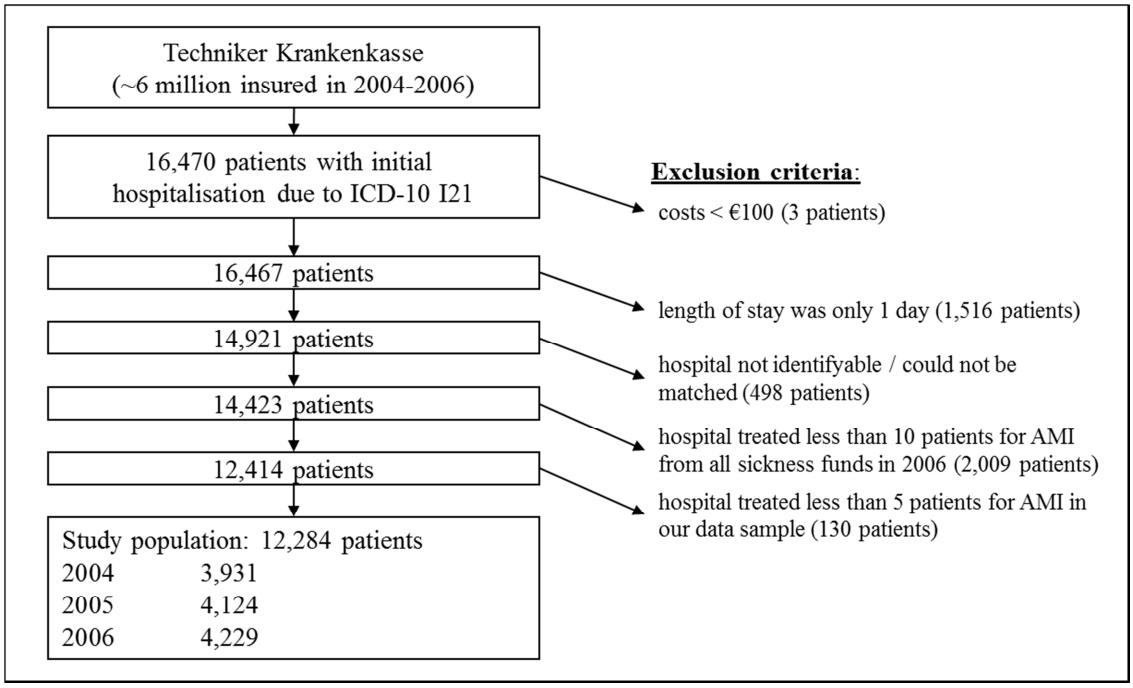
Figure 1. Summary of proposed methodological approach and implementation for AMI



4. Results

Of the 5.8 million insured members of the sickness fund, there were 16,470 patients with an initial hospitalisation due to ICD-10 'I21' between 2004 and 2006. Of these patients, 4,186 had to be excluded because costs were below €100 (3 patients), length of stay was only one day (1,516 patients), the hospital could not be identified (498 patients), the hospital treated less than 10 patients for AMI from all sickness funds in Germany in 2006 (2,009 patients), and the hospital had treated less than 5 patients in our dataset (130 patients). The final study population therefore comprised 12,284 patients (318 hospitals) that were about uniformly distributed between 2004, 2005 and 2006 (see figure 2).

Figure 2. Study population, in- and exclusion criteria



Mean age of patients was 64.1 years. 81.6% of the population were male. 365-day- mortality was 9.9% with 30.3% of the study population being readmitted during the one year follow-up. Average costs of treatment were € 6.936. The average hospital in our sample treated 570 patients for AMI in 2006 and had approximately 772 beds. 73.1% of the hospitals were also teaching hospitals implying a special cost structure and slightly different treatment patterns. 30.5% of hospitals had a specialisation on cardiovascular diseases (see table 1).

Table 1. Patient Characteristics

	Mean	Standard deviation
number of patients	12,284	
number hospitals	318	
Costs	6,936 €	5,767 €
Outcome variables (%)		
Mortality 30 days	5.3%	
Mortality 60 days	6.0%	
Mortality 90 days	6.3%	
Mortality 365 days	8.7%	
Age (mean), gender (%), and distance to hospital		
Age	64.1	11.8
Gender (=female)	18.4%	
Disposable income per inhabitant in postal code area	18,583 €	2,416 €
Distance to hospital in km	14.1	11.7
Structural characteristics of the hospital		
Beds	772.3	529.3
Number of patients with AMI in hospital	570.4	372.5
Size of nursing staff in FTE	630.9	501.2
Specialization on cardiovascular diseases	30.5%	
Teaching	73.1%	
Co-morbidities (%)		
Acute renal failure	2.5%	
Chronic renal failure	12.2%	
Cancer	2.4%	
Cardiac dysrhythmia	21.0%	
Cerebrovascular disease	4.9%	
Ischemic heart disease	88.4%	
Congestive heart failure	21.7%	
Diabetes without complications	13.0%	
Diabetes with complications	7.2%	
Pulmonary edema	1.8%	
Shock	3.5%	

