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Cost measurement and estimation of cost functions

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Introduction

The purposes of this paper are two: First, to introduce the reader to the challenges of estimating health care costs and suggested solutions to these challenges, and second, to approach a strategy for cost estimation in EuroHOPE.

There are two distinct tasks. In general, data on health care costs are not available at the individual patient level in most countries. Hence, the first task is to construct a one-dimensional measure of costs based on indicators of resource use that are contained in the data sets. Next, given a one-dimensional cost-indicator the second task is to estimate the relation between measured cost and patient characteristics in addition to other variables. The result is estimated cost adjusted for patient risk and supply side variables that we would like to take account of.

Our general strategy is to start simple with descriptives and then add additional analytical features when we become more familiar with the data and the methods.

This paper is work under progress. All sections will be elaborated on based on feedback from the project participants, further literature studies and on actual experience with data. In addition to references from the literature, this paper makes use of notes from preconference course on "Modeling Health Care Costs and Counts" by Partha Deb, Willard Manning and Edward Norton at the International Health Economics Association's conference in Toronto in 2011 (Deb, Manning and Norton, 2011).

Estimating health care costs

Estimating costs in fixed period of time

In a special issue of the journal Medical Care from 2009 several experienced researchers in the field of health care cost estimation sum up the status and challenges ahead. Mullahy (2009) starts out by describing four prominent features of health care expenditures that are typically important to accommodate. First, health expenditure data are nonnegative. Second, in many cases a sizable fraction of the observations are zero, as many people do not make use of health care during a particular period. Third, the data have heavy right hand tails. Forth, data are right-skewed. In addition, there may be nonlinearity in response to covariates and cost response may change by level of consumption. Since EuroHOPE is dealing with patient data, the second concern is less of a problem while the other three are. In addition, there are the problems of potential endogenous covariates, the problem of retransformation when analysis is based on nonlinear transformation of health care cost measures, and censoring of longitudinal cost data. A brief description of censoring and how to deal with it is given in Section 2.2. A more detailed description is found in Appendix A.

Manning (2006, 2012) summarizes the same kinds of characteristics. He explains that the top one per cent of the distribution will often account for a quarter of the health care costs. Sometimes it might be even more skewed with the top tenth of the distribution accounting for half of all costs.

According to Mullahy (2009) most empirical analysis of health care cost data are regression based. This means a statistical estimation of features of the statistical distribution of costs (y) conditional on covariates (x). The application of ordinary least squares regression (OLS) typically gives inconsistent or inefficient results when at least one of the above mentioned characteristics are prevalent. If the data set is big enough, it is claimed that this is less of an issue (e.g. (Manning, 2006)). For instance, cost estimation to

adjust for heterogeneity among Medicare patients in the US is done my means of OLS. For smaller data sets, as in EuroHOPE, OLS is unlikely to be a good choice and hence, the alternatives to OLS become an important issue.

In addition to the references already given, there is in particular one recent study that summarizes statistical methods used for analyzing health care resources and costs. Mihaylova et al. (2011) systematically reviewed papers that are likely to be applicable to randomized trial data. In total 97 manuscripts were included in the review. No explicit quality criteria for the reviewed studies were employed. Their review is also relevant for studies that make use of administrative register data, as EuroHOPE.

Mihaylova et al. (2011) distinguish between 12 categories of analytical approaches currently employed. These are: (I) methods based on the normal distribution, (II) methods following transformation of data, (III) single-distribution generalized linear models (GLMs), (IV) parametric models based on skewed distributions outside the GLM family, (V) models based on mixtures of parametric distributions, (VI) two (or multi)-part and Tobit models, (VII) survival methods, (VIII) non-parametric methods, (IX) methods based on truncation or trimming of data, (X) data components models, (XI) methods based on averaging across models, and (XII) Markov chain methods.

Mihaylova et al. find from the literature survey that (I) methods based on the normal distribution (such as ordinary least squares) are widely used. They find that the estimates are sensitive to extreme values and likely to be inefficient in small to medium sample sizes if the underlying distribution is not normal. It can produce out-of-range predictions, as for instance negative predicted costs. Generalized least squares estimators or Huber/white estimate of the variance- covariance matrix for OLS regressions are often used to achieve consistent estimates of standard errors and covariances in such situations. E.g. Gutacker et al. (2012) report results from a linear cost model to be similar to those from a GLM with log link and gamma/Poisson distribution. On the other hand Garrido et al. (2012) in a setting with nonlinearity and endogeneity report significantly different treatment effects for models that are linear for costs or log-costs compared with e.g. GLM with gamma distribution and log link.

(II) Methods following transformation of data are applied to take the problem of skewness into account. These methods are common in the literature, especially in the log(y) version. The log(y) is a special case of the more general Box-Cox transformation

$$f(y) = \frac{y^{\lambda} - 1}{\lambda}$$

which has been widely used. The transformation implies untransformed *y* for λ=1 and ln(*y*) for λ=0. The parameter λ can be estimated by maximum likelihood. It reduces robustness problem by focusing on symmetry, and gives improved precision if y is skewed right. It may reduce (but not eliminate) heteroscedasticity. Manning (2006) summarizes technical issues that arise with Box-Cox models. These include how to deal with observations where *y*=0 and that the estimates of power transform are sensitive to extreme outliers. A disadvantage with the method is that decision-makers are not interested in the transformed cost estimates. Hence, the cost estimate has to be retransformed from the scale of estimation to the scale of actual interest. Since the Box-Cox transformation is non-linear, we cannot simply invert the transformation to obtain unbiased estimates of E(y|x) because in general E(f(y|x))≠ f(E(y|x)). This is the retransformation problem discussed in the literature, and where Duan's (1983) smearing factor can be

applied if the error term is homoscedastic and its analogue in the heteroscedastic case. More references are provided by Manning (2006) and by Manning et al. (2005).

(III) Single-distribution generalized linear models (GLMs) specify a distribution of the dependent variable and a link function between the linear model *x'β* and the mean such that g(E(y|x))= *x'β*. Since the estimation is directly on the scale of raw data, there is no need for back transformation. GLMs deal with skewness in the data. These models are used for modelling costs as well as for items of resource use. When used for modelling costs the Gamma distribution combined with the log link is the most common while the Poisson and negative binomial specification with a log link are common for counts of resource use. In classical GLM the variance function is implied by the choice of a particular member from the family of exponential distributions and by the mean function. For example, the gamma distribution has the property that $V[y|x]$ is proportional to $\left[E[y|x]\right]^2$ while for the Poisson distribution $E[y|x] = V[y|x]$. According to Mihaylova et al. (2011) the most widely used GLM with log link has been shown to suffer substantial efficiency losses when the log scale variance is large or the error distribution of the log scale is symmetric, but heavy-tailed. The classical GLM approach maximizes the likelihood by iterative reweighted least squares solving at each stage an equation depending only on the mean and variance functions of the model (e.g. McCullagh and Nelder, 1989). The generalized estimating equations (GEE) approach is less assuming in that it requires only the mean and variance functions to be specified, without full distributional assumptions. Manning (2006) suggested testing the form of the variance function with a Park test. If, for example the variance is defined as a power function of the mean $V(y|x) = \theta_1 \mu^{\theta_2}$, where $\mu = E(y|x)$, $\theta_2 = 0$ would correspond to a variance as in a normal distribution, while $\theta_2 = 1$, $\theta_2 = 2$ and $\theta_2 = 3$ would correspond to Poisson, gamma and inverse Gaussian variances, respectively. The Park test amounts to estimating and testing θ_1 and (in particular) θ_2 in a simple regression after having obtained with a first step regression estimates of $E(y|x)$ and $V(y|x)$ for each observation. In Stata maximum likelihood estimation is obtained with the glm command, while GEE is pursued with xtgee. Basu (2005) and Basu and Rathouz (2005) extend GEE to flexible link and variance functions. Cantoni and Ronchetti (2006) present a GEE approach more robust to outliers.

(IV) Parametric models based on skewed distributions outside the GLM family. Methods based on distribution outside the GLM family (as noted, a GLM has a probability distribution from the exponential family) have been used to improve the flexibility of the previous parametric models. As most notable here we regard the Generalized Beta of Second Kind (GB2), (Jones et al. 2011). This model contains several other suggestions, like the Generalised Gamma (Manning et al. 2005), as special or limiting cases. Hence the GB2 seems to provide a useful, flexible and general framework for testing and comparing models and choosing a distribution to apply. There seems to be both Stata and R modules available for GB2 (Jenkins 2009, Graf and Nedyalkova 2010).

(V) Models based on mixtures of parametric distributions. These models are introduced to account for excess zeros, overdispersion and heavy tails and may lead to more robust estimates. The models mix several distributions. For example, the zero inflated Poisson/binomial model is used to take into account excess zeros, where zeros are assumed to be generated by two different processes. Say we are interested in estimating the expected number of a particular hospital service a population receives. A zero can then both be obtained because a person is not admitted to the hospital (a healthy person) and because it was decided not to provide the service even though the patient was admitted to the hospital.

(VI) Two (or multi)-part and Tobit models. The two part model usually consists of first estimating the probability that medical service is used and then the number or quantity of services received given that service is received. The two parts are estimated independent of each other. The two part model is perhaps best known from the Rand Health Insurance Experiment in the 1970s. As noted above, the need for back transformation of estimated magnitudes to the original scale has received much attention in the literature. The retransformation problem appears if health care costs are estimated by some kind of nonlinear transformation of the cost variable, for instance a log transformation, the retransformation back to natural units may be complicated. This is particularly so if error term in the transformation regression is heteroskedastic in x.

(VII) survival methods is covered by Section 2.2

(viii) Non-parametric methods. This approach has been receiving much attention in statistics and econometrics. However, in health economics we have not yet seen much development or applications. Mihaylova et al. (2010) gives a short review.

(ix) Methods based on truncation or trimming of data. Mihaylova et al. (2010) notes that this approach is based on the assumption that data are contaminated which is not the case with health care resource use and costs where zero or high observations are true values.

(x) Data component models. Mihaylova et al. (2010) describes an emerging area of research where components of resource use or costs are modeled separately. Better fit is often reported, though with limited evidence on whether data are overfit and on efficiency of the estimators. Mihaylova et al. (2010) note that these models represent possibilities for research.

(xi) Methods based on averaging across a number of models. This is another recent area with not many contributions so far within health economics.

(xii) Markov chain methods. This amounts to modelling resource use over different phases of health care and requires detailed data. Mihaylova et al. (2010) see some promise but conclude that more research is needed into robustness and efficiency of this approach.

When it comes to the specification of covariates, Mullahy (2009) considers at least two considerations to be particularly important: interaction effects and endogenous covariates. In non-linear model the interpretation of interaction effects is typically more complicated than in linear models.

Endogenous covariates and/or considering outcome jointly with costs

An endogenous regressor means that the regressor is correlated with the error term in the regression. This could for instance happen if there is a third unobservable variable that is related to both the regressor and the dependent variable. For instance, some variables that describe behavior may be related to some more fundamental personal characteristics that also have an impact on health care costs. Endogenous covariates call for instrumental variables. Good instruments are often hard to find.

In Schreyögg and Stargardt (2010), the authors study the relationship between hospital costs and health outcomes for patients with myocardial infarction (AMI) in Veteran Health Administration hospitals. They use individual data both for costs and outcomes. Costs are defined as all costs during the index

hospitalization for treatment of AMI Clinical outcome is measured as mortality and readmission assessed one year after the index hospitalization. The authors estimate a two level model with patients nested within hospitals. They estimate random effects proportional hazard models (frailty models). Competing risks (death and readmission) are accounted for. They also take into account that costs are endogenous to health outcomes. They estimate a model of two-stage residual inclusion (2SRI). They use the Medicare Wage Index and the general overhead cost per day at the hospital level as instruments. They argue that these instruments are related to costs without being related to health outcomes. A key result is that there is a trade-off between costs and outcomes.

Hvenegaard et al. (2010) argue theoretically for a U-shaped function between costs and quality. They estimate separately a linear model for costs and a logit model for a binary outcome/quality variable (30 days mortality and wound complications), each of the two models including fixed effects for hospital departments. An advantage with fixed effects compared with random effects is that the fixed effects are allowed to correlate with the other explanatory variables which likely correspond to reality. The fixed effects approach gives unbiased estimates even if risk adjustment factors and departmental effects are correlated and it directly produces explicit estimates of department effects. Hvenegaard et al. 2010 handle the simultaneity between costs and outcomes, i.e. describes potential covariance between cost and quality, by bootstrap sampling jointly of costs and quality from the estimated models, and construct two-dimensional confidence regions for cost and quality. They conclude that ranking of departments may alter considerably when quality is taken into account and they cautiously conclude that there appears to be cost/quality tradeoff between costs and mortality. This approach does not need weights to be defined for different criteria/objects like costs and quality, nor causality relations between the endogenous variables to be specified. The estimated equations can be seen as reduced forms but still the authors also note that estimated equations might suffer from omitted variable bias.

Gutacker et al. (2012) estimate cost function with health outcomes as input. They argue for random rather than fixed provider effects and find some evidence of a U-shaped relationship between risk-adjusted costs and outcomes.

