MOX–Report No. 21/2010

Provider Profiling Using Mixed Effects Models on a Case Study concerning STEMI Patients

Niccolo' Grieco, Francesca Ieva, Anna Maria Paganoni

MOX, Dipartimento di Matematica "F. Brioschi"
Politecnico di Milano, Via Bonardi 9 - 20133 Milano (Italy)

mox@mate.polimi.it http://mox.polimi.it

Provider Profiling Using Mixed Effects Models on a Case Study concerning STEMI Patients

Niccolò Grieco[1], Francesca Ieva[2], Anna Maria Paganoni[2]

June 1, 2010

[1] A.O. Niguarda Cà Granda,
AAT 118 - Milano, Italy
niccolo.grieco@118milano.it

[2] MOX - Modellistica e Calcolo Scientifico
Dipartimento di Matematica "F. Brioschi"
Politecnico di Milano
via Bonardi 9, 20133 Milano, Italy
francesca.ieva@fastwebnet.it
anna.paganoni@polimi.it

Abstract

"Provider profiling" is the evaluation process of the performance of hospitals, doctors, and other medical practitioners to enhance the quality of medical care. In this work we describe statistical analyses conducted on MOMI^2 (MOnth MOnitoring Myocardial Infarction in MIlan) survey, a collection of data concerning patients admitted with STEMI (ST-Elevation Myocardial Infarction) diagnosis in one of the hospitals belonging to the Milan urban area Network, with the aim of pointing out process indicators to be used in health-care evaluation. An effective statistical support to decisional process for clinical and organizational governance is then obtained analyzing and modelling data coming from clinical registers and administrative data banks. Typically this kind of data are grouped at first level by structure where patients are admitted to, so multilevel models have been considered and fitted to catch and explain overdispersion phenomena. Moreover, we compare three different techniques of hospitals classification based respectively on traditional survival rates comparison, on analysis of variance components in fitted generalized linear mixed effects models and non parametric random effects estimation.

Key words: Generalized Linear Mixed Models, In-hospital survival, ST-Elevation Myocardial Infarction, Provider Profiling

1 Introduction

Performance indicators for assessing quality in health care contexts have drawn more and more attention over recent years, because they may measure some aspects of the health-care process, clinical outcomes and disease incidence. At the same time, questions about the right use of such indicators as measure of quality of care have emerged. In this work we purpose the use of performance indicators in modelling outcome of clinical structures, in order to identify "similar behaviour" among clinical structure. These models take into account variability between institutions, adjusting for case-mix, and performance indicators are computed starting from data collected trough clinical registers. The purpose of the present work is, in fact, to highlight how advanced statistical methods can be used to identify suitable models for complex data coming from clinical registers in order to classify and evaluate health-care providers.

Procedures for analyzing and comparing health-care providers effects on health services delivery and outcomes have been referred to as *provider profiling*. In a typical profiling procedure, patient-level responses are measured for clusters of patients treated by different providers. We believe that statistical analyses of data coming from clinical registers focused on specific diseases might point out suitable indicators of hospital quality of care. Once data have been collected or obtained from clinical registers and/or administrative data banks, a study to assess the correlation among hospital quality of care and outcomes can be performed.

Several examples, available in clinical literature (see Saia *et al.* 2009, Hasday *et al.* 2002, Dalby *et al.* 2003), make use of clinical registers to evaluate performances of medical institutions. These databases are very useful: they enable people concerned with the health-care governance to plan activities on real epidemiological evidence and needs: in fact, they provide the knowledge of the number of cases and incidence, of the survival etc., concerning a specific disease. In general, health-care service scheduling is strictly connected with a deep knowledge of current health needs, of innovative surgery practices efficacy and of measurement of clinical outcomes.