Results from the first stage regression showed that our instruments were reliable predictors of hospital costs. Average costs in federal state (p=0.0196) as well as price per square meter (p=0.0085) were associated with increased hospital costs (see table 2). F-statistics for both instruments, average costs in federal state (F-value: 39.47) and price per square meter (F-value: 16.59), were well above the usually assumed thresholds for weak correlation. Thus, bias from IV-regression is lower than bias from standard regression techniques. Co-morbidities and hospital level variables generally also had the expected signs. Results show that hospital size significantly decreased treatment costs (p=0.0366). Size of nursing staff in full time equivalents (p=0.0001) and specialization on cardiovascular diseases (p <0.0001) significantly increased costs. The total number of AMIs treated by the hospital and teaching had no effect on treatment costs.

Second stage regression showed increasing costs to decrease mortality (p=0.0145) (see table 2). A reduction in hospital costs by €100 would thus increase the hazard of dying, i.e. mortality, by 0.43%. This result is also illustrated by figure 3. The significant trade-off remained if analyzed for each year separately. The hazard of dying would have been increased by a reduction in hospital costs of €100 by 0.79% in 2004 (p=0.0080), by 0.06% in 2005 (p=0.0005), and by 1.25% in 2006 (p=0.0125), respectively. Thus the step-by-step introduction of the DRG system did not create a consistent trend in the cost-quality trade-off.

According to the regressions of Schoenfeld residuals against time, the proportional assumption seems to have been violated for age, cancer, cardiac dysrhythmia, chronic renal failure, and specialization on cardiovascular diseases. However, this might also be due to the OLS regression being heavily influenced by outliers (Thompson et al. 2003). When plotting scaled Schoenfeld residuals against event time for the above mentioned variables, both models appeared to be a good fit to the data.

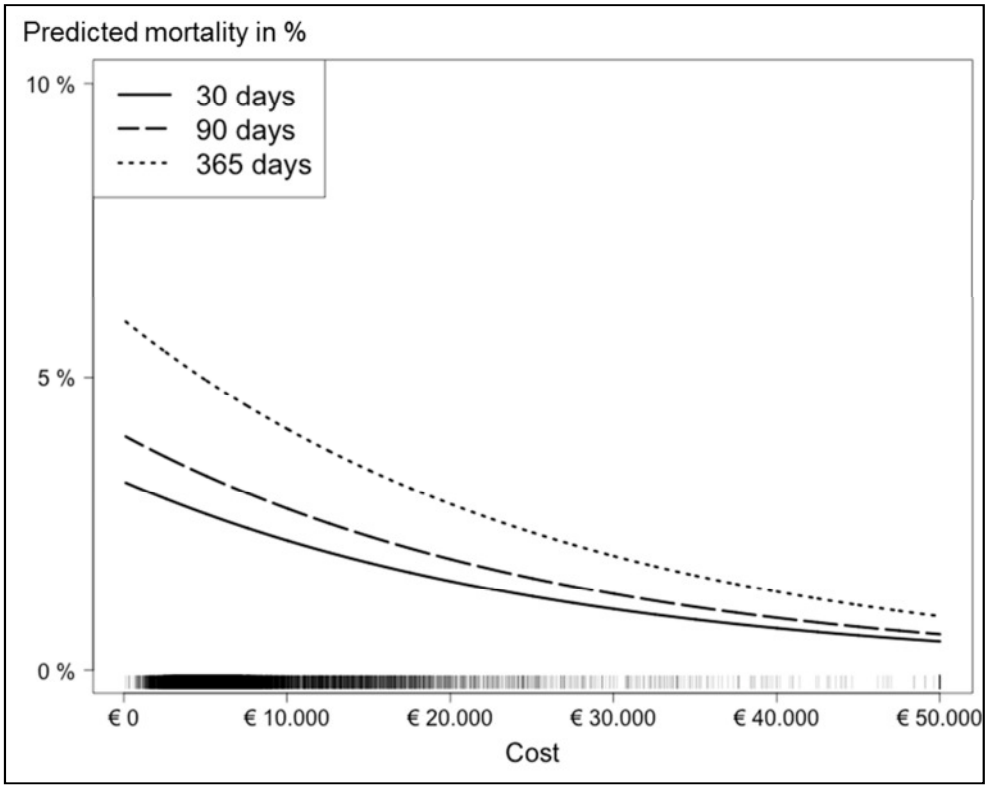
Table 2. Results from first and second stage regression