Kaestner and Silber (2010), Skinner and Fischer (2010) and Stukel et al. (2012) argue for using instrumental variables to counteract potential reverse causality (here: that unobserved health characteristics may impact on resource use). The authors motivate their choice with previous studies having shown that the intensity of treatment and use of resources for patients in a hospital is strongly associated with the intensity of treatment for patients at the end of life in that same hospital. Accordingly, they use these end-of-life measures of treatment of decedents in particular hospitals as an instrument for inpatient spending for patients in those hospitals. Their identifying assumption is that the variation among hospitals in end-of-life spending on decedents who have several chronic conditions is not correlated with unmeasured differences among hospitals regarding their patients' health. They provide evidence to support that assumption. In general, they find that increased spending is associated with reduced mortality.

In a recent paper Garrido et al. (2012) compare methods for handling endogeneity in nonlinear models for costs. The model is set up as

$$P(d_i = 1|\boldsymbol{z}_i, I_i) = g(\boldsymbol{z}_i'\boldsymbol{\alpha} + \delta I_i)$$
$$E(Y|\boldsymbol{x}_i, d_i, I_i) = f(\boldsymbol{x}_i'\boldsymbol{\beta} + \gamma d_i + \delta I_i)$$

where $\boldsymbol{z}$ and $\boldsymbol{x}$ denote vectors of observed covariates, Y is outcome (costs) and d_i is a binary variable (treatment, outcome or selection) which also appears as an endogenous regressor in the cost equation. I_i denotes latent (unobserved characteristics) common to treatment/selection and costs. For identification $\boldsymbol{z}$ has to include at least one variable (instrumental variable) not included in $\boldsymbol{x}$. It is illuminating to take note of the approaches considered by Garrido et al. (2012):

(i) two stage least square after having tested for the appropriateness of their instrument variable.

(ii) two stage least square on log transformed dependent variable with homoskedastic nonparametric retransformation (Duan 1983).

(iii) control function (CF) approaches. This amounts to adding to the cost equation, which is a gamma GLM with log link, residuals from the quality equation. Various forms of residuals are used (raw residuals, Pearson residuals, etc) and they are included in the cost equation in up to third degree polynomial form. The two-stage residual inclusion estimation of Terza et al. (2008) is a limited special case of this. For linear models with jointly normal errors the approach is related to generalized Tobit models and to two stage estimation procedures suggested by Vella (1993) and Heckman (1979). Häkkinen et al. (2012) used a version of this with a linear cost function for logarithmized costs and assuming jointly normally distributed error terms.

(iv) maximum simulated likelihood. Apparently Garrido et al. (2012), following Deb and Trivedi (2006), assume that the unobserved latent characteristics I_i follow a normal distribution. Then it is easy to generate random samples of I_i . Given I_i , cost and outcome are independent.

The 2SLS on costs and on log costs give in their example surprisingly much bigger estimated treatment effects than the CF and maximum simulated likelihood approaches. Häkkinen et al. (2012) specify the model as

$$\ln(c_{ik}) = x'_{1ik}\beta_1 + \delta q_{ik} + u_k + \epsilon_{1ik}$$

and

$$q^*_{ik} = x'_{2ik}\beta_2 + v_k + \epsilon_{2ik}$$

where c_{ik} = costs for patient i in hospital k,

$$q_{ik} = \begin{matrix} 1 \text{ if discharged alive } (q^*_{ik} \geq 0) \\ 0 \text{ if died in hospital } (q^*_{ik} < 0) \end{matrix} ,$$

x_{1ik} and x_{2ik} = vectors of variables that describe patient *i* in hospital *k*, regarding their medical characteristics (diagnosis, severity, co-morbidities, age, gender), u_k and v_k = hospital specific effects (fixed, i.e. allowed to correlate with the included risk factors x as well as with each other), and ε_{1ik} and ε_{2ik} = patient level error terms (bivariate normal). This is simultaneously a linear model for costs and a probit model for quality, connected by correlated error terms as well as by the binary variable q_{ik} possibly effecting costs. With Chow F-test they tested whether the cost equation should be estimated separately for those who died in hospital and those who were discharged alive. If this division of the sample is done for the cost equation

the model is in fact a Roy model, which boils down to two Heckman selection models which can be estimated separately (Cameron and Trivedi, 2005).

Comparisons of models and approaches

Comparisons have been done on theoretical grounds, empirically and by simulation. Mihaylova et al. (2010) also summarizes comparisons of performance and note twenty identified papers on controlled environment of simulated data. Among conclusions they note that "Further research comparing the performance of different methods on simulated as well as experimental trial data is highly desirable".

Censoring in cost data

An important challenge in the estimation of medical costs, is that medical data often are observed with different length of spells (incompletely observed), indicating that we do not observe the total medical costs for all individuals in the sample, but within a limited observation period or "time-window", such as the period (0, τ) in Figure 1. Spells that both start and end within the "time-window", such as Spell 1 in Figure 1, would reflect the total medical costs. For all other spells, the observed spell will not represent the true total treatment costs due to either right, left or interval censoring. Right censoring occurs when the time-window includes the time of diagnosis (0, τ), but not the end of treatment (τ,∞), such as Spell 2 in Figure 1. Left censoring occurs when treatment started before time 0 and ended with the observed time-window (0,τ). A spell with interval censoring is defined by a starting point before time 0 and an endpoint later than time τ, (τ,∞). In survival analysis, right censoring is the most common, indicating that only those spells starting within 0 and τ, are included. With regard to costs, all types of censoring could be relevant.

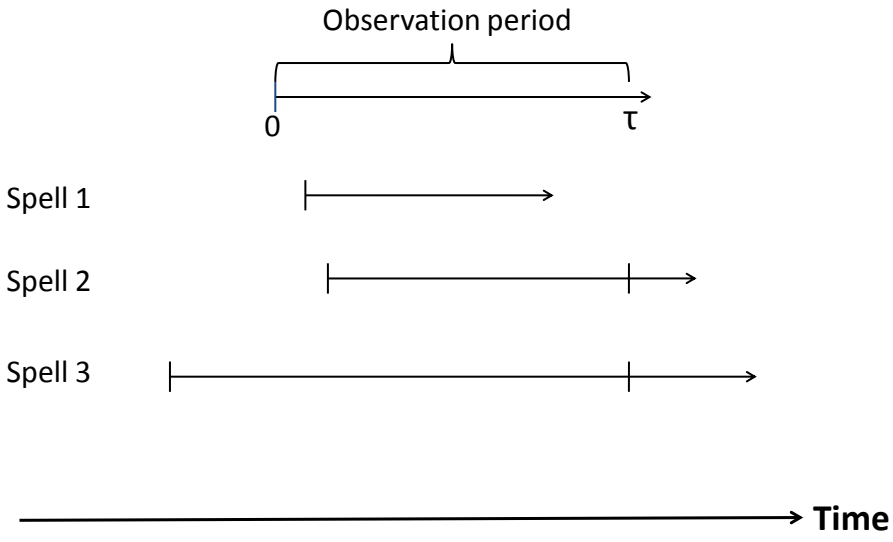

Figure 1: Different spells of treatment according to the time window, in which the medical data are observed

To demonstrate the challenges with censoring, let us assume that we have access to a dataset on treatment costs for patients with acute myocardial infarction (AMI) and the aim is to estimate total treatment costs. The available treatment data include individuals diagnosed between January 2008 (time 0) and December 2010 (time τ). Given the structure of the data, the observation period or duration of an AMI diagnosed September 1st 2010 will be four months, while the duration for a patient diagnosed in January 2008, could be up to three years. When spells could be equally long, but for different reasons, this could stem from censoring. If an individual diagnosed in January 2008 dies in May 2008, and the individual diagnosed in September 1st 2010 survives throughout the observation period (end of 2010), the treatment cost for the individual dying, reflects the true treatment cost for this individual, while that is not the case for the other individual, as he might receive treatment after December 2010. Thus, we need to include a mechanism that distinguishes between these two spells, where one dies, while the other does not.

In EuroHOPE, costs will be estimated together with survival and other indicators. With regard to estimation of costs, the aim is to estimate expected one year treatment costs for five different types of diseases, and not total treatment costs. As the perspective is one year and costs are observed for every individual for one year, unless they have died, censoring will not be an issue in the main cost analysis in EuroHOPE.

An extension of time horizon in EuroHOPE could result in right side censoring, as the cost data are observed from the time of diagnoses. When the aim is to estimate longer time series with different length of spells due to censoring, other models need to be considered, see Appendix A for a short review of relevant methods.

Comparing costs between countries in EuroHOPE

In EuroHOPE the purpose is to compare treatment costs between the participating countries. One aims at estimating the deviation in a country's treatment costs from the average. In this section we focus on specific methodological challenges in comparison of costs between countries. The challenges in the preceding sections of methods for estimating costs in general, are still valid. When comparing costs between countries or different regions, we aim at identifying differences in costs that stem from differences in how countries organize the treatment. Even if we are less interested in differences in composition of patients in itself, risk adjustment is crucial in order to obtain cost estimates that are comparable.

The presentation of methods in this section is based on three studies, applying different methods for cost comparisons (Street et al., 2012; Schreyögg and Stargardt, 2011; Peltola et al., 2011). In Street et al. (2012) regional differences, which easily could be applied for different countries, are modeled explicitly by including a fixed effect. In Schreyögg and Stargardt (2011) a multi-level approach with propensity score matching is applied, while Peltola et al. (2011) estimated differences between countries as the difference in predicted costs, based on estimated coefficients from a pooled data set, with observed costs from each country. The different methods have different pros and cons, which will be discussed below.

In Street et al. (2012) the aim is to estimate costs within the EuroDRG project. Estimation of costs includes regional differences within each country, but does not explicitly estimate differences between countries.

Thus, based on Street et al. (2012) it is only possible to compare differences in predicted costs based on country specific coefficients, and further explore factors that causes differences in costs. It is not possible to explicitly calculate differences in costs between the countries, only between regions. If data between countries could be merged, the method in Street et al. could be applied for across country comparison. Let us assume that regional variation in Street et al. (2012) is replaced with countries, and then differences in costs could be estimated by applying a log-linear model with fixed effects, given by

$$y_{ik}^{c} = \beta_0 + \boldsymbol{\beta}'\boldsymbol{x}_{ik} + u_k + \boldsymbol{\varepsilon}_{ik}$$

where $y_{ik}^{c}$is log-costs for individual *i* for country *k* and $\boldsymbol{x}_{ik}$ is a vector of individual characteristics adjusting for relative risk of individual *i* in country *k*. Country specific influence of costs are represented by u_k, while $\boldsymbol{\varepsilon}_{ik}$ is the standard disturbance. The differences in costs will be represented by u_k, estimated as fixed effect. High values of u_k could be interpeted as costs above average, after adjusting for individual characteristics. In addition, Street et al. (2012) also estimated the variation between regions (in EuroHOPE the parallel would be countries) by hospital characteristics.

Given that data for all countries could be merged into one pooled dataset, the above method could be applied to estimate across country cost differences in EuroHOPE, both with and without regional differences within each country. In the EuroDRG project a log-linear model was used to estimate expected costs. As re-transformation is not straight forward when covariates are included, this might cause some problems with estimating mean costs.

In Schreyögg and Stargardt (2011) costs among patients treated for AMI are compared between Germany and the US Veterans Health Administration (VHA). The comparison of costs between countries combines propensity score matching and multi-level modeling. First, they estimate the probability for undergoing treatment in Germany, adjusted for risk, such as comorbidity. Secondly, the patients from Germany and the VHA sample are matched by means propensity score matching with replacement. From predicted means of costs a new sample is defined based on a one-to-one match of individuals from Germany and the VHA sample. Based on the new matched sample, costs are both estimated separately for each country by means of a multi-level model and by matching. The two-level multi-level model approach assumes that there is correlation between individuals in the same region (or patients belonging to the same hospital). The structure is given by

$$y_{ij} = \beta_{0j} + \boldsymbol{\beta}'\boldsymbol{x}_{ij} + \beta_2 z_j + \boldsymbol{\varepsilon}_{ij}$$

$$\beta_{0j} = \beta_0 + \mu_j$$

where y_{ij} is log-linear costs for individual *i* for country *j* and $\boldsymbol{x}_{ij}$ is a vector of individual characteristics adjusting for risk for individual *i* in country *j*. Country specific influences of costs are represented by z_j, while $\boldsymbol{\varepsilon}_{ij}$ is the standard disturbance for individual i in region *j*, and μ_j is the standard disturbance at the hospital level. The multi-level cost function was estimated by means of both log-normal and gamma distribution.

The last approach is based on the estimations in PERFECT (Peltola et al., 2011). In this study, comparisons between regions were based on estimations from a pooled dataset. In this study all data were merged into one dataset. Then costs were estimated as a function of different risk components, such as age, severity and comorbidity. Based on the estimated coefficients, predicted costs for each region were compared with observed costs. Differences in costs between regions are then defined as the deviation in costs from the average. For region *j* the deviation in costs is an indicator (IND_j) given as the ratio of observed costs (O_j) to expected costs (E_j)

$$IND_j = O_j/E_j$$

In EuroHOPE we would like to say something very explicit about differences in costs across countries. The method applied in PERFECT is possible to apply if not data from all countries are included in the pooled dataset. It would be optimal, if all countries could contribute to the pooled dataset, but if that is not possible due to data restrictions, it will still be possible to compare costs by the indicator. All countries could apply the estimated coefficients from the pooled estimation.