As we will see in the next sections, in this work we use data coming from MOMI[2] clinical register on STEMI and we model survival outcome by means of suitable patient's covariates and process indicators, then we try to classify hospitals in groups of "similar behaviour". Particularly, we propose three different methodologies to evaluate hospital's performance in this provider profiling perspective: in the first one we estimate the in-hospital survival rates after fitting a Generalized Linear Model on outcome of interest; in the second one we fit a Generalized Linear Mixed Effects Model to explain in-hospital survival outcome, with a parametric random effect due to the hospital grouping factor, then we perform an explorative classification analysis on the estimated hospital effects; finally in the third one we classify the hospitals on the basis of the variance components analysis explained by a Generalized Linear Mixed Effects Model on outcome with a non parametric random effect.

The article is structured as follows: firstly we present cardiovascular diseases we are interested in from a clinical perspective, focusing on Lombardia

Region health-care policy (Section 2), then we discuss the role of statistician as supporter of management of cardiovascular health-care policy (Section 3). We describe the MOMI^2 clinical register (Section 4), the statistical models fitted on these data aiming at hospital classification (Section 5), and the results of statistical analyses (Section 6). Finally we conclude with discussion of results and suggestions for further developments of analyses (Section 7). All the analyses have been performed with R program (version 2.10.1, R Development Core Team 2009).

2 Cardiovascular disease and health policy in Lombardia Region

It is known that cardiovascular diseases are nowadays one of the main causes of death all over the world. In fact, the American Hearth Association refers to them as the largest major killer in the clinical context, because of the mortality they often induce.

Among them, we are particularly interested in Acute Coronary Syndromes (ACS) and specifically in Acute Myocardial Infarction with ST segment elevation (STEMI), which is a disease characterized by a great incidence (650 - 700 events per month have been estimated only in Lombardia Region) and serious mortality (Italy 8%, data coming from *Istituto Superiore della Sanità*). As we said before, it is one of the main causes of death all over the world. In general, the Acute Myocardial Infarction (AMI) is the most frequent disease among the class of ACS. These pathologies are caused by a stenotic plaque detachment, which causes a coronary thrombosis and a sudden critical reduction of blood flow in coronary vessels. This process causes a widespread necrosis of myocardial tissues and leads to an inadequate feeding of myocardial muscle itself.

A case of STEMI can be diagnosed through the electrocardiogram (ECG). It highlights bad patterns, for example those characterized by ST-segment elevation. This subgroup of patients must be treated as soon as possible (American Hearth Association and American College of Cardiology suggest less than 90 min since arrival at Emergency Room and treatment time). Up to now, Thrombolytic therapy and Percutaneous Transluminal Coronary Angioplasty (PTCA) are the most common procedures in dealing with STEMI events. The former one consists in a pharmacological treatment which causes a breakdown of the blood clots, while in the latter one an empty and collapsed balloon on a guide wise, known as *Balloon* catheter, is passed into the narrowed or obstructed vessels and then inflated to a fixed size. The balloon crushes the fatty deposit, so that the vessel can be opened up, the blood flow improved, and then balloon is collapsed and withdrawn. In our data on Milan reality, patients always undergo directly PTCA procedure avoiding the Thrombolysis, even if the two treatments are not mutually exclusive. A good practice can be evaluated by observing firstly the in-hospital survival of inpatients, then quantifying the reduction of ST segment elevation one hour later the surgery: if the reduction is larger than 70% we could consider the procedure effective. Both survival and quantity of myocardial tissue saved from permanent injury depend strongly on time saved during the process. So treatment times (i.e. time of first ECG, time since the arrival at Emergency Room (ER) up to PTCA,...) assume a key role in influencing outcomes (see Cannon *et al.* 2000) and stand as candidates of process indicators, to evaluate the performance of a clinical institutions.