	1st stage: Cost (mixed gamma)			2nd stage: Mortality (frailty cox)			
	coef.	std.	p-value	Hazard ratio	coef.	std.	p-value
Fixed effects							
Intercept	3.7313	0.1960	<0.0001				
Cost in €100				0.996	-0.0043	0.0018	0.0145
Residual from 1st stage				0.994	-0.0060	0.0018	0.0009
Instruments							
Average cost in federal state	0.0046	0.0020	0.0196				
Price per m²	0.0002	0.0001	0.0085				
Co-morbidities & other covariates							
Age	-0.0018	0.0005	0.0003	1.051	0.0500	0.0033	<0.0001
sex	0.0000	0.0000	0.0186	1.000	0.0000	0.0732	0.6820
Disposable income per inhabitant in postal code area	-0.0501	0.0140	0.0003	1.030	0.0300	0.0000	0.4651
Distance to hospital in km	0.0007	0.0005	0.1268	1.002	0.0016	0.0028	0.5680
renal_fail_acute	0.3378	0.0352	<0.0001	3.255	1.1801	0.1180	<0.0001
cancer	-0.1219	0.0348	0.0005	2.786	1.0245	0.1108	<0.0001
cardiac_dysrhythmia	0.2402	0.0137	<0.0001	2.365	0.8610	0.0745	<0.0001
cerebrovascular	0.1581	0.0248	<0.0001	1.710	0.5365	0.1024	<0.0001
heart_ischemic	0.1827	0.0171	<0.0001	0.425	-0.8554	0.0803	<0.0001
renal_fail_chronic	0.0865	0.0173	<0.0001	1.403	0.3383	0.0752	<0.0001
heart_fail	0.1578	0.0140	<0.0001	1.558	0.4436	0.0721	<0.0001
diabetes	0.0599	0.0159	0.0002	1.242	0.2170	0.0833	0.0092
diabetes_comp	0.0817	0.0212	0.0001	1.483	0.3944	0.0909	<0.0001
pulmonary	0.1700	0.0412	<0.0001	1.827	0.6029	0.1252	<0.0001
shock	0.5112	0.0303	<0.0001	5.872	1.7702	0.1397	<0.0001
Hospital level variables							
Beds	-0.0001	0.0001	0.0366	1.000	0.0001	0.0002	0.5297
Number of patients with AMI in hospital	0.0000	0.0000	0.3109	1.000	-0.0001	0.0001	0.4539
Size of nursing staff in FTE	0.0003	0.0001	0.0001	1.000	0.0000	0.0002	0.8450

Teaching	-0.0346	0.0242	0.1534	1.097	0.0929	0.0900	0.3021
Specialisation on cardiovascular diseases	0.1524	0.0290	<0.0001	1.039	0.0384	0.0987	0.6969
Time							
2006	0.0338	0.0131	0.0097	0.813	-0.2068	0.0764	0.0068
2005	0.0513	0.0131	<0.0001	0.766	-0.2661	0.0771	0.0006
2004	reference group			reference group			

Note: Dependent variables: time to death and time to readmission within one year of discharge. The coefficients for beds were multiplied by 100.