Aspects of comparison are also dealt with by Hvenegaard et al. (2010), Gutacker et al. (2012), and Häkkinen et al. (2012).

Costing: Calculating costs

The problem

In order to estimate how treatment cost depends on patient characteristics and supply side variables, one first has to provide the cost variable. Cost figures only rarely are provided at the individual patient level (bottom-up approach). Hence, one often has to rely on a figures derived from a top down approach, perhaps supplemented with information from hospitals that make use of bottom-up cost per patient (CPP) figures. Alternative methods for cost-calculations may result in variation in cost figures and may potentially have a considerable impact on cost estimation. This issue is illustrated in Geue et al. (2012). Using data from Scotland as an illustrative example, five costing methods are compared. Cost variables are derived using two forms of DRG-type costs, costs per diem, costs per episode (that distinguishes between variable and fixed costs and incorporates individual length of stay), and costs per episode using national average length of stay. Descriptive statistics show substantial variation in the cost figures that emerge from the alternative costing methods. These differences also carry over to differences of cost estimates found in the regression analyses. The authors conclude that any inference made from econometric modelling of costs, where the marginal effect of explanatory variables is assessed, is substantially influenced by the costing method.

This conclusion is also highlighted by the EuroDRG-project that finds a considerable variation with regard to the explanatory power of DRGs across countries and types of treatment (Busse, 2012).

Costing in Perfect

Finland has for many years done comparative outcome and cost analysis across hospital districts. A description of the method of cost estimation is described in Peltola and Häkkinen (2011) and more briefly, in Peltola et al. (2011). The Finnish approach is an episode of care approach, also adopted by EuroHOPE. In

general, the inspiration to the EuroHOPE approach comes from Perfect. During an episode of care, hospital cost (inpatient and outpatient) and pharmaceutical cost outside hospital are included.

In general, calculation of hospital cost is not done at the level of individual patients. Since DRG-weights are assigned to all inpatient stays and outpatient consultations, they are used for cost calculations in most cases. For some treatments DRG-weights are considered to be too crude as hospital cost indicators. For example for hip and knee replacement there is only one DRG irrespective of whether it is the first replacement or a repeated replacement. In these cases, the availability of individual level cost accounting data from the biggest hospital district (Helsinki and Uusimaa, HUS) are made use of. The contributions to cost of variables like procedures, length of stay, discharge status and various disease specific variables are estimated. The cost of prescribed medicine outside hospital is taken from the Social Insurance Institution.

Available data of resource use and cost in EuroHOPE

Comparative studies of treatment costs across countries entail additional problems. These problems relate to the absence of standardized systems for registering diagnoses and in particular, procedures and resource use across countries.

Each country in EuroHOPE has provided information of registration of resources that is available from the register data to be used in EuroHOPE. The information is both given at a general level and at a disease specific level.

A summary of the information provided at the general level is given in Appendix B. Finland, Hungary, Italy, Norway and Sweden have a DRG-system, although the DRG grouper varies across the countries. Finland, Norway and Sweden have all the same grouper, namely the NordDRG system (http://www.nordcase.org/eng/nordic_drg-system). Netherlands has a DRG-type system, the DTC-system (DTC = Diagnosis Treatment Combination) while Scotland uses HRGs (Health Related Groups) as the basis for assigning treatments into groups with similar use of resources. It is also a variation across countries in whether or not outpatient consultations and procedures are included in the classification system. Length of stay information is available in the data files in all countries. The coding system for surgical operations and procedures varies across countries. Again, the Nordic countries make use of the same system, NCSP (Nordic Classification of the surgical Procedures). All countries report that they have approximations to costs of the various procedures. In most cases these will be fees and price lists related to the various procedures. At last, we registered the possible occurrence of a cost per patient system in at least one hospital in the country. Such systems seem to be best developed in Sweden and Finland. Hungary, Netherlands and Scotland do not report of any such systems in their countries while Italy and Norway is in between.

We have also collected information from the partners about disease specific registrations of use of resources and costs. A summary of the information is included in the appendix. The summary considers main elements of diagnostics and treatment of the EuroHOPE diseases in the EuroHOPE countries. Of particular interest is the availability of information in the registers to be used in EuroHOPE. A main impression from the collected information is that treatment procedures are registered although there is some variation among countries. The recording of diagnostic procedures seems to be less comprehensive. Take Acute Myocardial Infarction (AMI) as an example. Treatments by PCI and CABG are registered in all countries while the registration of Thrombolytic treatment varies. When it comes to diagnostics, it seems to be more variation regarding what is registered. For instance ECG is registered in some countries and

Troponin testing is registered in only two of the countries. An impression is nevertheless that the most costly procedures are registered in all countries.

Calculating costs in EuroHOPE

Considerations common to all diseases

A preliminary conclusion from the description of data availability at the general level and disease specific level is that a measure of total cost of care of the individual disease episode is not available from all countries. It is hardly available from any of the participating countries.

This result did not come as a surprise and we have to consider other approaches. One possibility might have been to take advantage of NordDRG system and calculate DRG codes with assigned codes for all countries according to the Nordic system and cost weights from one or several of the Nordic countries. Registrations of diagnoses, procedures, length of stay etc at the individual patient level from all countries would then be fed into the NordDRG grouper in order to create the DRG codes. One problem with this approach is the variety of systems for coding of procedures across the EuroHOPE countries. In order to apply the NordDRG grouper procedures, data from all countries would have to be coded according to Nordic Classification, which might have been possible, but is considered to be too costly. However, costing according to the NordDRG system could be done as a sub-project based on data from the three participating Nordic countries.

After having considered various approaches we decided on two specific approaches that are supposed to supplement each other.

Approach I:

All countries have in their discharge registers and pharmaceutical prescription data bases registrations that indicate main components of use of resources. The registered components are mainly related to procedures and hospital length of stay. One can easily imagine that relative costs of the treatment components differ between patients. For instance, one patient may experience complications during surgery making the relative cost of surgery more expensive compared with another patient. This individual variation in relative costs cannot be accounted for within this approach. The relative cost of the different components of resource use is approximated by data from the cost per patient (KPP) data base (http://www.skl.se/vi_arbetar_med/statistik/sjukvard/kpp/databas) by Swedish Association of Local Authorities and Regions (SALAR). Cost in Swedish Kronor (SEK) is then converted to Euros by means of the input –based Purchasing Power Parity index for hospital services developed by Eurostat (2012). Hospital costs are calculated during first hospital episode and during 365 days after the index admission date. Then pharmaceutical cost during the first year after the index admission in national currency is added and converted to Euros by means of the Purchasing Power Parity index for GDP developed by Eurostat (2012).

This is a somewhat more precise exposition of the approach. There are two cost components: Hospital costs and Cost of medicines outside hospital.

x_{ijklt} =number of resource item *i* to patient j for disease k in country *l* in period *t*

p_{iklt} = cost in SEK from the Swedish Cost Per Patient data base attached to resource item *i* for disease k in country *l* in period *t*

m_{jklt} = cost in local currency of medicines to patient *j* for disease *k* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

m_{jlt} = total cost in local currency of medicines (irrespective of ATC code) to patient *j* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

c_{hlt} = adjustment of cost level of hospital services (h) in country *l* (Sweden) in period *t* by Eurostat PPP index for hospital services

c_{mlt} = adjustment of cost level of pharmaceuticals (m) in country *l* in period *t* Eurostat PPP index for GDP

The total cost of patient j with disease k in country *l* in period *t* with adjustment for differences in cost level is then:

$$C_{jklt} = c_{hlt}\left\{\sum_i p_{iklt} x_{ijklt}\right\} + c_{mlt} m_{jklt}$$

Approach II:

Approach II prescribes that each country contributes with their best cost estimate given their own system of cost calculations. For some hospitals, for instance in Sweden, it would then be possible to calculate a cost per patient. In Norway, the cost estimates generated by the DRG system is used and costs of medicines based on data from prescription register are added. In this approach we would have to check that identical treatment components are included from each country. In this approach the different currencies would have to be transformed to a common currency and adjustment for differences in cost levels between countries would have to be done. The chosen converter is the PPP for hospital services and the PPP for GDP developed by OECD and Eurostat and referred to above.

Some countries have more detailed data available than others. We aim at using the countries with most detailed data to run robustness analysis in order the check to what extent the choice of method has an impact on the results.

To illustrate the application of Approach I, we now describe the adoption of Approach I to acute myocardial infarction (AMI). More detailed descriptions are found in appendix C (AMI), appendix D (stroke) and appendix E (hip fracture).

Acute myocardial infarction (AMI)

Costs should be registered during two intervals: First episode after index admission and one year after index admission.

The following resource items are included:

A. Hospital costs: The following information according to each individual patient is registered:

A1. Total number of coronary by-pass surgery (CABG)

A2. Total number (regular, stent, drug eluting stent) of percutaneous coronary intervention (PCI)

A3. Total number of admissions related to AMI (ICD 10: I20-I25 and I44-I50)

A4. Total number of admissions for other diagnoses (also rehabilitation if possible)

A5. Total number of inpatient days related to AMI (ICD 10: I20-I25 and I44-I50)

A6. Total number of inpatient days for other diagnoses

A7. Total number of outpatient consultations irrespective of diagnosis

B. Cost of medicines outside hospitals

B1. Calculate from the prescription register the total sum of medicines (irrespective of ATC code) dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included

B2. Calculate from the prescription register the sum of medicines with an ATC related to AMI dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included. The relevant ATCs are described in Appendix C:

C. Assigning Hospital Costs

Unit cost is based on data from the Swedish cost per patient (KPP) data base provided by Swedish Association of Local Authorities and Regions (SALAR).

C1. Hospital cost components from the Swedish KKP data base (outliers are excluded) are calculated for procedures (CABG and PCI), basic ward cost per day for AMI patients, mean cost per day for all inpatient stays and for outpatient visits.

D. Adjust for cost level in Sweden using Eurostat PPP: http://epp.eurostat.ec.europa.eu/portal/page/portal/purchasing_power_parities/data/database. PPP for GDP are used for pharmaceuticals and PPP for hospital services (input-based) for procedures and ward related cost.

Cost estimation in EuroHOPE

Sections 2 – 4 have shown that estimation of treatment cost is a challenging task. The econometrics is challenging and many difficult trade-offs are involved. In addition, due to privacy concern, a pooled data set will not contain data from all countries in EuroHOPE. We also consider it as a virtue in itself that methods used should be transparent also for non-experts. EuroHOPE is oriented towards surveillance and policy-making. The project is likely to receive more impact among policy-makers if policy-makers are able to understand the intuition (not necessarily all technical details) of the used methods.

We start out with the approach from PERFECT (Peltola et al., 2011). Based on estimated coefficients from a pooled data set from some of the countries (Finland, Hungary, Norway, Sweden), predicted costs for each region and country will be compared with observed costs. As described in Section 4, differences in costs between regions and countries are then expressed as the ratio between observed costs and expected costs. Methodologically it is sound practice to embed and test a selected model in a more general framework, like generalised beta suggested by Jones et al. 2011 and/or the flexible link and variance functions of Basu (2005).

We plan to proceed with approaches that take the endogeneity of outcome (mortality) into account. The approach by Hvenegaard et al. (2010), as explained in Section 2.2, is an approach that will be further explored. Also the method with simultaneous cost and quality estimation in Häkkinen et al. (2012) will be further explored (see some explanation in Section 2.2). Models we actually end up with will depend on the experience that we gain during the work.

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Appendix A:

Censoring

To take censoring into account in the estimation of costs, one important assumption, is the requirement of independent censoring, i.e. independency between the censoring times and time of death and independency between cumulative costs at censoring and cumulative costs at death for survival and costs, respectively. It could be expected that time of death is independent of the time of censoring, but it is not clear whether this is the case for treatment costs, due to underlying latent classes of patients (as severity). Thus, some patients accrue costs at higher rates independent of whether they die or not, just because they tend to have higher costs in general. A consequence of this is that the cost at death and costs at censoring are correlated, but the practical problem is that we observe only one of the situations.

The problem with dependency could be illustrated by Table A1, where rows represent patients (i) and columns (j) represent time from diagnosis. A + sign indicate that the individual has survived until that time period and observed during the period. When estimating expected cumulative costs per patient, Etzioni et al. presented two different methods; firstly, by means of treatment costs for each period (column) or secondly, for each individual (row). Estimation based on columns is the sum of average treatment costs among the individuals alive at the beginning of a period (j) weighted by the probability of surviving to the period (j). Total expected costs, based on row is defined as sum over all periods of the average total treatment costs among individuals dying in period (j) weighted by the probability of dying in the same period (j). The two different methods are described by Equations (A1) and (A2). The expected cumulative treatment cost based on columns is given by:

$$\hat{C}_{cols} = \sum \bar{c}_j S_j \qquad \text{(A1)}$$

where $\bar{c}_j$ is average costs in period j among the individuals survived at the beginning of the period, based on Table 1, $\bar{c}_1 = C_1 / 5$, and S_j is the probability of survival until period j. The summation is over periods. The other approach is based on total costs observed for the individual and given by

$$\hat{C}_{rows} = \sum \bar{C}_i s_i \qquad \text{(A2)}$$

Where $\bar{C}_i$ is the mean total cost for individuals dying in period j, thus based on Table 1, $\bar{C}_2 = (C_2 + C_4)/2$, and s_i is the probability of dying in period j for individual *i*. The summation is over periods. The estimation of costs could only be based on the individuals who actually die within the observation period. Without censoring, (A1) is equal to two (A2).