In 2005, February 11th, the *Piano Cardio-Cerebro Vascolare* has been approved in Lombardia Region through D.G.R.20592. This law set favourable conditions for using clinical registers in health-care process planning. Several clinical registers have been made in Lombardia Region up to now. In fact Lombardia Region is very sensitive to cardiovascular topics, as proved by the huge amount of social and scientific initiatives concerning these syndromes. Some of the most important clinical and scientific projects conducted and funded by Lombardia Region during last years are:

- **Strategic Program** (2008-2011) → Identification and development of new diagnostic, therapeutic and organizational strategies to be applied to patients with Acute Coronary Syndromes (ACS), in order to improve the occurrence of clinical outcomes;
- **Nuove Reti Sanitarie** (2004-2009) → Tele-monitoring activities for patients affected by Chronical cardiac insufficiency and those concerned with in-home care after cardiac admittance to hospital;
- **PROMETEO - PROgetto Milano Ecg Teletrasmessi Extra Ospedaliero** (2009) → All Basic Rescue Units working on Milan urban area have been equipped with ECG telemonitoring machinery;
- **MOMI^2 - MOnth MOnitoring Myocardial Infarction in MIlan** (2006 -2008) → Six time periods data collection (lasting from 30 to 60 days, MOMI^2.1 - MOMI^2.6) on STEMI patients in Milan urban area, performed by Working Group for Cardiac Emergency of Milan, Cardiology Societies, and 118 (national free toll number for emergencies) Dispatch Center;
- **GestIMA: Gestione dello STEMI in Lombardia** (2003) → Bimontly data collection (Oct 15th - Nov 14, 2003), 612 patients with ST-segment Elevation Myiocardial Infarction diagnosys were enrolled (see Oltrona *et al.* 2005).

It can be argued that control and use of such huge amount of complex data for clinical and epidemiological scopes are very hard tasks. In this context the role of statistician and of statistical analysis for management of health-care become central.

In next sections, we will focus our interest, modelling efforts and analyses only on MOMI^2 survey.

3 The role of statistic and statistician in managing cardiovascular health-care

The role of statistician in management of cardiovascular health care assumes complex connotation. Firstly he is asked to comprehend and point out the mechanisms connecting the health-care process itself and inpatients outcomes, which incase of STEMI are in-hospital survival and reduction of ST segment elevation after angioplasty surgery. The way the statistician can do this is through monitoring, analyzing and modelling data collected by clinical surveys or available from already existing databases.

In all these cases, we can resume the work of statistician through the pattern reported in Figure 1: starting from the existing health-care process (in our case, the process since infarction symptoms onset time to pharmaceutical therapy or surgery), the comprehension of process dynamics passes through statistical analyses of previous data collection. This enable the statistician to give a first feedback to the players involved into the process (hospitals, institutions, clinicians, governance and so on) and to plan and realize new data collections designed on specific needs. The analyses on these new databases let the statistician to model phenomena and evaluate process indicator in order to point out new gold standards and protocols and to give again feedback to the involved players, so that health-care process improvements can be obtained.

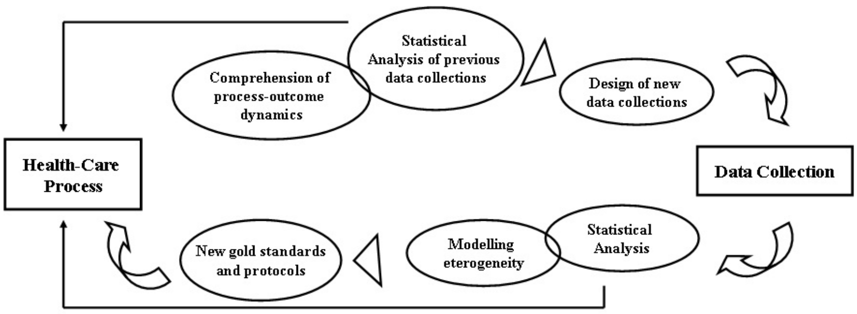

Figure 1: Flow chart representing the statistician's role in managing health-care process

4 The MOMI^2 Clinical Register

The MOMI^2 project arises from a collaboration between the Working Group for Cardiac Emergency (ACEU) of Lombardia Region, Dispatch Center of 118 and Niguarda Cà Granda hospital, concerning the management of the Network, activated in the Milan urban area since 2001, in order to connect the territory to hospitals by a centralized coordination of the emergency resources. Its primary aims are promoting the best utilization of the different reperfusion strategies, reducing transport and decisional delays connected with logistic matters and therapies, and increasing the number of patients undergoing primary PTCA before 90 minutes since the arrival at ER, limit suggested by the American Heart Association/American College of Cardiology (AHA/ACC) guidelines (see Antman *et al.* 2008, Ting *et al.* 2008). Difficulties in reaching these goals are primary due to the fact that Milan urban area is a complex territory with high density of population (2.9 million resident and 1 million commuters daily) and a great number of hospitals (n = 27). Twenty-three of them have a cardiology division and a Critical Care Unit; 18 offer a 24 hour available Cath Lab for primary PTCA, 5 are completed with a Cardiac Surgery unit.