Figure 3. Predicted mortality depending on costs



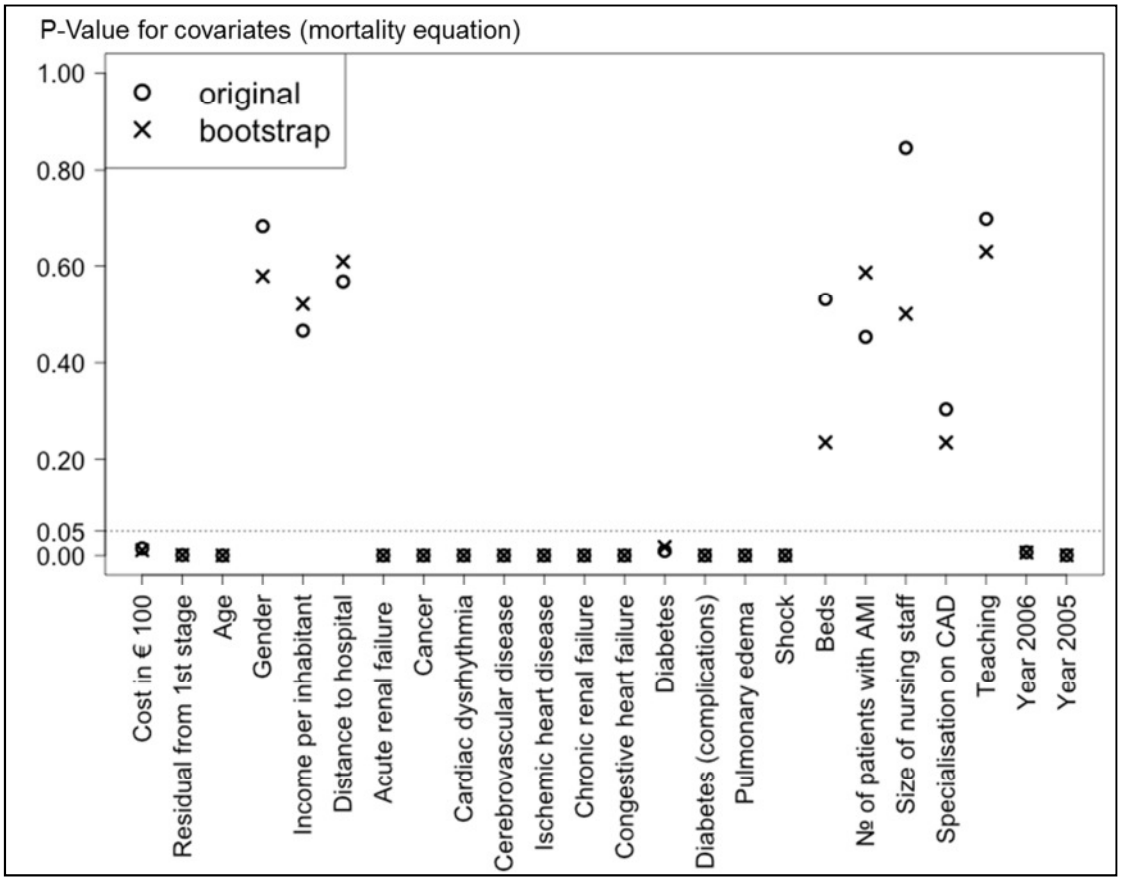
All other sensitivity analyses did not have a major impact on results. Change in functional form did not improve model fit or change results (Table 3). Bootstrapping showed that p-values were very stable and not affected by outliers, in particular for the most important covariate costs (see figure 4). Exclusion of the 2,074 patients that had been transferred during their initial hospital stay, slightly increased the magnitude of outcomes (hazard ratio: 0.990 for alternative model vs. 0.996 for base model). If followed-up from admission instead of from discharge, results remained nearly unchanged (hazard ratio: 0.995 for alternative model vs.

0.996 for base model). Extending our observation period to 2 years instead of 1 year in the base model also did not affect results (hazard ratio 0.996 for alternative model vs. 0.996 for base model).

Table 3. Results from second stage regression, change in functional form

	2nd stage: Mortality (frailty cox)		
	hazard ratio	coefficient	p-value
Base model			
Costs	0.9962	-0.0038	0.0145
Including cost²			
Costs	0.9957	-0.0043	0.0470
Costs²	1.0000	-0.000002	0.5000

Figure 4. Original and bootstrapped p-values for covariates



5. Discussion

In this paper, we propose a methodological approach to measure the relationship between hospital costs and health outcomes. We suggest to use two-stage residual inclusion with a gamma model for costs in the first stage and a random intercept cox proportional hazard model for mortality in the second stage. To obtain consistent estimates of the standard errors, Murphy-Topel adjustment was applied. To demonstrate our model, we investigated the relationship between hospital costs and health outcomes for patients with AMI in Germany. Our results suggest that there is a negative association between hospital costs and mortality.

Our results confirm the often hypothesized trade-off between costs and outcomes. An increase of costs by €100 leads to a reduction of mortality risk by 0.4%. The results are generally in line with previous studies examining the relationship of costs and outcomes for AMI who also find a significant positive association (Romley et al. 2011; Stukel et al. 2012; Schreyögg & Stargardt 2010), while Jha et al., 2009 did not find any significant association. However, comparability to some of the previous studies is limited by a number of differences in study design, methods and setting. The study by Romley et al. (2011) is quite different, because they used in-hospital mortality as outcome measure, categorized spending into quintiles and performed a logistic regression. Similarly, the study by Jha et al., (2009) is hardly comparable because they used 30-day post hospital mortality for AMI, categorized spending into quartiles and compared mortality rates between quartiles based on t-tests. Both Stukel et al. (2012) and Schreyögg & Stargardt (2010) also performed cox-proportional hazard models by using one year post-hospitalization mortality as outcome. The major difference of Stukel et al. (2012) to our study is that they categorized spending into terziles and performed one stage cox-proportional hazard models without multilevel structure. Schreyögg & Stargardt (2010) found that an increase of costs by US$100 leads to a reduction of mortality risk by 0.63%. Stukel et al. (2012) found that being treated by a hospital of the highest spending terzile compared to being treated by a hospital of the lowest spending terzile reduces the mortality risk by 0.99%.