Period *j*		1	2	3	4	5	Total row
	A	+	+	+			C_1
	B	+	+				C_2
Person (i)	C	+	+	+			C_3
	D	+	+				C_4
	E	+	+	+	+	+	C_5
Total column		c_1	c_2	c_3	c_4	c_5	

Table A1. Presentation of different hypothetical treatment spells according to time of diagnosis, based on Table 1 in Etzioni et al. (2002)

To account for potential violation of required assumption with regard to censoring, such as representativeness in equation (A2), an alternative approach was proposed by Etzioni et al. (1999) and Lin et al. (1997). Let time be restricted to τ. As Equation (A2) includes costs for those dying, individuals dying after the observation period, is excluded. In order to include and use the information from the individuals dying after time τ, an alternative approach that is more similar to Equation (A1), where the two approaches is combined and is given by

$$\hat{C}_{alt} = \sum_{i=1}^{I} \bar{C}_i s_i + \bar{c}_\tau S_\tau \qquad \text{(A3)}$$

where S_τ is the probability of surviving beyond time τ, and $\bar{c}_\tau$ is the average costs in period τ among individuals surviving beyond τ.

Empirical specifications

The choice of empirical specifications of survival and costs could either be non-parametric or parametric. The proposed specifications over the last years have varied between these two approaches. In this section we will discuss these two types of methods and discuss briefly which properties that are needed for the methods to be unbiased and efficient. The presentation will be done chronologically, starting with the methods presented at the end of the 1990's. As bases for the following discussion, two spells are illustrated in Figure 1 to show the different periods that are relevant with regard to estimating costs.

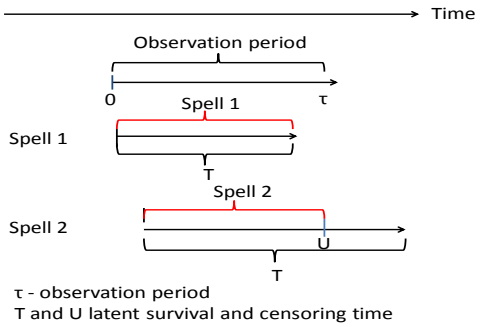

Figure A1: Different spells of treatment according to the observation period, censoring and death (using the notation in Lin et al. (1997).

Let us assume that X=min(T,U), were X is defined as the latest contact date observed. Further, let δ=I(T≤U) be an indicator function. We observe the set of (X, δ, $\tilde{C}$), were $\tilde{C}$ is the observed total costs. If δ=1 or X=T, then the observed costs are equal to the true costs ($\tilde{C} = C$). This is the case for Spell 1 in Figure A1. The individual dies within the observation period, thus T<U and we observe the last contact date, X. Thus from Spell 1 we are able to observe the true total costs. But, in Spell 2, δ=0 and X = U, thus this dataset is censored and we cannot conclude that the observed costs reflects the true total costs.

In the estimation of treatment costs, choosing methods that do not depend on the distribution of the costs should be considered, thus non-parametric approaches has been suggested and applied in several settings. As we are interested in expected accumulated costs, we need to adjust for individuals alive at each point of time (Etzioni et al. 2002). The two most known approaches are estimations based on Kaplan Meier Sample Average (KMSA) applied in Etzioni et al. 1996 and Lin et al. 1997, also named LIN97 in Basu and Manning (2009). This method has been applied in both Equation (A1) and (A3). The starting point is costs for individuals alive in a period and not censored at the beginning of the period. Survival is estimated by means of Kaplan Meier.

The KMSA estimator

In the presence of no censoring, the estimation of average treatment costs, C_{NoCens}, are given by

$$C_{NoCens} = \bar{c}(1) + \frac{n_2 \bar{c}(2)}{n_1} + \frac{n_3 \bar{c}(3)}{n_1} + ... \qquad \text{(A4)}$$

where $\bar{c}(j)$ and $\frac{n_j}{n_1}$ represent average treatment costs in time period *j* (among those alive in that period) and the proportion alive at the beginning of time period *j,* respectively. If censoring is present, this is account for in the Kaplan-Meier estimator S_t given by

$$\hat{S}_t = \prod_{j:t_j \le t} \frac{n_j - d_j}{n_j} \qquad \text{(A5)}$$

where d_j is the number of individuals dying during time period *j*. If 100 individual was eligible at the beginning of period 1, five died during the first period and 15 was lost to follow-up, then n_1 and n_2 will be 100 and 80, respectively. By substituting (5) with $\frac{n_j}{n_1}$ in (4), we are able to estimate expected costs by means of the Kaplan-Meier sample average (KMSA), similar to Equation (A1) and given by Lin et al. (1997)

$$E = \sum_{j=1}^{J} S_j E_j \qquad \text{(A6)}$$

where S_j is defined by (5) and E_j is estimated by

$$E_j = \frac{\sum_{i=1}^{n} Y_{ji} \tilde{C}_i}{\sum_{i=1}^{n} Y_{ji}} \qquad \text{(A7)}$$

where Y_{ji} is an indicator given the values 0 if observed average costs ($\tilde{C}_i$) are missing observed in period j and 1 otherwise.

Estimation of expected costs based on (6) is an unbiased estimate (indicating the observed average costs equals the true costs, $\tilde{C}_i = C_i$) when all individuals are censored at the end or the very beginning of each observed period. As the starting point of this estimation is individuals alive at the beginning of the period, the cost of individuals censored during time period j, is included in the estimation of costs. Further, as time of censoring during period j is not taken into account in the estimation (as time is discrete), average costs could be downward bias. The bias will most likely increase with the length of the time periods and the degree of censoring. In Lin et al. (1997) it is suggested prorating the costs of the censored could reduce the bias given heavy censoring. Another important factor is the independency between censoring time and survival and/or costs. The first relates to the fact that individuals who are censored are of different risk of death, while the latter relates to that censored individuals accumulate higher or lower costs than uncensored individuals.

In Lin et al. (1997) it is also suggested that estimating total costs could be based on Equation (A2), i.e. of total costs. In this estimation, the cost history is not relevant and costs are estimated only among the individuals dying during the given time period (j).

$$E = \sum_{j=1}^{J+1} A_j (S_j - S_{j+1}) \qquad \text{(A8)}$$

where S_j is survival in time period *j* (hence, $S_j - S_{j+1}$ is the probability of dying within time period *j*) and $A_j = \varepsilon(C \mid a_j \leq T < a_{j+1})$ is the expected costs given that that the individual dies within the time period $[a_j, a_{j+1})$. Given the independent assumption, the expected costs among individuals censored are assumed

to be the same as the expected costs for those dying. Assuming censoring at the end of the period, j, A_j could be estimated consistently, by

$$A_j = \frac{\sum_{i=1}^{n} Y_{ji}\tilde{C}_i}{\sum_{i=1}^{n} Y_{ji}} \qquad \text{(A9)}$$

where Y_{ji} is an indicator for whether or not the individual is dying during the period. If all individuals are censored at the end of the period, then Y_{ji} =1 and *E* an unbiased estimate of the costs, i.e. $\tilde{C}_i = C_i$. If censoring takes place at the start of the interval, then given $X_i \geq a_k$, the $T_i's$ (latent survival) have the same probability of being censored during the interval. Given these assumptions, the individuals observed to die in the interval are a random sample of all the deaths, and Equation (8) is a consistent estimate. If censoring is spread out in the interval, then estimated costs in Equation (9) tends to be driven by the individual dying early, because given the same distribution of censoring, larger survival times are more likely to be censored. It is suggested that splitting the total observation period into small intervals will reduce the bias.

Inverse probability weighting (IPW)

An alternative non-parametric method, quite similar to the one above, is the one presented by Bang and Tsiatis (2000). If L is the restricted survival time, Horvitz-Thompson-type method could be applied (Horvitz 1952) to reweight complete cases. If the survivor function of the censoring time is given by $S_U(t) = \Pr(U > t)$, i.e. the probability of being censored in time period *j*, given that you were in the sample at the end of the interval. In such a situation, censoring is taken care of by weighting each uncensored individual with S_U^{-1}, where $T = X$ for an uncensored individual. A subscript *i=1,2,….n* is added to each random variable for individual *i.* Derived from the above argument, a weighted estimator could be applied (Bang and Tsiatis, 2000) often referred to the IPW estimator (inverse probability weighting):

$$\mu_{IPW} = n^{-1}\sum_{i=1}^{n} \frac{\delta_i \tilde{C}_i}{\hat{S}_U} \qquad \text{(A10)}$$

where $\hat{S}_U$ could be estimated by means of Kaplan-Meier within the restricted time period U. The Biang and Tsiatis (2000) estimator is always consistent as it only includes individuals dying within each period. The estimation of Equation (10) is closely related to Equation (A8) above. Splitting of the restricted time [0,U] in small intervals, making Horvitz-Thompson like estimators within each interval before summing over all intervals, similar to Equation (A6). Biang and Tsiatis (2000) also proposed a partitioned estimator based on Equation (A3), that is comparable with the method given by Equation (A3). For a further discussion, see O'Hagen and Stevens (2004).

Cox - regression

The estimation of the equations by Lin et al. (1997) and Bang and Tsiatsi (2000), may not fulfil the assumption of independent censoring in time and representativeness of the estimated mean treatment costs. If the cost structure of those censored is different from those dying, the costs would not be representative and biased. The total costs, may depend on individual characteristics, such as severity, co-morbidity, age etc that are correlated with survival and censoring. As stated in Lin (2000) the problem is related to the fact that

"*Because a patient who accumulates costs over time at relatively higher rates tend to generate larger cumulative costs at both the survival time and censoring time, the cumulative costs at the survival time (the lifetime cost) are positively correlated with the cumulative cost at the censoring time (i.e., the censoring variable for the lifetime cost) even if the underlying survival time and censoring time is independent. (Lin 2000, p 775)*

To adjust for this, Lin (2000) presented a model, called the proportional means regression. Let $C(t)$ be the cumulative treatment costs up to time X. As costs cannot occur after death, thus $C(.)$ are not affected after time T, where T defines the survival time. Further, let Z be a set of covariates that are relevant for the study. Mean cumulative treatment costs are defined by $\mu(t \mid Z) = E(C(t) \mid Z)$ and specified by the proportional means model given by

$$\mu(t \mid Z) = \mu_0(t) e^{\beta' Z} \qquad \text{(A11)}$$

Where μ_0 is an arbitrary baseline mean function and β is a vector of regression parameters that are to be estimated. In this model there is no link between T and C*. The estimation is done by a Cox proportional hazard model. With censoring, C* may not be fully observed, which needs to be adjusted for. Assuming that the samples consists of n independent triplets C_i, U_i, Z_i (i= 1,2, ...n), then the coefficients could be estimated by means of

$$H^*(\beta) = \sum_{i=1}^{n} \int_0^{\infty} Z_i - \bar{Z}(\beta, t) \; dM_i(t) \qquad \text{(A12)}$$

where $M_i(t) = \int_0^t I(U_i \geq s) \; dC_i(s) - e^{\beta' Z} \, d\mu_0(s)$ are zero-mean stochastic processes. Very often we do not observe the information needed, thus adjustments need to be carried out. Details on this could be found in Lin (2000a).

In Lin (2000b) accumulated costs are estimated by means of a linear regression model, censoring are adjusted for by weighting the costs inversely with the probabilities of being included, i.e. similar to the IPW presented by Bang and Tsiatis (2000). But contrary to Bang and Tsiatis (2000), the survival probabilities are estimated by means of a Cox regression that is used to adjust for the fact that covariates could affect the probability of being censored. The model in Lin (2000b) are defined by

$$\sum_{i=1}^{n} \frac{\delta_i^*}{\hat{S}(T_i^*)} (Y_i - \beta' Z_i) Z_i = 0 \qquad \text{(A13)}$$

where $\hat{S}(T_i^*)$ is estimated by means of a Cox regression, and δ is an indicator function.

A difference between the two different approaches by Lin (2000a and b) is that the covariate effect is modelled as a multiplicative versus and additive effect. Further, a general criticism for theses models are the assumptions relating the use of Cox regressions. In a Cox regression it is assumed that there is non-proportionality in the costs accumulation, and violations from this assumption occurs when the risk of observing costs greater than any given value does not increase linearly with covariates' value, Etzione et al. (1999).

Another model was presented by Bang and Tsiatis (2002) where they used quantile regression to estimated expected costs. In this model Kaplan-Meier was used to estimate survival.