The aim of this project is the activation, on the Milan urban area, of a register on Acute Myocardial Infarction to collect also process indicators (Symptom Onset time, first ECG time, Door to Balloon time and so on), to be used in profiling providers' service. Specifically, the main purpose of the study is the identification and development of new diagnostic, therapeutic and organizational strategies to be applied (by Lombardia Region, 118 and hospitals) to patients with STEMI, in order to improve the occurrence of clinical outcomes and the health-care offer to the patients. In order to do this, it is firstly necessary to understand which organizational aspects can be considered as predictive of reduction of time to treatment. Therefore, a special attention is focused on the mode of admittance; five different types of patients can be pointed out:

- **self-presented** patients, i.e. patients who came to the hospital by themselves;
- patients delivered by advanced life support units with tele-transmission of ECG (**ALS + tele-ECG**), i.e by rescue units with doctors on it and equipped with LIFEPACK 12, a box which enable clinicians to make ECG and forecast it to the Dispatch Center and to the hospital where the patient will be admitted to;
- patients delivered by advanced rescue units (**ALS**), i.e. by a rescue unit with doctors on it but without ECG tele-transmission equipment;
- patients delivered by basic life support units (**BLS**), i.e. the common ambulances;
- patients **transferred**, i.e. patients admitted to a certain hospital and then undergone to angioplasty in another one.

Beyond the mode of admittance, several other information can be found in the MOMI^2 dataset: for example, demographic data as age and sex, clinical data like declared symptoms, Killip class (which quantify in four categories the severity of infarction) and received therapy, organizational data like mode, hospital of admission and activation of Fast-Track, data concerning all procedure times and finally, clinical outcomes: in-hospital survival and reperfusion efficacy.

The MOMI^2 survey is then a retrospective observational study. Anyway, it is a study who enables us to give a "real time" feedback on the monitored activities. In fact the MOMI^2 survey is composed by six collections, planned and made during monthly/bimestral periods. In particular:

$MOMI^2$.1:	90 pcs.	Jun 1st - Jun 30th 2006
$MOMI^2$.2:	147 pcs.	Nov 15th - Dec 15th 2006
$MOMI^2$.3:	220 pcs.	Jun 1st - Jul 31st 2007
$MOMI^2$.4:	131 pcs.	Nov 15th - Dec 15th 2007
$MOMI^2$.5:	120 pcs.	Jun 1st - Jun 30th 2008

MOMI^2.6: 133 pcs. Jan 28th - Feb 28th 2009

The whole dataset collects data concerning 841 patients.

Now, in the diagram proposed in Figure 1, the MOMI^2 analysis can be seen as the step of analysis of data collection in order to give real time feedback to providers and to point out critical situation to work on. In fact, in the first analysis we performed on it (see Ieva 2008), the crucial importance of ECG tele-transmission was pointed out, and PROMETEO project was planned for equipping all Milan basic rescue units with ECG machinery. Moreover, the results achieved by that work confirmed Lombardia Region governance to intensify and widen MOMI^2 paradigm of data collection and monitoring, extending to the whole Lombardia Region territory a new data collection on Cardiological diseases, namely *STEMI Archive* (see Barbieri *et al.* 2010, Grieco *et al.* 2008, Ieva & Paganoni 2009,2010, for further details). Finally, the main feedback of our analysis for providers is the hospital classification we performed once we described outcomes by means of suitable covariates, taking into account process indicators and case mix. In next sections, the use of advanced statistical techniques for clustering providers' behaviour in terms of in-hospital survival will be shown, starting from data of MOMI^2 survey.