Our study has a number of strengths and adds to previous research on the trade-off between costs and outcomes, particularly from a methodological perspective. First, we use patient level data and focus on one episode of care facilitating adequate risk adjustment. Second, there are reasons to believe that the cost-outcomes relationship varies between different countries, e.g. due to higher risk of malpractice claims which may affect resource input. This study is – according to our knowledge – the first paper that addresses the trade-off between costs and

outcomes in Europe, i.e. in a health care system primarily driven by public health insurance. Third, it proposes the application of Murphy-Topel adjustment to obtain consistent estimates of the standard deviation in two stage regression models for a mixed gamma model in the first stage and a frailty cox proportional hazard model in the second stage. Fourth, we introduce the distance between the patient's residence and the hospital that treated the patient as a proxy for time to care increasing the precision of point estimates. Finally, we allow for different functional forms for costs in the outcome equations.

For the purpose of investigating the cost-outcome relationship our proposed model represents a feasible option to use the available information more efficiently. When investigating the cost-outcome relationship researchers should take the following points into their methodological considerations. First, a focus on selected conditions facilitates controlling for patient severity and address potential differences in the cost-outcome relationship between conditions. Second, if available researchers should use patient-level data for both costs and outcomes to be able to fully exploit the variance of these measures between patients in a given hospital. Although actual costs may seem the best choice to measure costs there is a certain danger that differences in costs may be due varying cost accounting practices. While introducing some limitations (see below), individual reimbursement charges may – in many cases – be a more reliable proxy of costs. Third, it is very likely that the cost-outcome relationship varies between hospitals. Multilevel models are capable of considering the hospital-level variance and allow for inclusion of hospital-level variables controlling for differences in structural quality, e.g. volume performed for a certain condition. Finally, it is important to recognize and address the endogenous character of costs in the cost-outcome relationship. In doing so, instrumental variable approaches represent one option to deal with this. Suitable instruments that are highly correlated to costs, but that are unrelated to outcomes are most likely found among regional aggregates that influence costs, e.g. wage indices, prices for rent etc.

However, our study has also several limitations. As we use reimbursement as a proxy for hospital costs, we were – on the one hand – not able to capture actual resource input for each patient. On the other hand, the DRG system differentiates for the intensity of AMI treatment according to 8 different DRGs (11 in 2006) and 6 different AMI-specific supplementary fees (5 in 2006). Thus, our data still allows for a substantial variation of costs according to treatment intensity, i.e. through DRGs/supplementary fees, and the general level of costs of the hospital, i.e. through the base rate still heavily depending on actual costs for each hospital. In addition

the use of reimbursement rates reduced the vulnerability to different accounting practices between hospitals. Thus using hospital costs assessed by the hospitals' information system may have created the problem that differences in accounting practices explain some of the variation in outcomes.

Although we included a comprehensive set of important covariates we have to acknowledge that risk-adjustment may never be complete. This partly due to the unavailability of data, i.e. other important structural characteristics, such as the volume of procedures performed by a particular surgeon or staffing patterns of the nursing units (Birkmeyer et al. 2002), were not available to us. We also did not have access to data for outpatient care which may have been important, as subsequent treatment in the outpatient sector, e.g. drug treatment, may have impacted the hazard of dying.

Finally, generalization to other health care systems and conditions should be treated with caution. Other studies, although based on different methods, suggest that the cost-outcome relationship may vary according to the conditions (Chen et al. 2010) and may vary according to the settings (Chen et al. 2010; Romley et al. 2011). This study investigates the cost-outcome relationship for AMI as one particular condition; for Germany as one selected health care system.

6. Conclusion

Research on the hospital cost-outcome relationship has emerged in recent years and developed in different stages. The first stage included pioneering studies that examined the relationship on a general hospital level. In the second stage, studies focused on selected conditions and found that cost-outcome relationships may vary between conditions and settings. The current study addressed methodological limitations of previous studies to increase the reliability of results on the cost-outcome relationship. In the next stage studies should try to answer the question, why the cost-outcome relationship may vary according to conditions and settings investigated. In doing so researchers will have to decompose hospital treatment processes into numerous activities identifying mechanisms that drive the cost-outcome relationship over time. These studies will require in-depth activity data, e.g. standardized patient records, from each hospital in addition to the administrative data that has been used so far. If studies were able to identify the underlying reason for varying cost-outcome relationships, results may be highly relevant for decision-makers.

References

Birkmeyer JD, Gust C, Dimick JB, Birkmeyer NJ, Skinner JS. (2012) Hospital quality and the cost of inpatient surgery in the United States. *Ann Surg*. 2012 Jan; 255(1):1-5.