Jain and Strawderman (2002) presented an alternative method, a flexible hazard regression model. In this model Cox regression is used combined with the inverse probability weighting (IPW) method first presented by Bang and Tsiatis (2000). In this method complete observed individuals are upweighted, but cost information from the individuals censored is also included. In addition, the way of modelling avoids restrictive assumptions about the relationship between costs, survival and covariates. The method is not so useful for marginal analysis and to illustrate conditional distribution of costs given covariates (C|Z).

In O'Hagen and Stevens (2004) there is a review of the different methods at that time. They presented some recommendations that could support choices of methods.

Naive estimations of average costs can lead to serious biases in the presence of censoring. The method of Lin (1997) and B&T (2000) presented here are demonstrably better and are simple to use.

When only total costs are available on each patient, the B&T complete case estimator is recommended. We have shown its equivalence to a limiting form of Lin's second estimator.

More efficiency can be obtained from having more information on accrual, and we recommend the cost per patient in each of a number of time periods should always be recorded in trials with censoring. If enough time periods are used, then the relative loss of information from the B&T partitioned estimator will be small and this estimator is then recommended for its consistency. If the loss of information is small, Lins's (1997) estimator in EQ (A1) may be preferred because it uses more information.

Other non-parametric estimators may be more efficient, but have been little used in practice. It is not clear in general that their gains outweigh the extra complexity of using them. However, where covariate adjustment is needed, the methods of Lin (2000a and 2000b) and Jain and Strawderman (2002) should be considered.

Parametric modelling has the potential to address the skewness in the cost data and to extract more information from censored data by modelling cost accrual. Parametric modelling of survivor function would also permit for extrapolation of conclusions beyond the length of the trial. We are not aware of any general work of this kind in the literature, but suggest that this is an important direction for research.

O'Hagen and Stevens (2004), pp 623

The additive approach

The motivation for the paper by Pagano et al. (2008) and Gregori et al. (2011) is that the Cox model has some strong assumptions, such as the non-proportionality of the accumulation of costs in presence of censoring (has also been shown to occur in a non-censoring framework). Further, attempts to model medical costs by means of parametric models have been several, but none of these have applied a functional form with additivity of covariates effects on the accumulation of costs. Such a model is presented by Pagano et al. (2008), who base their model on the Aalen model (Aalen, 1989 and 1993). In the Aalen model, observed costs, $\tilde{C}_i$, are observed for each individual (*i = 1, 2, ……k)* and depend on *h* explanatory variables, Z_j (*j = 1,2,.....h).* The hazard function, i.e. the conditional probability of stopping the accumulation of costs, given that a certain cumulative cost has been reached is given by

$$\lambda(c_i \mid Z_h) = \lambda_0 + \sum_{j=1}^{h} \alpha_j(c) Z_j(c) \qquad \text{(A14)}$$

and is a linear combination of the baseline hazard, λ_0 and the explanatory variables $Z_j(c)$ and $\alpha_j(c)$, that results in *h* functions based on Equation (14). The aim of the estimation is for given levels of c to find the cumulative regression coefficient, defined by

$$A(c) = \int_0^c \alpha(s) ds \qquad \text{(A15)}$$

The slope of the *h* cumulative regression functions indicates the weight of each covariate on the hazard function. When plotted for a specific level on costs, $\hat{A}_j(c)$, the confidence bands (asymptotic normal distribution) indicate if a covariate has a significant effect of costs, significant when not crossing the cost-axis (the coefficient is a straight line close to zero). When comparing this model with other parametric models (lognormal and gamma), the results based on simulations shows that the gamma distribution and the Aalen model have good results. With a high degree of censoring, the Aalen approach tends to give slightly better results.

Basu and Manning (2009)

The next step in the development of the estimation of lifetime costs or treatment costs, Basu and Manning (2009), claims that no other papers have distinguished between the effect of covariates on survival and intensity of utilization, which jointly determine costs. This method is compared with prior proposed models (Bang and Tsiatsi, 2000). Basu and Manning (2009) points that the models presented in Lin (1997) and Bang and Tsiatsi (2000) are suited to analyse differential in the covariates impact on costs due to survival versus those due to changes in intensity of utilization. Under continuous time of death and censoring, the estimator presented by Lin (1997) is biased, but by dividing the period in small intervals, the bias is reduced. Bang and Tsiatsi (2009) extend the approach by Lin (1997) by allowing for continuous distribution of survival time and censoring. Based on the estimator it is also possible to distinguish between the covariates effect on survival and how they affect the rates of cost accumulation conditioned on being alive. As rates are important in the estimator, they are able to evaluate end of life treatment, that often are very intensive. The contribution in the paper is summed up by – 1) *Use of non-linear two-part models*

appropriate for modeling skewed outcomes in the presence of censoring; 2) Variable rates of accumulation of costs over time; 3) Spikes in cost-accumulation due to end-of-life care; and 4)estimator consistency in the presence of heavy censoring and covariates affecting survival conditions under which properties of inverse probability weighting (IPW) approaches are not clearly established. (Basu and Manning, 2009, pp1011)

The estimation in Basu and Manning are carried out in several steps to ensure that the estimator could allow for continuous death and censoring times and in addition include individual characteristics to influence the accumulation of costs. Let U be the duration within an interval. The different steps are as follows:

a) Estimation of survival ($\hat{S}_j(X)$ and hazard, $\hat{h}_j(X)$)by means of a flexible survival model (for instance generalized gamma distribution).

b) In the next step, individuals observed to die within the interval, costs are estimated by means of a generalized linear model to account for individual characteristics and the distribution of deaths within the interval, U. In the estimation of costs the prediction of the distribution on U is accounted for by weighting the costs by the predicted distribution of U, given by $\hat{\mu}_{1j}(X) = \int \hat{\mu}_{1j}(X) dF(U \mid a_b < V^{obs} \leq a_{b+1})$

c) In the third step, the costs among individuals not dying and not censored within a specific interval are estimated by means of a generalized linear model. Based on this model, it is possible to predict costs, $\hat{\mu}_{2j}(X)$, for all intervals.

d) Based on the three first steps, the estimated cost function for interval *j* for any individual is given as

$$\hat{\mu}_j(X) = \hat{S}_j(X)[\hat{h}_j(X)\mu_{1j}(X) + (1-\hat{h}_j(X))\mu_{2j}(X)] \quad \text{and} \quad \hat{\mu}(X) = \sum_{i=1}^{K} \hat{\mu}_j(X) \qquad \text{(A16)}$$

where $\mu_{1j}(X)$ is the expected costs for the individuals dying within the interval j, while $\mu_{2j}(X)$ is the expected costs for those alive in the observation period, but not censored.

Appendix B: Costing information summary

	Finland	Hungary	Italy	Netherlands	Norway	Scotland	Sweden
1: Is DRG information available from register data and included in the EuroHOPE data files?	Yes	Yes	Yes. Now regions have different DRGs systems and these differences exist also across selected pathologies.	DRGtype system, the DTC-system (DTC = Diagnosis Treatment Combination). Also voluntary *National Medical Register* (NMR)	Yes	In Scotland the National Tariff Project uses HRGs as a method of grouping/classifying hospital discharges into iso-resource groups.	Yes
2: Are outpatient consultations and procedures included in the DRG system?	Yes	No	No. The system only pertains to ordinary admissions, day-hospital and day-surgery.	DTC register for 2008 and 2009 (see above)	Yes, from 2010	No	Yes
2b: If outpatient consultations and procedures are not included in the DRG system: Is there another classification system available?		Yes. It is called "german point" system. It is basically a fee-for-service type financing scheme	Yes - specific classification of outpatients services used for funding providers. Tariffs for the same service may vary from region to region.		Before 2010 specific codes for various outpatient fees		
3: What is the method for the revision of cost elements reimbursed in DRG ystem?	Reference provided	Committee - decisions not transparent	Revision of tariffs is very unsystematic. The national system is rarely revised.		DRG-weights are annually updated based on detailed cost information	Please see National Tariff Project http: //www. isdscotland .org/isd/ 3552.html	_

	Finland	Hungary	Italy	Netherlands	Norway	Scotland	Sweden
4: Is there a description of the DRG-system (or similar patient classification system) for your country in English language. If yes, please provide reference(s).	Reference provided	In the HEALTHBASKET PROJECT: Reference provided	No	There is no official document, but information can be found in the HiT-report	Not very detailed – link provided	http://www.isdscotland.org/isd/3552.html	N0
5: Is length-of-stay (LOS) information explicitly reported for each inpatient stay and will it be included in the EuroHOPE data files?	Yes	Yes	Yes	Available in NMR	Yes	Yes	Yes
6: What is the coding system used for surgical operations and procedures?	A Finnish version of the NCSP (Nordic Classification of the Surgical Procedures).	Much like the outpatient coding system. Originally based on icpm	ICD-9-CM	Dutch classification System of procedures (CvV) related to ICPM.	NCMP Link provided	ICD10 and OPCS4 http://www.isdscotland.org/isd/4363.html?text-size=3	"Klassifikation av vårdåtgärder", where NCSP is included. Please find link below: http://www.socialstyrelsen.se/klassificeringochkoder/atgardskoder/kva

	Finland	Hungary	Italy	Netherlands	Norway	Scotland	Sweden
7: Are there approximations to costs of the various procedures (for instance fees)? If yes, describe briefly: Laboratory tests and analyses:	Finnish Unit Prices in Health Care in 2006 [accessible at http://www.stakes.fi/verkkojulkaisut/tyopaperit/T3-2008-VERKKO.pdf, unit prices for many laboratory activities and radiology.	Yes. For those procedures also in the outpatient procedure list (mostly lab tests and other diagnostic procedures),	Uunpublished sources that can be used to estimate costs of specific procedures. Typically, from a limited no. of organizations.	We can use the tariffs set by the Dutch government to get an indication of costs of procedures.	There is a system of fees used for reimbursement purposes to hospitals. Fees are very crude approximations to costs	total costs/budget attributed to a department.	Pricelists order to identify specific costs for specific tests and investigations. There are no average estimations.
Radiology:							
Surgery:							
8: Is there available information about average salary level for hospital personnel groups according to profession and position?	At national level we can acquire information on salaries. data is owned by the Statistics Finland	Table provided	Provides national data from 2009. Aailable from 2001.	Not directly available – can be calculated	Yes, Link provided – also table	NHS workforce in Scotland http://www.isdscotland.org/isd/6127.html	Yes, information is provided with links to more details
9: Is there a cost per patient system in at least one hospital in the country? Describe in some detail	In some hospitals / hospital districts there are some hospitals' cost data on individual level. Iin the Helsinki region access individual patient level cost data.	Does not know about any	One or two private providers have accounting system that allow to cost each patient (mainly based on an ABC)	No	Development projects – should be availble for at least one hospital.	No	Kostnad per patient (KPP) 2010 it included ~65% of all somatic inpatient care and 49% of all somatic outpatients. Link provided

	Finland	Hungary	Italy	Netherlands	Norway	Scotland	Sweden
10: Explain briefly the funding system for hospital teaching and research activities? In particular, is teaching and research compensated in the DRG-system or is it funded separately?	Teaching and research is not compensated in the DRG system, they are funded separately by the Ministry of Social Affairs and Health. The Ministry of Social Affairs and Health sets the total annual budget for teaching and research and the total budget is divided into teaching and research budgets. These budgets are allocated to hospitals according to their teaching and research outputs.	Teaching is funded separately as educational costs. University hospitals get the same drg financing as any other hospital	Research and teaching are not funded through DRGs although there are cases where the DRG may be slightly higher if the provider is a teaching/research institution.	Hospital teaching and research activities are separately funded.	Some research financed from general budgets, som directly from Ministry of Health	Separate funding for hospital teaching and research activities.	Teaching is funded within the DRG system, research is not.
11: How is the cost of capital resources defined and measured within accounting systems? In particular, is the user cost of capital accounted for in the weights of the DRG-system?	Capital costs are included in the national DRG weights. In hospitals where they have cost per patient, they have similar accounting methods as in any enterprise and capital cost items are handled accordingly	Owners of medical insitutions cover capital costs. Aaccounting depends on the operating form (public institute, ltd, non-profit company, etc)	For NHS-owned hospitals DRGs do not cover capital costs. Buildings (e.g. a new hospital) are generally funded with ad hoc grants	Since 2006, the cost of capital has been taken into account in the DTC-tariffs	Similar to private firms. The user cost of capital is not accounted for in the weights of the DRG-system	The user cost of capital is not included in the National Tariffs.	No, cost of capital is not included in the DRG weights, which are derived from the KPP system.