5 Models for classification

We propose three different methodologies to evaluate hospital's performance in this provider profiling perspective. In the first one we estimate the in-hospital survival rates after fitting a Generalized Linear Model on outcome of interest. In the second one we fit a Generalized Linear Mixed Effects Model to explain in-hospital survival outcome, with a parametric random effect due to the hospital grouping factor, then we perform an explorative classification analysis on the estimated hospital effects. In the third one we classify the hospitals on the basis of the variance components analysis explained by a Generalized Linear Mixed Effects Model on outcome with a non parametric random effect.

5.1 Generalized Linear Models (GLM)

Generalized Linear Models (GLMs) represent a class of fixed effects regression models for several types of dependent variables (i.e., continuous, dichotomous, counts) see McCullagh & Nelder 1989. Common Generalized linear models (GLMs) include linear regression, logistic regression, and Poisson regression.

There are three specifications in a GLM. First, the linear predictor, denoted as η_i, which is of the form $\eta_i = \mathbf{x}_i^{'}\beta$ where $\mathbf{x}_i$ is the vector of regressors for unit i with fixed effects β. Then, a link function $g(\cdot)$ is specified which converts the expected value μ_i of the outcome variable Y_i (i.e., $\mu_i = \mathbb{E}[Y_i]$) to the linear predictor η_i, i.e. $g(\mu_i) = \eta_i$. Finally, a specification for the form of the variance in terms of the mean μ_i is made. The latter two specifications usually depend on the distribution of the outcome

Y_i , which is assumed to belong to the exponential family of distributions. Fixed effects models, which assume that all observations are independent of each other, are not appropriate for analysis of several types of correlated data structures, in particular, for clustered and/or longitudinal data, anyway they can be considered a first straightforward attempt to model these data, which are typical in clinical literature. The New York State Department of Health (NYS DOH), a leader in provider profiling, assesses hospital performance by computing in-hospital survival rates adjusted for differences in patient severity (see Racz & Sedransk 2010). Then, starting from GLM model fitting, we define the Statewide Survival Rate (SSR) for hospital j as

$$SSR_j = \frac{\sum_{i=1}^{n_j} y_{ij}^{obs}}{\sum_{i=1}^{n_j} \hat{p}_{ij}},$$

where y_{ij}^{obs} is the observed value of outcome for patient i treated in the hospital j, and $\hat{p}_{ij}$ is the corresponding survival probability estimated by using, for example, a GLM. SSR_j relates the actual survival at the $j-$hospital to the expected survival in the same hospital, adjusted for different patient severity resumed in the covariates of the GLM. An elementary assessment of hospital j can be obtained by comparison of SSR_j with 1.

5.2 Generalized Linear Mixed effects Models (GLMM)

In clustered designs subjects are observed nested within larger units (schools, hospitals, neighborhoods, workplaces, and so on). These are often referred to as *multilevel* or *hierarchical* data, in which the level-1 observations (subjects) are nested within the higher level-2 observations (clusters). Higher levels are also possible, for example, a three-level design could have repeated observations (level-1) nested within subjects (level-2) who are nested within clusters (level-3).

For statistical analysis of such multilevel data, random cluster effects can be added into the regression model to account for the correlation of the data. The resulting model is a mixed model including the usual fixed effects for the regressors plus the random effects. Mixed models for continuous normal outcomes have been extensively developed, anyway many developments have been produced also for non-normal data. Many of these developments fall under the name of Generalized Linear Mixed Models (GLMMs), which extend GLMs by the inclusion of parametric gaussian random effect in the predictor. An alternative way to assessment the performance of hospitals can be obtained by analysing the estimated values of random effect for every hospital.

Since the goal of analyses performed on MOMI^2 survey is also to find a model for grouped data, clustered by providers where patients are admitted to, our case can be thought as belonging to the class of problems for which Fixed Effects Models poorly perform in explaining phenomenon variability, and then GLMM is straightforward to be considered. In this case, the method for classifying providers is strongly related to the GLMM definition. In fact, in this section we would like to build a suitable model for MOMI^2 data. We considered a GLMM (see Pinheiro & Bates 2000 and Goldstein 2003) to model binary response of grouped data.