Birkmeyer JA, Siewers E, Finlayson T, Stukel F, Lucas I, Batista H, Welch D, Wennberg DE. Hospital volume and surgical mortality in the United States. *New England Journal of Medicine* 2002; **346**(15): 1128-1137.

Bound J, Jaeger DA, Baker RM. Problems with Instrumental Variables Estimation When the Correlation Between the Instruments and the Endogeneous Explanatory Variable is Weak. *Journal of the American Statistical Association 1995;* **90**(430): 443-450.

Breslow NE. Discussion of Regression models and life-tables by D. R. Cox. *Journal of the Royal Statistical Society, Series B* 1972; **34**(2): 216-217.

Carey K, Burgess JF. On measuring the hospital cost/quality trade-off. *Health Economics* 1999; **8**(6): 509-520.

Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases* 1987; 40(5): 373-383.

Chen LM, Jha AK, Guterman S, Ridgway AB, Orav EJ, et al. (2010) Hospital cost of care, quality of care, and readmission rates: penny wise and pound foolish? Arch Intern Med 22; 170(4):340-6.

Cox DR. Partial likelihood. *Biometrika* 1975; **62**(2): 269-276.

Deily ME, McKay NL. Cost inefficiency and mortality rates in Florida hospitals. *Health Economics* 2006; **15**(4): 419-431.

Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *Journal of Clinical Epidemiology* 1992; 45(6): 613-619.

Efron B, Tibshirani R. *An introduction to the bootstrap*, Chapters 6-7, 9. Exton, PA: Chapman & Hall; 1993.

Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity Measures for Use with Administrative Data. *Medical Care* 1998; 36(1): 8-27.

Evans E, Imanaka Y, Sekimoto M, Ishizaki T, Hayashida K, Fukuda H, Oh EH. Risk adjusted resource utilization for AMI patients treated in Japanese hospitals. *Health Economics* 2007; **16**(4): 347-59.

Fahrmeir L, Tutz G. *Multivariate statistical modelling based on generalized linear models*, Chapter 7. Berlin: Springer; 2001.

Finkler SA, Ward DM, Baker J. Essentials of Cost Accounting for Health Care Organizations. 3rd Edition, MA: Jones & Bartlett; 2006.

Flood A, Scott W, Ewy W. Does practice make perfect? Part II: The relation between volume and outcomes and other hospital characteristics. *Medical Care 1984*; **22**(2): 115-125.

Grambsch PM, Therneau TM. Proportional hazard tests and diagnostics based on weighted residuals. *Biometrika* 1994; **81**(3): 515-526.

Greene WH. *Econometric Analysis*. Upper Saddle River, NJ: Pearson Prentice Hall; 2008.

Hughes RG, Hunt SS, Luft HS. Effects of surgeon volume and hospital volume on quality of care in hospitals. *Medical Care 1987;* **25**(6):489-503.

Jha AK, Orav EJ, Dobson A, Book RA, Epstein AM. (2009) Measuring efficiency: the association of hospital costs and quality of care. *Health Aff* 28(3):897-906.

Lagu T, Rothberg MB, Nathanson BH, Pekow PS, Steingrub JS, et al. (2011) The relationship between hospital spending and mortality in patients with sepsis. *Arch Intern Med*. 2011 Feb 28;171(4):292-9.

Landrum MB, Guadagnoli E, Zummo R, Chin D, McNeil BJ. Care following acute myocardial infarction in the Veterans Administration Medical Centers: a comparison with Medicare. *Health Services Research* 2004; **39**(6 Pt 1): 1773-1792.

Malkin JD, Broder MS, Keeler E. Do longer postpartum stays reduce newborn readmissions? Analysis using instrumental variables. *Health Services Research* 2000; **35**(5 Pt 2): 1071-1091.

Manning WG, Mullahy J. Estimating log models: to transform or not to transform? *Journal of Health Economics 2001*. **20**(4): 461-494.

McClellan M, Staiger D. Comparing the quality of health care providers. In: Garber, A. (ed.), *Frontiers in Health Policy Research*, vol. 3: 113-136, Cambridge, MA: MIT Press; 2000.

McKay NL, Deily ME. Cost inefficiency and hospital health outcomes. *Health Economics* 2008; **17**(7): 833-848.

Morey RC, Fine DJ, Loree SW, Retzlaff-Roberts DL, Tsubakitani S. The trade-off between hospital cost and quality of care. An exploratory empirical analysis. *Medical Care* 1992; **30**(8): 677-698.

Mukamel DB, Spector WD. Nursing home costs and risk-adjusted outcome measures of quality. *Medical Care* 2000; **38**(1): 78-89.

Murphy K, Topel R. Estimation and inference in two-step econometric models. *Journal of Business and Economic Statistics* 1985; **3**(4): 370-379.