AMI

	Finland		Hungary		Italy		Netherlands		Norway		Scotland		Sweden	
1: The most important diagnostic procedures	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**
	Cardiac ultrasound (echocardiography)	Yes, poor coding	Chest pain	No	ECG all	No	Coronary angiography	Yes	EKG	No	ECG	No		
	EKG (electrocardiography)	Yes, poor coding	ECG	Yes	Markers (Troponin T or I and CK-MB) all	No	ECG	Yes	Troponin tests	No	Coronary arteriography	Yes		
	troponin tests	No	Labtest (Troponin, CKMB)	Yes	Coronorary Angiography	Yes	Troponin	Yes	Clinical evaluation	No	Echocardiograph	No		
			Echocardiography	Yes	Echocardiogram	No	other cardiac enzymes	Yes			Blood tests - Troponin	No?		
			Coronarography	Yes							ECG	No		
3: Main types of treatments for the disease?	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**
	Thrombo-lysis	Yes, poor coding	(PCI (~70%)	Yes	PCI (angiography with BMS or DES)	Yes	PCI	Yes	Medication	Yes	Angioplasty	Yes		
	PCI	Yes	Thrombolysis (~2-3%)	Yes	Thrombolysis	No	fibrinolytic therapy	Yes	PCI	Yes	Thrombolysis	NO		
	CABG	Yes	Ventilation (~7%)	Yes	with other medical therapies	No	CABG	Yes	ACB (aorto coronar bypass operation)	Yes	Medical treatment for second. prevention	No		
			Intraaortic ballon pump (~10%)	Yes			medication	Yes						
			Coronary Care Unit observation (~ 2days)	No										
			Optimal Medical Therapy)	Yes?										

Breast cancer

	Finland		Hungary		Italy		Netherlands		Norway		Scotland		Sweden	
1: The most important diagnostic procedures	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**
	Mammography	Yes, coding is poor.	Mammography + breast and axilla Ultrasound	Yes			Mammography, Echo, needle biopsy and pathology (cytology/histology), excision biopsy, sometimes MRI, HER2r determination, microarray	The data files do not include out-patient records. Data only for admitted patients	Clinical examination Mammogram, ultrasound and sometimes MR of mamma FNAC (Fine Needle Aspiration Cytology) or cylinderbiopsi	Not complete	Clinical examination	?		
	Ultrasound	Yes, coding is poor.	Chest+ abdomen CT,bone scintigraphy	yes							Mammography	Yes		
	Thick(Or fine) needle biopsy	Yes, coding is poor.	PET/CT	yes							Ultrasound of breast and axilla	Yes		
	MRI	Yes, coding is poor.	Histology type, Eostrogen, Progesteron, Her-2 receptor status	yes							Histology	Yes		
			Tumor marker: Ca 15-3: elevated or normal	yes										

	Finland		Hungary		Italy		Netherlands		Norway		Scotland		Sweden	
3: What are the main types of treatments for the disease?	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**
	Surgery	Yes.	Surgery	Yes			Surgery (breast-saving, or mastectomy), radiotherapy, chemotherapy	Yes	Surgery – w/ and wo/ breast conserving	Yes	Surgery	Yes		
	Radiation treatment	Yes	Chemotherapy	Yes					Chemotherapy	Yes	Systemic therapy – hormonal or cytotoxic therapy	Yes		
	Chemotherapy	Not reliably	Targeted therapy	Yes					Radiation	No	Radiation	Yes		
	Hormonal treatment (drugs)	Yes, if prescribed drugs.	Radiotherapy	Yes					Hormon therapy	Some				
			Palliation	No										

Hip fracture

	Finland		Hungary		Italy		Netherlands		Norway		Scotland		Sweden	
1: The most important diagnostic procedures	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**
	X-ray of the pelvis and hip	Yes, with poor coding	Anteroposterior view and lateral view X-ray about hip joint	Yes	Phisical examination	yes	X-ray, pre-operative "work-up" (lung function, coagulation, etc)	Yes, whether or not performed	(Clinical examination)		Hip X-ray	No	X-rays preop, postop and at follow-up	No
	Computed tomography in uncertain cases	Yes, with poor coding			Hip standard roentgenograms	yes			X rays golden standard		Occasionally MR imaging	No	MRI/CT (if unclear if the patient has a fracture or not)	No
									CT-scan (rare) MRI (rare)				Blood test , preop, postop (eg Hb)	No

	Finland		Hungary		Italy		Netherlands		Norway		Scotland		Sweden	
3: Main types of treatments	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**
	Femoral neck fractures: Hemiprothesis or cannulated screws	Yes, based on procedure codes.	Surgical intervention, osteosynthesis or hip replacement (prothese)	Yes	Trochanteric fracture (820.2):	yes	Surgery: different types of operations, depending on specific characteristics of fracture; Early rehabilitation and physiotherapy	yes	Neck fractures: Hemiarthroplasty		Surgical treatment	yes	Surgical procedure: open reduction and internal fixation (screws, plates etc) or prosthesis – depending on the fracture type and the patient	Yes
	Pertrochanteric fractures: Sliding hip plate or intrameddullary nail	Yes, based on procedure codes.			Neck fracture (820.0):	yes			Neck fractures: Internal fixation with parallel screws		Conservative treatment		Rehabilitation, physiotherapy, waking aids	No
	Subtrochanteric fractures: intramedullary nailing	Yes, based on procedure codes.							Trochanteric fractures: Sliding hip screw plate				Pain medication	Yes
									Trochanteric fractures: Nail				Examination regarding osteoporosis and	No
													Medication if osteoporosis is apparent	Yes

Stroke

	Finland		Hungary		Italy		Netherlands		Scotland		Sweden	
1: The most important diagnostic procedures	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**	**Name**	**Avail-able**
	Head computer tomography (CT)	Yes, coding is poor.	clinical examination including history	No	Head CT/MRI	Y	CT scan, MRI. Secondary: ultrasound, MRA, CTA	Yes	CT brain	Yes		
	Head magnetic resonance imaging (MRI)	Yes, coding is poor	neurimaging (CT or MRI)	Yes	Head CT-angiography/MR-angiography/DSA	Y	CT scan, MRI. Secondary: ultrasound, MRA, CTA	Yes	MRI Brain	Yes		
	CT angio (CTA)	Yes, coding is poor			Carotid Doppler	N			Carotid Duplex ultrasound	No		
	MR angio (MRA)	Yes, coding is poor			ECG	N			MR angiography	No		
	Conventional digital subtraction angiography (DSA)	Yes, coding is poor			Echocardiography	N			Echocardiography	No		
	Carotid ultrasound	Yes, coding is poor										

	Finland		Hungary		Italy		Netherlands		Scotland		Sweden	
3: main types of treatments for the disease?	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**	**Name**	**Avail**
	Thrombolytic therapy (tPA): alteplase for acute ischemic stroke within 4.5 hours of stroke onset.	Yes, coding is poor	Treatment on stroke unit	No	Thrombolytic therapy	Y	Thrombolysis,	yes	Stroke unit care	Yes		
	Stroke unit care: specialized multidisciplinary care within a ward or unit dedicated to stroke patients	Yes, classification of the hospitals.	Thrombolysis in the time window	Yes	Other medical therapies	N	treatment in stroke unit,	yes	Thrombolysis	Yes		
	Medical secondary prevention for ischemic stroke: antihrombotic medications, antihypertensives, and statins	Yes, if prescribed drugs or entitle to special reimbursement.	ASA for those who can not have thrombolysis	No	Mechanical thrombectomy	Y	anti-platelet agents, anti-hypertensive drugs, statins,	yes	Aspirin	Yes		
	Surgical secondary prevention for ischemic stroke: carotid endarterectomy or stenting	Yes, coding is poor	Craniectomy for malignant MCA syndrome (48h, 60y)	Yes	Carotid endarterectomy Carotid stenting	Y Y	sometimes carotid artery surgery	yes	Anticoagulation	Yes		
					ICH evacuation Aneurysm coiling Aneurysm clipping Hemicraniectomy Tracheostomy	Y Y Y Y Y			Carotid surgery	Yes		

Appendix C: Costing approach I: AMI

There are two cost components: Hospital costs and Cost of medicines outside hospital.

x_{ijklt} =number of resource item *i* to patient j for disease k in country *l* in period *t*

p_{iklt} = cost attached to resource item *i* for disease k in country *l* in period *t*

m_{jklt} = cost of medicines to patient *j* for disease *k* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

m_{jlt} = total cost of medicines (irrespective of ATC code) to patient *j* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

c_{hlt} = adjustment of cost level of hospital services (h) in country *l* in period *t*

c_{mlt} = adjustment of cost level of pharmaceuticals (m) in country *l* in period *t*

The total cost of patient j with disease k in country *l* in period *t* with adjustment for differences in cost level is then:

$$C_{jklt} = c_{hlt}\left\{\sum_i p_{iklt}x_{ijklt}\right\} + c_{mlt}m_{jklt}$$

Application to AMI

Costs should be registered during two intervals: First episode after index admission and one year after index admission.

The following resource items are included:

A. Hospital costs: Register the following information according to each individual patient:

A1. Total number of coronary by-pass surgery (CABG)

A2. Total number (regular, stent, drug eluting stent) of percutaneous coronary intervention (PCI)

A3. Total number of admissions related to AMI (ICD 10: I20-I25 and I44-I50)

A4. Total number of admissions for other diagnoses (also rehabilitation if possible)

A5. Total number of inpatient days related to AMI (ICD 10: I20-I25 and I44-I50)

A6. Total number of inpatient days for other diagnoses

A7. Total number of outpatient consultations irrespective of diagnosis

B. Cost of medicines outside hospitals

B1. Calculate from the prescription register the total sum of medicines (irrespective of ATC code) dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included

B2. Calculate from the prescription register the sum of medicines with an ATC related to AMI dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included. The following ATCs should be included:

- Antithrombotic agents: B01AC04, B01AC05, B01AC06, B01AC07, B01AC14, B01AC30
- Digoxin: C01AA05
- Proscillaridin: C01AB01
- Anti-arrhythmic drugs: C01BA01, C01BA03, C01BB02, C01BC03, C01BC04, C01BD01
- Nitrates: C01CA01, C01CA24, C01DA02, C01DA08, C01DA14, C01DA70
- Antihypertensives: C02AB01, C02AC01, C02AC05, C02CA01, C02DC01, C02LA01
- Diuretics: C03AA03, C03BA08, C03BA11, C03CA01, C03CA02, C03DA01, C03DB01, C03DB02, C03EA01, C03EA02, C03EB01
- Beta-blockers: C07AA01, C07AA02, C07AA03, C07AA05, C07AA06, C07AA07, C07AB02, C07AB03, C07AB04, C07AB05, C07AB07, C07AB08, C07AB52, C07AG01, C07AG02, C07BB02, C07BB07, C07AG02, C07BB02, C07BB07, C07FB02, C07FB03
- Calcium channel blockers: C08CA01, C08CA02, C08CA03, C08CA05, C08CA06, C08CA07, C08CA10, C08CA13, C08CX01, C08DA01, C08DB01
- ACE inhibitors: C09AA01, C09AA02, C09AA03, C09AA04, C09AA05, C09AA06, C09AA08, C09AA16, C09BA02, C09BA03, C09BA04, C09BA05, C09BA06, C09BB05, C09BB10
- AII inhibitors: C09CA01, C09CA02, C09CA03, C09CA06, C09CA07, C09DA01, C09DA03, C09DA06, C09CA

Assigning Hospital Costs

Several approaches are considered. Here I use data from the Swedish cost per patient (KPP) data base provided by Swedish Association of Local Authorities and Regions (SALAR).

1. Calculate Swedish hospital cost components from KKP data base – outliers are excluded
2. Adjust for cost level in Sweden using Eurostat PPP: http://epp.eurostat.ec.europa.eu/portal/page/portal/purchasing_power_parities/data/database

   Two alternatives are used: PPP for GDP and PPP for hospital services (input-based). Figures in the two last columns in the table below then come up.

Service	Year	Cost SEK	PPP GDP	PPP hospital services	COST € PPP GDP	COST € PPP hospital services
CABG	2006	106948	10.5809	9.99232	10108	10703
PCI	2006	45356	10.5809	9.99232	4287	4539
Cost per hospital day AMI (KPP DRG 121 + 122)	2006	5852	10.5809	9.99232	553	586
Cost per hospital day general	2006	8851	10.5809	9.99232	837	886
Cost per outpatient visit	2006		10.5809	9.99232		
CABG	2007	92954	10.3928	10.03235	8944	9265
PCI	2007	42870	10.3928	10.03235	4125	4273
Cost per hospital day AMI (KPP DRG 121 + 122)	2007	6350	10.3928	10.03235	611	633
Cost per hospital day general	2007	9061	10.3928	10.03235	872	903
Cost per outpatient visit	2007		10.3928	10.03235		
CABG	2008	101709	10.7058	9.98883	9500	10182
PCI	2008	46414	10.7058	9.98883	4335	4647
Cost per hospital day AMI (KPP DRG 121 + 122)	2008	6275	10.7058	9.98883	586	628
Cost per hospital day general	2008	9257	10.7058	9.98883	865	927
Cost per outpatient visit	2008		10.7058	9.98883		
CABG	2009	103144	11.2258	10.02061	9188	10293
PCI	2009	43452	11.2258	10.02061	3871	4336
Cost per hospital day AMI (KPP DRG 121 + 122)	2009	6777	11.2258	10.02061	604	676
Cost per hospital day general	2009	9642	11.2258	10.02061	859	962
Cost per outpatient visit	2009	2372	11.2258	10.02061	211	237
CABG	2010	107967	11.1165	10.1657	9712	10621
PCI	2010	37006	11.1165	10.1657	3329	3640
Cost per hospital day AMI (KPP DRG 121 + 122)	2010	6703	11.1165	10.1657	603	659
Cost per hospital day general	2010	9753	11.1165	10.1657	877	959
Cost per outpatient visit	2010	2386	11.1165	10.1657	215	235

These figures give us the treatment cost as it occurs on average in Sweden adjusted to the average cost level of hospital services in EU-15.