Let Y_{ij} be the binary outcome of subject i of j-*th* group, and p_{ij} the related probability of success. A GLMM could be written in the following way:

$$logit\left(\mathbb{E}\left[Y_{ij}|b_j\right]\right) = logit(p_{ij}) = \beta_0 + \sum_k \beta_k x_{ijk} + b_j$$

where x_{ijk} are significant covariates; $b_j \sim \mathcal{N}(0, \sigma_b^2)$ are additive random effects Normally distributed. The first two terms of the linear predictor $(\beta_0 + \sum_k \beta_k x_{ijk})$ are commonly called fixed effect. We fitted a Generalized Linear Mixed Model on in-hospital survival outcome; the hospital of admission is the grouping factor assumed as an additive random term with Normal distribution. Estimates for fixed effects coefficients (β_i) and standard deviation of Normal random effect (σ^2) can then be obtained via maximization of Likelihood function

$$L(\beta, \sigma) = \prod_j \int \prod_i f(y_{ij}|\beta, \sigma, b_j)\pi(b_j)db_j$$

where $\pi(b_j)$ is the Normal density function. This integral does not have a closed form except for Normal outcomes, then approximations need to be computed. We fitted GLMM models on our data with `lme4` package, which make use of Laplace approximation for computing high-dimensional integrals (Bates & Maechler 2010).

Once we obtain estimates of fixed effects $\hat{\beta}_j$ and random effect variance $\hat{\sigma}^2$, agglomerative alghoritms (for example k-means) on the estimated values of random effect for each hospital can be implemented in order to detect clustering structure, i.e. to establish how many groups, in terms of suitable similarity indexes, can be detected starting from data.

5.3 Non Parametric Maximum Likekihood Estimator for GLMM

In modelling data overdispersed and grouped the use of a fully paramatric model for random effects can result quite binding, so we consider also the idea of Non Parametric Maximum Likelihood (NPLM) estimation (see Aitkin 1999) for joint distribution of random effects. This idea is based on replacing normal random effect by a finite sum of mass points z_k with masses π_k. The study of estimated z_k and related probabilities that observed outcomes related with hospital j come from component k is an alternative procedure to classify different hospitals. The algorithm idea is based on replacing integrals over normal b_j by a finite sums over K Gaussian quadrature mass point z_k with masses π_k. Then estimates of masses and fixed effects coefficients can be obtained via maximization of

$$L(\beta, \sigma) = \prod_{j=1} \sum_{k=1}^{K} \pi_k \prod_{i=1} f_{ik}$$

where $f_{ik} = \prod_j f(y_{ij}|\beta, \sigma, z_k)$.

The likelihood is thus (approximately) the likelihood of a finite mixture of exponential family densities with mixture proportions π_k at mass points z_k, with the linear predictor for the ij-th observation in the k-th mixture component being

$$\eta_{ijk} = \beta^{'} x_{ij} + z_k$$

.
The score equations we have to solve turn out to be a weighted version of the single distribution score equations with weights $w_{ik} = \pi_k f_{ik} / \sum_l \pi_l f_{il}$. The estimates of these weights can be interpreted as posterior probabilities that the observation y_i comes from component k. We computed non parametric maximum likelihood estimations on our data with `npmlreg` package (Einbeck *et al.* 2009)

6 Statistical Analysis

We focus our readings on patients undergone primary angioplasty. We counted out patients with "transferred" as way of admittance, because, concerning treatment times, they represent a different population with respect to all other patients. So the population considered for all the following analyses consists of 536 statistical patients admitted in 17 different hospitals.

We fitted a Generalized Linear Model and a Generalized Linear Mixed Model on survival outcome. In the latter case, the hospital of admission is the grouping factor assumed as an additive random term with Normal distribution.