Park RE. Estimation with heteroscedastic error terms. *Econometrica;* **34**: 888.

Picone GA, Sloan FA, Chou SY, Taylor DH. Does higher hospital cost imply higher quality of care? *The Review of Economics and Statistics* 2003, **85**(1): 51-62.

Pregibon D. Goodness of Link Tests for Generalized Linear Models. *Applied Statistics* 1980; **29**: 15-24.

Romley JA, Jena AB, Goldman DP. (2011) Hospital spending and inpatient mortality: evidence from California: an observational study. Ann Intern Med 154(3):160-7.

Schreyögg J, Stargardt T. On Measuring the Hospital Cost/Quality Trade-Off: The Case of Acute Myocardial Infarction, *Health Services Research* 2010; **45**(6): 1585-1601.

Schreyögg J, Stargardt T, Tiemann O. Cost and quality of hospitals in different health care systems: a multi-level approach with propensity score matching. *Health Economics* 2011; **20**(1): 85–100.

Schreyögg J, Tiemann O, Busse R. Cost accounting to determine prices: how well do prices reflect costs in the German DRG-system? *Health Care Management Science* 2006; **9**(3): 269-279.

Shen YC, Hsia RY. Association between ambulance diversion and survival among patients with acute myocardial infarction. *Journal of the American Medical Association* 2011; **305**(23): 2440-7.

Shen YC. The effects of hospital ownership choice on patient outcomes after treatment for acute myocardial infarction. *Journal of Health Economics* 2002; **21**(5): 901-922.

Staiger D, Stock JH. Instrumental Variables Regression with Weak Instruments. *Econometrica 1997;* **65**(3): 557-586.

Stukel TA, Fisher ES, Alter DA, Guttmann A, Ko DT, et al. (2012) Association of Hospital Spending Intensity With Mortality and Readmission Rates in Ontario Hospitals *The Journal of the American Medical Association 2012;* **307**(10): 1037-1045 .

Terza JV, Basu A, Rathouz PJ. Two-stage residual inclusion estimation: addressing endogeneity in health econometric modeling. *Journal of Health Economics* 2008; **27**(3): 531-543.

Thompson L, Chhikara R, Conkin J. *Cox proportional hazards models for modeling the time to onset of decompression sickness*. NASA Technical Publication 2003-210791, Johnson Space Center: Houston; 2003.

Tu JV, Austin PC, Walld R, Roos L, Agras J, McDonald KM. Development and validation of the Ontario acute myocardial infarction mortality prediction rules. *Journal of the American College of Cardiology* 2001; **37**(4): 992-997.

Vermeulen MJ, Tu JV, Schull MJ. ICD-10 adaptations of the Ontario acute myocardial infarction mortality prediction rules performed as well as the original versions. *Journal of Clinical Epidemiology* 2007; **60**(9): 971-974.

Weech-Maldonado R, Shea D, Mor V. The relationship between quality of care and costs in nursing homes. *American Journal of Medical Quality* 2006; **21**(1): 40-48.

Yaisawarng S, Burgess JF, Jr. Performance-based budgeting in the public sector: an illustration from the VA health care system. *Health Economics* 2006; **15**(3): 295-310.

Appendix: Murphy-Topel-Adjustment

$$\boldsymbol{V_1} = \widehat{\boldsymbol{F}}_{\boldsymbol{1}}^{-\boldsymbol{1}}$$

with

$$F_1(\alpha_1, \alpha_2, \xi) = \begin{pmatrix} \sum_{i=1}^{n} x_{Ii} x_{Ii}' \exp(2\,\eta_{Ii}) \sigma^{-1} & \sum_{i=1}^{n} x_{Ii} z_{Ii}' \exp(2\,\eta_{Ii}) \sigma^{-1} \\ \sum_{i=1}^{n} z_{Ii} x_{Ii}' \exp(2\,\eta_{Ii}) \sigma^{-1} & \sum_{i=1}^{n} z_{Ii} z' \exp(2\,\eta_{Ii}) \sigma^{-1} + G(\xi)^{-1} \end{pmatrix}$$

$$\boldsymbol{V_2} = \widehat{\boldsymbol{F}}_{\boldsymbol{2}}^{-\boldsymbol{1}}$$