There have also been done (by Mikko) some analyses on Finnish cost per patient data from Helsinki and Uusimaa -region, years 2002-2010. It seems that cost estimates do not differ a lot from the Swedish data. In the OLS analysis without constant term and LOS, CABG and PCI as independent variables these estimated parameters came out:

	Estimated cost € 2002-2010	Appr PPP GDP 2002-2010	Estimated cost EU-15 cost level
LOS	566.7	1.10	515
cabg	10199.7	1.10	9273
pci	4216.8	1.10	3834

Absolute figures come out somewhat lower in Finland than in Sweden. One reason for that can be that outliers are identified and dropped based on the cost of discharge with a bilateral trim of ±3 standard deviations from the mean in the Finnish data.

Assigning Pharmaceutical Costs

Cost in national currencies are adjusted for differences in cost level using Eurostat PPP GDP

GEO/TIME	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
European Union (15 countries)	1	1	1	1	1	1	1	1	1	1
Italy (Normalized to EU-15 = 1)	0.93811	0.95426	0.97708	0.98079	0.97099	0.95559	0.96262	0.98249	0.99118	0.97381
Hungary (Normalized to EU-15 = 1)	127.475	134.691	141.398	145.53	149.654	153.616	157.939	159.175	160.425	161.118
Netherlands (Normalized to EU-15 = 1)	1.00083	1.03595	1.0177	1.01418	1.01124	1.00293	1.02787	1.0555	1.03488	1.03819
Finland (Normalized to EU-15 = 1)	1.11325	1.12937	1.09181	1.10594	1.10663	1.10022	1.11975	1.13606	1.1307	1.15148
Sweden (Normalized to EU-15 = 1)	10.3769	10.4334	10.193	10.6136	10.5809	10.3928	10.7058	11.2258	11.1165	11.0312
UK (Normalized to EU-15 = 1)	0.69644	0.71622	0.70809	0.71996	0.73003	0.75487	0.7942	0.82088	0.81381	0.83613
Norway (Normalized to EU-15 = 1)	10.1101	10.1838	10.0618	10.0682	10.1237	10.2651	10.6798	11.1985	11.0817	10.9472

Cost in national currency is divided by the adjustment figure to standardize all cost to the cost level of EU-15.

Appendix D: Costing approach I: Stroke

Resources and adjusted costs

There are two cost components: Hospital costs and Cost of medicines outside hospital.

x_{ijklt} =number of resource item *i* to patient j for disease k in country *l* in period *t*

p_{iklt} = cost attached to resource item *i* for disease k in country *l* in period *t*

m_{jklt} = cost of medicines to patient *j* for disease *k* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

m_{jlt} = total cost of medicines (irrespective of ATC code) to patient *j* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

c_{hlt} = adjustment of cost level of hospital services (h) in country *l* in period *t*

c_{mlt} = adjustment of cost level of pharmaceuticals (m) in country *l* in period *t*

The total cost of patient j with disease k in country *l* in period *t* with adjustment for differences in cost level is then:

$$C_{jklt} = c_{hlt}\left\{\sum_i p_{iklt}x_{ijklt}\right\} + c_{mlt}m_{jklt}$$

Application to Stroke

Costs should be registered during two intervals: First episode after index admission and one year after index admission.

The following resource items are included:

C. Hospital costs: Register the following information according to each individual patient:

A1. Identify all inpatient stays each year 2006-2011 for patients with ICD-10: I63.

A2. Calculate mean and median cost (outliers excluded) per inpatient stay and distinguish between stays without registered thrombolytic treatment and stays with thrombolytic treatment (AAL10).

A3. Also calculate mean and median cost (outliers excluded) per inpatient stay including at least one of the following procedure codes: PAF*, AAC00, AAL00, AAD15, AAB30, AAF*, A* (excluding codes above).

A4. Also calculate mean and median cost (outliers excluded) per patient stay for DRG 14a and 14b for ICD-10 I63 and for all patients.

D. Cost of medicines outside hospitals

B1. Calculate from the prescription register the total sum of medicines (irrespective of ATC code) dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included

B2. Calculate from the prescription register the sum of medicines with an ATC related to Stroke dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included. The following ATCs should be included (according to list of variables):

Clopidogrel	B01AC04
Dipyridamole	B01AC07, B01AC30
Diuretic	C03*, C07BB*, C09BA*, C09DA*
Beta blocker	C07*
ACE inhibitor	C09A*, C09B*
Angiotensin receptor blockers	C09C*, C09D*
Calsium channel blockers	C08*, C07FB*, C09BB*
Insulin	A10A*
Blood glucose lowering drugs, excluding insulins	A10B*
Statin	C10AA*
Warfarin	B01AA03
Antidepressants	N06A*
Anti-dementia drugs	N06D*
Antiepileptics	N03A*

Assigning Hospital Costs

This approach uses data from the Swedish cost per patient (KPP) data base provided by Swedish Association of Local Authorities and Regions (SALAR).

3. Calculate Swedish hospital cost components from KKP data base – outliers are excluded

4. Adjust for cost level in Sweden using Eurostat PPP: http://epp.eurostat.ec.europa.eu/portal/page/portal/purchasing_power_parities/data/database

   In the table below PPP for hospital services (input-based) is used.

   The distinction between stays without registered thrombolytic treatment and stays with thrombolytic treatment (AAL10) has not worked out so far because of a surprisingly low number of registered thrombolytic treatments. This has to be further checked with the KPP manager.

   As described for hip fracture, another important question is whether we should calculate mean cost per stay or mean cost per day. If we calculate mean cost per stay, differences in length of stay across countries will not be accounted for. Then, the only source of cost variation across countries will consist of inpatient stays additional to the index stay. With mean cost per day we would also

take into account use of resources related to variation in the LOS. If we use mean cost per day, we probably overestimate the additional cost of a long stay since more than a proportional part of the treatment cost occurs during the first days of the stay. Hence, it is a trade-off here, given the level of degree of detailedness of the data we have access to. I am inclined to suggest that we make us of cost per day multiplied by number of days.

	Year	mean LOS	Mean Cost SEK	Mean Cost per day SEK	PPP GDP	PPP hospital services	COST per day € PPP hospital services
ICD-10 I63	2006	9.8	52243	5303.9	10.581	9.99231945	531
Vårddag generelt	2006			8851	10.581	9.99231945	886
Outpatient visit	2006				10.581	9.99231945	
ICD-10 I63	2007	9.6	53853	5601.1	10.393	10.03234952	558
Vårddag generelt	2007			9061	10.393	10.03234952	903
Outpatient visit	2007				10.393	10.03234952	
ICD-10 I63	2008	9.3	54562	5877.1	10.706	9.988830634	588
Vårddag generelt	2008			9257	10.706	9.988830634	927
Outpatient visit	2008				10.706	9.988830634	
ICD-10 I63	2009	9.3	55737	5999.7	11.226	10.02060848	599
Vårddag generelt	2009			9642	11.226	10.02060848	962
Outpatient visit	2009		2376	2376	11.226	10.02060848	237
ICD-10 I63	2010	9.0	53411	5916.4	11.116	10.1656979	582
Vårddag generelt	2010			9753	11.116	10.1656979	959
Outpatient visit	2010		2386	2386	11.116	10.1656979	235
ICD-10 I63	2011	8.6	54030	6302.7			
Vårddag generelt	2011			10097			
Outpatient visit	2011	9.8	2392	2392			

These figures give us the treatment cost as it occurs on average in Sweden adjusted to the average cost level of hospital services in EU-15.

Assigning Pharmaceutical Costs

Cost in national currencies are adjusted for differences in cost level using Eurostat PPP GDP

GEO/TIME	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
European Union (15 countries)	1	1	1	1	1	1	1	1	1	1
Italy (Normalized to EU-15 = 1)	0.93811	0.95426	0.97708	0.98079	0.97099	0.95559	0.96262	0.98249	0.99118	0.97381
Hungary (Normalized to EU-15 = 1)	127.475	134.691	141.398	145.53	149.654	153.616	157.939	159.175	160.425	161.118
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Finland (Normalized to EU-15 = 1)	1.11325	1.12937	1.09181	1.10594	1.10663	1.10022	1.11975	1.13606	1.1307	1.15148
Sweden (Normalized to EU-15 = 1)	10.3769	10.4334	10.193	10.6136	10.5809	10.3928	10.7058	11.2258	11.1165	11.0312
UK (Normalized to EU-15 = 1)	0.69644	0.71622	0.70809	0.71996	0.73003	0.75487	0.7942	0.82088	0.81381	0.83613

Norway (Normalized to EU-15 = 1)	10.1101	10.1838	10.0618	10.0682	10.1237	10.2651	10.6798	11.1985	11.0817	10.9472

Cost in national currency is divided by the adjustment figure to standardize all cost to the cost level of EU-15.

Appendix E: Costing approach I: Hip fracture

Resources and adjusted costs

There are two cost components: Hospital costs and Cost of medicines outside hospital.

x_{ijklt} =number of resource item *i* to patient j for disease k in country *l* in period *t*

p_{iklt} = cost attached to resource item *i* for disease k in country *l* in period *t*

m_{jklt} = cost of medicines to patient *j* for disease *k* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

m_{jlt} = total cost of medicines (irrespective of ATC code) to patient *j* in country *l* in period *t* dispensed outside hospital in local currency calculated at the pharmacy's retail price VAT included

c_{hlt} = adjustment of cost level of hospital services (h) in country *l* in period *t*

c_{mlt} = adjustment of cost level of pharmaceuticals (m) in country *l* in period *t*

The total cost of patient j with disease k in country *l* in period *t* with adjustment for differences in cost level is then:

$$C_{jklt} = c_{hlt}\left\{\sum_i p_{iklt}x_{ijklt}\right\} + c_{mlt}m_{jklt}$$

Application to Hip fracture

Costs should be registered during two intervals: First episode after index admission and one year after index admission.

The following resource items are included:

E. Hospital costs: Register the following information according to each individual patient:

A1. Total number of inpatient days related to Hip Fracture , defined by:

- Fracture in neck of femur (ICD-9: 820.0-1; ICD-10: S72.0)
- Fracture in other areas of femur (subtrochanter, pertrochanter) (ICD9: 820.2-9; ICD-10: S72.1, S72.2)

A2. Total number of inpatient days for other diagnoses

A3. Total number of outpatient consultations irrespective of diagnosis

F. Cost of medicines outside hospitals

B1. Calculate from the prescription register the total sum of medicines (irrespective of ATC code) dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included

B2. Calculate from the prescription register the sum of medicines with an ATC related to Hip Fracture dispensed outside hospital calculated at the pharmacy's retail price in local currency VAT included. The following ATCs should be included (according to list of variables by EM):

VIT	Vitamins	A11*, A12A*
CD	Calcium + D	A12AX*
BD	Drugs for treatment of bone diseases	M05*, H05AA*, H05BA*, G03DC05, G03XC*
EST	Estrogens	G03C*
GC	Glucocorticoids	H02AB*
FE	Fenantoin	N03AB02, N03AB04, N03AB05
LE	Levothyroxin	H03AA01
PPI	Proton pump inhibitor	A02BC

Assigning Hospital Unit Costs

We use data from the Swedish cost per patient (KPP) data base provided by Swedish Association of Local Authorities and Regions (SALAR):

5. Calculate Swedish hospital cost components from KKP data base – outliers are excluded. SALAR has identified all inpatient stays in Swedish hospitals each year 2006-2011 for patients with ICD-10: S72.0, S72.1 and S72.2. Within each diagnosis mean cost (outliers excluded) is calculated as a whole and according to four subgroups: Group 1 (with prosthetic replacement of hip joint: NFB09, NFB19, NFB29, NFB39, NFB49), Group 2 (Internal fixation of fracture: NFJ79, NFJ69, NFJ89, NFJ59, NFJ89, NFJ99), Group 3 (Other surgical procedure codes: NFJ09, NFJ19, NFJ29, NFJ39, NFJ49 and Group 4 (without any of the procedure codes above). A distinction is made between procedure cost (surgery and related procedures) and cost occurring at the bed ward.

Table 1 shows cost in SEK according to the four groups and diagnoses in 2009.