with

$$F_2(\beta_1, \beta_2, \psi) = \begin{pmatrix} \sum_{i=1}^{n} \delta_i \left(\frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, x_{IIi} x_{IIi}' \exp(\eta_{IIi}) - x_{IIi} \exp(\eta_{IIi}) \sum_{j=R(t_i)} \exp(\eta_{IIj}) x_{IIj}'}{\left(\sum_{j=R(t_i)} \exp(\eta_{IIj})\right)^2} \right) \\ \sum_{i=1}^{n} \delta_i \left(\frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, x_{IIi} z_{IIi}' \exp(\eta_{IIi}) - x_{IIi} \exp(\eta_{IIi}) \sum_{j=R(t_i)} \exp(\eta_{IIj}) z_{IIj}'}{\left(\sum_{j=R(t_i)} \exp(\eta_{IIj})\right)^2} \right), \\ \sum_{i=1}^{n} \delta_i \left(\frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, u_i\; x_{IIi}' \exp(\eta_{IIi}) - z_{IIi} \exp(\eta_{IIi}) \sum_{j=R(t_i)} \exp(\eta_{IIj}) x_{IIj}'}{\left(\sum_{j=R(t_i)} \exp(\eta_{IIj})\right)^2} \right) \\ \sum_{i=1}^{n} \delta_i \left(\frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, z_{IIi} z_{IIi}' \exp(\eta_{IIi}) - z_{IIi} \exp(\eta_{IIi}) \sum_{j=R(t_i)} \exp(\eta_{IIj}) z_{IIj}'}{\left(\sum_{j=R(t_i)} \exp(\eta_{IIj})\right)^2} \right) \end{pmatrix}$$

$$\boldsymbol{C} = \hat{\boldsymbol{s}}_{\boldsymbol{2}} \hat{\boldsymbol{s}}_{\boldsymbol{21}} \qquad \text{and} \qquad \boldsymbol{R} = \hat{\boldsymbol{s}}_{\boldsymbol{2}} \hat{\boldsymbol{s}}_{\boldsymbol{1}}$$

with

$$s_1(\alpha_1, \alpha_2, \xi) = \begin{pmatrix} \sum_{i=1}^{n} x_{Ii} \exp(\eta_{Ii})\, (y_{Ii} - \mu_{Ii})\, \sigma^{-1} \\ \sum_{i=1}^{n} z_{Ii} \exp(\eta_{Ii})\, (y_{Ii} - \mu_{Ii})\, \sigma^{-1} - G(\xi)^{-1} \alpha_2 \end{pmatrix}$$

$$s_2(\beta_1, \beta_2, \psi) = \begin{pmatrix} \sum_{i=1}^{n} \delta_i \left(x_{IIi} - \frac{x_{IIi} \exp(\eta_{IIi})}{\sum_{j=R(t_i)} \exp(\eta_{IIj})} \right) \\ \sum_{i=1}^{n} \delta_i \left(z_{IIi} - \frac{z_{IIi} \exp(\eta_{IIi})}{\sum_{j=R(t_i)} \exp(\eta_{IIj})} \right) - \ D(\psi)^{-1} \beta_2 \end{pmatrix}$$

$$s_{21}(\alpha_1, \alpha_2, \beta_1, \beta_2) = \begin{pmatrix} \sum_{i=1}^{n} \delta_i \left(-\alpha_{1r} \exp(\eta_{Ii})\, x_{Ii} + \frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, \alpha_{1r} \exp(\eta_{Ij}) x_{Ij}}{\sum_{j=R(t_i)} \exp(\eta_{IIj})} \right) \\ \sum_{i=1}^{n} \delta_i \left(-\alpha_{1r} \exp(\eta_{Ii})\, z_{Ii} + \frac{\sum_{j=R(t_i)} \exp(\eta_{IIj})\, \alpha_{1r} \exp(\eta_{Ij}) z_{Ij}}{\sum_{j=R(t_i)} \exp(\eta_{IIj})} \right) \end{pmatrix}$$

hche | Hamburg Center for Health Economics

The Hamburg Center for Health Economics is a joint center of the School of Business, Economics and Social Sciences and the Medical School at the University of Hamburg.

Contact: Hamburg Center for Health Economics
Esplanade 36, 20354 Hamburg, Germany
Tel. +49 (0) 42838-8041, Fax: +49 (0) 42838-8043
Email: office@hche.eu, http://www.hche.eu

hche Research Paper Series, ISSN 2191-6233 (Print), ISSN 2192-2519 (Internet)

2011/1 Mathias Kifmann and Kerstin Roeder, Premium Subsidies and Social Insurance: Substitutes or Complements? March 2011

2011/2 Oliver Tiemann and Jonas Schreyögg, Changes in Hospital Efficiency after Privatization, June 2011

2011/3 Kathrin Roll, Tom Stargardt and Jonas Schreyögg, Effect of Type of Insurance and Income on Waiting Time for Outpatient Care, July 2011

2012/4 Tom Stargardt, Jonas Schreyögg and Ivan Kondofersky, Measuring the Relationship between Costs and Outcomes: the Example of Acute Myocardial Infarction in German Hospitals, August 2012