Table 1. Cost in SEK according to group in year 2009

Group #	Main diagnosis	#obs	LOS Mean	Total cost Mean	Ward cost Mean	Procedure cost Mean	LOS Median	Total cost Median
All	S72.0 Kollumfraktur	6135	8	71107	41128	29979	7	68628
All	S72.1 Pertrokantär fraktur	4649	9	72649	44299	28350	8	68256
All	S72.2 Subtrokantär fraktur	970	9	85413	45729	39684	8	80837
1	S72.0 Kollumfraktur	2911	9	84115	44666	39449	8	81570
1	S72.1 Pertrokantär fraktur	44	8	83655	43619	40036	8	81559
1	S72.2 Subtrokantär fraktur	10	9	94544	50428	44116	9	86916
2	S72.0 Kollumfraktur	1022	7	56873	33644	23229	5	50076
2	S72.1 Pertrokantär fraktur	2516	8	72491	42014	30477	7	66434
2	S72.2 Subtrokantär fraktur	510	8	85146	44054	41092	7	80255
3	S72.0 Kollumfraktur	1445	8	63357	39759	23597	7	58973
3	S72.1 Pertrokantär fraktur	1474	10	81701	50068	31633	9	78249
3	S72.2 Subtrokantär fraktur	316	10	98334	51239	47095	9	90667
4	S72.0 Kollumfraktur	745	8	54265	40119	14146	6	49116
4	S72.1 Pertrokantär fraktur	615	8	50815	39872	10943	7	43713
4	S72.2 Subtrokantär fraktur	134	8	55278	38757	16522	6	47096

Table 1 shows costs in 2009. We see from Table 1 that S72.2 shows the highest treatment cost irrespective of sub-group. We also see that the procedure costs are considerably smaller in group 4 compared with the other groups, which makes sense. Group 4 has also the smallest total costs among the four sub-groups.

We also see from Table 1 that for both S72.0 and S72.1, Mean Cost group 1 > Mean Cost group 3 > Mean Cost group 2 > Mean Cost group 4. For S72.2 Cost group 3 > Mean Cost group 1 > Mean Cost group 2 > Mean Cost group 4. We also see that S72.2 has the highest total mean cost irrespective of sub-group, while the position of S72.1 relative to S72.2 varies according to sub-group.

A difficult question is whether or not we should describe each diagnosis according to sub-groups of surgery. If the composition of types of surgery within a diagnosis varies between countries, having one cost figure for each diagnosis, could misrepresent cost differences across countries. On the other hand, variation in composition of types of surgery probably also implies variation in types of patients within each sub-group which is likely to impact on the mean cost in each group. One option might be to isolate sub-group 4 (those

without mentioned procedure codes as an indicator of not having surgery). For each diagnosis would we then distinguish between having surgery and not having surgery.

Another important question is whether we should calculate mean cost per stay or mean cost per day. If we calculate mean cost per stay, differences in length of stay across countries will not be accounted for. Then, the only source of cost variation across countries will consist of inpatient stays additional to the index stay. With mean cost per day we would also take into account use of resources related to variation in the LOS. If we use mean cost per day, we probably overestimate the additional cost of a long stay since more than a proportional part of the treatment cost occurs during the first days of the stay. Hence, it is a trade-off here, given the level of detailedness of the data we have access to. The solution suggested here is to take the (procedure cost) + (the ward cost per day * the length of stay). By using the ward cost rather than total cost, the potential bias is expected to be reduced.

Below we describe four types of calculations that may supplement each other. The types have declining robustness with regard to data availability across countries:

A. Distinguish patients according to whether they have surgery (Groups 1- 3) or not (Group 4). Take the weighted mean procedure cost and add weighted mean ward cost per day times mean length of stay.

B. Option 1 according to the diagnoses S72.0, S72.1 and S72.2.

C. Option 1 with Groups 1 – 4 separately (irrespective of diagnosis).

D. Option 1 according to the diagnoses S72.0, S72.1 and S72.2 and with a distinction between Groups 1 – 3.

II. Adjust for cost level in Sweden using Eurostat PPP: http://epp.eurostat.ec.europa.eu/portal/page/portal/purchasing_power_parities/data/database

Below results from calculations types A – C are presented. At the bottom of Table 2 we also present mean ward cost for hip fracture patients in total.

The figures give us the treatment cost as it occurs on average in Sweden adjusted to the average cost level of hospital services in EU-15.

Table 2. Type A: Procedure cost and ward cost per day according to whether or not a patient had surgery

Year	Group	Mean LOS	Mean ward cost per stay SEK	Mean Ward cost per day SEK	Mean proce-dure cost SEK	PPP hospital services	Mean proce-dure cost €	Mean Ward cost per day (€) PPP hospital services
2006	Surgery	8.06	37661	4673	29391	9.9923	2941	468
2006	NoSurgery	8.61	36719	4263	13103	9.9923	1311	427
2006	Mean inpatient day			8851		9.9923		886
2006	Mean outpatient visit					9.9923		
2007	Surgery	8.91	42513	4770	28146	10.0323	2806	476
2007	NoSurgery	9.25	40311	4357	9136	10.0323	911	434
2007	Mean inpatient day			9061		10.0323		903
2007	Mean outpatient visit					10.0323		0
2008	Surgery	8.97	44294	4940	31737	9.9888	3177	495
2008	NoSurgery	8.36	37521	4490	12065	9.9888	1208	449
2008	Mean inpatient day			8846		9.9888		886
2008	Mean outpatient visit					9.9888		
2009	Surgery	8.52	43174	5065	32594	10.0206	3253	505
2009	NoSurgery	8.24	39895	4843	13040	10.0206	1301	483
2009	Mean inpatient day			9642		10.0206		962
2009	Mean outpatient visit			2376		10.0206		237
2010	Surgery	8.31	40567	4884	32957	10.1657	3242	480
2010	NoSurgery	8.63	40322	4674	10686	10.1657	1051	460
2010	Mean inpatient day			9753		10.1657		959
2010	Mean outpatient visit			2386		10.1657		235
2011	Surgery	8.06	41045	5091	32732			
2006	Hip fracture total	8	37570	4633		9.9923		464
2007	Hip fracture total	9	42264	4722		10.0323		471
2008	Hip fracture total	9	43576	4895		9.9888		490
2009	Hip fracture total	8	42762	5037		10.0206		503
2010	Hip fracture total	8	40539	4856		10.1657		478

Table 3. Type B: Procedure cost and ward cost per day according to diagnosis and whether or not a patient had surgery

Year	Diagnosis	Group	Mean LOS	Mean Ward cost per stay SEK	Mean Ward cost per day SEK	Mean proce-dure cost SEK	PPP hosp. service	Mean proce-dure cost €	Mean Ward cost per day (€)
2006	ICD-10 72.0	Surgery	7.66	36414	4751	28552	9.99	2857	475
2006	ICD-10 72.1	Surgery	8.55	39100	4575	28475	9.99	2850	458
2006	ICD-10 72.2	Surgery	8.31	38912	4683	39123	9.99	3915	469
2006	ICD-10 72.0	NoSurgery	8	35716	4278	12788	9.99	1280	428
2006	ICD-10 72.1	NoSurgery	9	37146	4359	10270	9.99	1028	436
2006	ICD-10 72.2	NoSurgery	10	39155	3850	27183	9.99	2720	385
2006		Inpatient day			8851		9.99		886
2006		Outpatient visit					9.99		
2007	ICD-10 72.0	Surgery	8.48	40914	4826	28641	10.03	2855	481
2007	ICD-10 72.1	Surgery	9.33	43967	4712	25655	10.03	2557	470
2007	ICD-10 72.2	Surgery	9.76	46030	4715	35806	10.03	3569	470
2007	ICD-10 72.0	NoSurgery	9.17	40235	4386	11073	10.03	1104	437
2007	ICD-10 72.1	NoSurgery	9.22	39789	4317	6072	10.03	605	430
2007	ICD-10 72.2	NoSurgery	9.84	43099	4381	12785	10.03	1274	437
2007		Inpatient day			9061		10.03		903
2007		Outpatient visit					10.03		
2008	ICD-10 72.0	Surgery	8.48	42405	5001	31615	9.99	3165	501
2008	ICD-10 72.1	Surgery	9.55	46267	4844	30436	9.99	3047	485
2008	ICD-10 72.2	Surgery	9.45	47563	5031	38745	9.99	3879	504
2008	ICD-10 72.0	NoSurgery	8.12	36648	4515	12248	9.99	1226	452
2008	ICD-10 72.1	NoSurgery	8.16	36553	4479	9948	9.99	996	448
2008	ICD-10 72.2	NoSurgery	10.25	45477	4438	20101	9.99	2012	444
2008		Inpatient day			8846		9.99		886
2008		Outpatient visit					9.99		
2009	ICD-10 72.0	Surgery	8.03	41253	5136	32107	10.02	3204	513
2009	ICD-10 72.1	Surgery	9.07	44974	4959	31003	10.02	3094	495
2009	ICD-10 72.2	Surgery	9.07	46846	5166	43397	10.02	4331	516
2009	ICD-10 72.0	NoSurgery	8.18	40119	4902	14146	10.02	1412	489
2009	ICD-10 72.1	NoSurgery	8.37	39872	4764	10943	10.02	1092	475
2009	ICD-10 72.2	NoSurgery	7.93	38757	4886	16522	10.02	1649	488
2009		Inpatient day			9642		10.02		962
2009		Outpatient visit			2376		10.02		237
2010	ICD-10 72.0	Surgery	7.87	39381	5006	33169	10.17	3263	492
2010	ICD-10 72.1	Surgery	8.81	41487	4711	31051	10.17	3054	463
2010	ICD-10 72.2	Surgery	8.70	43551	5004	40260	10.17	3960	492
2010	ICD-10 72.0	NoSurgery	8.28	38864	4694	11008	10.17	1083	462
2010	ICD-10 72.1	NoSurgery	8.64	40224	4657	8735	10.17	859	458
2010	ICD-10 72.2	NoSurgery	10.51	48891	4653	18436	10.17	1814	458
2010		Inpatient day			9753		10.17		959
2010		Outpatient visit			2386		10.17		235

Table 4. Type C: Procedure cost and ward cost per day according Groups 1 – 4 separately (irrespective of diagnosis).

Year	Group	Mean LOS	Mean Ward cost per stay SEK	Mean Ward cost per day SEK	Mean proce-dure cost SEK	PPP hospital services	Mean proce-dure cost €	Mean Ward cost per day (€) PPP hospital services
2006	Group1	8.6	41457	4821	36133	9.99	3616	483
2006	Group2	7.1	32404	4563	26594	9.99	2661	457
2006	Group3	9.8	46201	4709	27943	9.99	2796	471
2006	Group4	8.6	36719	4263	13103	9.99	1311	427
2006	Inpatient day			8851		9.99		886
2006	Outpatient visit					9.99		
2007	Group1	9.3	45043	4836	35929	10.03	3581	482
2007	Group2	7.9	38295	4838	25738	10.03	2566	482
2007	Group3	9.9	45914	4643	24416	10.03	2434	463
2007	Group4	9.3	40311	4357	9136	10.03	911	434
2007	Inpatient day			9061		10.03		903
2007	Outpatient visit					10.03		
2008	Group1	9.3	47040	5065	38979	9.99	3902	507
2008	Group2	8.4	41583	4973	30199	9.99	3023	498
2008	Group3	9.4	45277	4792	27186	9.99	2722	480
2008	Group4	8.4	37521	4490	12065	9.99	1208	449
2008	Inpatient day			8846		9.99		886
2008	Outpatient visit					9.99		
2009	Group1	8.6	44670	5209	39473	10.02	3939	520
2009	Group2	8.0	40158	5034	29984	10.02	2992	502
2009	Group3	9.2	45578	4974	29554	10.02	2949	496
2009	Group4	8.2	39895	4843	13040	10.02	1301	483
2009	Inpatient day			9642		10.02		962
2009	Outpatient visit			2376		10.02		237
2010	Group1	8.5	43478	5122	39294	10.17	3865	504
2010	Group2	7.9	38502	4899	30725	10.17	3022	482
2010	Group3	8.8	40601	4620	29619	10.17	2914	454
2010	Group4	8.6	40322	4674	10686	10.17	1051	460
2010	Inpatient day			9753		10.17		959
2010	Outpatient visit			2386		10.17		235

Assigning Pharmaceutical Costs

Cost in national currencies are adjusted for differences in cost level using Eurostat PPP GDP

GEO/TIME	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
European Union (15 countries)	1	1	1	1	1	1	1	1	1	1
Italy (Normalized to EU-15 = 1)	0.93811	0.95426	0.97708	0.98079	0.97099	0.95559	0.96262	0.98249	0.99118	0.97381
Hungary (Normalized to EU-15 = 1)	127.475	134.691	141.398	145.53	149.654	153.616	157.939	159.175	160.425	161.118
Netherlands (Normalized to EU-15 = 1)	1.00083	1.03595	1.0177	1.01418	1.01124	1.00293	1.02787	1.0555	1.03488	1.03819
Finland (Normalized to EU-15 = 1)	1.11325	1.12937	1.09181	1.10594	1.10663	1.10022	1.11975	1.13606	1.1307	1.15148
Sweden (Normalized to EU-15 = 1)	10.3769	10.4334	10.193	10.6136	10.5809	10.3928	10.7058	11.2258	11.1165	11.0312
UK (Normalized to EU-15 = 1)	0.69644	0.71622	0.70809	0.71996	0.73003	0.75487	0.7942	0.82088	0.81381	0.83613
Norway (Normalized to EU-15 = 1)	10.1101	10.1838	10.0618	10.0682	10.1237	10.2651	10.6798	11.1985	11.0817	10.9472

Cost in national currency is divided by the adjustment figure to standardize all cost to the cost level of EU-15.