In order to choose significant covariates for the model, we considered stepwise regression methods (AIC criterion) on the fixed effect part of the model and clinical best practice. These criteria pointed out the logarithm of Symptom Onset to Balloon time (log(OB)) ($p - value = 0.1838$), killip ($p - value = 0.0038$) and age ($p - value = 8.27 \times 10^{-5}$) of patient as significant factors in order to explain survival probability from a statistical and clinical point of view (see also Rathore *et al.* 2009). The killip variable is now a binary categorization of Killip class, whose values are zero for less severe (Killip class 1 or 2) and more severe (Killip class 3 or 4) infarction. The choice of these covariates is confirmed also in a Bayesian framework as explained in details in Guglielmi *et al.* 2010.

Therefore, calling Y_{ij} the binary random variable representing in-hospital survival of patient $i = 1, \ldots, 536$ treated in the hospital $j = 1, \ldots, 17$, the models fitted are respectively:

$$\begin{aligned} logit\left(\mathbb{E}\left[Y_{ij}\right]\right) &= \beta_0 + \beta_1 age_i + \beta_2 \log(OB)_i + \beta_3 killip_i && (1) \\ logit\left(\mathbb{E}\left[Y_{ij}|b_j\right]\right) &= \beta_0 + \beta_1 age_i + \beta_2 \log(OB)_i + \beta_3 killip_i + b_j && (2) \end{aligned}$$

where, in (2), $b_j \sim \mathcal{N}(0, \sigma_b^2)$ is the Normal random effect of the grouping factor (i.e. hospital where $i - th$ patient is admitted to). For details about this model see Ieva & Paganoni 2010.

6.1 Classification analysis

Once we fitted a model to MOMI[2] data in order to explain in-hospital survival by means of suitable patients' covariates and process indicators, eventually taking into account overdispersion induced by grouping factor adding a random effect, in this section we point out comparative analyses on performances.

We now propose and compare three different approaches to catch some clustering structure in the hospital performances (for a deeper discussion about this problem see Racz & Sedransk 2010).

(1) According to NYS DOH methodology we compute the SSR_j for every hospital; the expected survival probability $\hat{p}_{ij}$ is estimated with a GLM for survival outcomes with for log(OB), killip and age as covariates (1). We call "Good" the institutions such that their SSR is greater than or equal to one, and "Bad" the remaining ones. This procedure splits the hospitals in two groups: only hospitals $2, 3, 5, 9, 10, 13$ are clustered in the lower category ("Bad"), and the twelve remaining medical institutions are in the upper category ("Good").

(2) We fit the (2) model and we obtain estimates of additive contribution of each hospital to estimated survival probability. Let us call them $\hat{b}_j$, $j = 1, ..., 17$.

In Table 1 estimates of fixed effects coefficients and standard deviation of random effect are reported with corresponding 95% confidence intervals.

Table 1: Model parameters estimates and relatives asymptotic confidence intervals.

		estimate	Asymptotic CI (95%)
Intercept	$\hat{\beta}_0$	12.957	[7.867,18.047]
Age	$\hat{\beta}_1$	-0.105	[-0.157,-0.052]
log(OB)	$\hat{\beta}_2$	-0.402	[-0.986,0.182]
Killip	$\hat{\beta}_3$	-1.719	[-2.885,-0.553]
Std. Dev.	$\hat{\sigma}_b$	0.261	/

We partition with a k-means clustering algorithm (see Hartigan, & Wong 1979) $\hat{b}_j$. A robustness analysis for the number of clusters using the average silhouette width (Struyf *et al.* 1996) supported the optimal choice of $k = 2$. Indeed Fig. 2 shows the silhouette plot of this clustering procedure, and the value of average silhouette width equal to 0.67 indicate that a reasonable clustering structure has been found.

The means of the two clusters are -0.0875 and 0.03456, representing a "Bad" and a "Good" behavior respectively. Then we analyze the two groups detected by this agglomerative clustering algorithm. In fact in this case only hospitals $2, 3, 5, 9, 10$ belongs to cluster with center equal to -0.0875. We observe that the result of this clustering procedure is in agreement with the previous one, except for hospital 13.

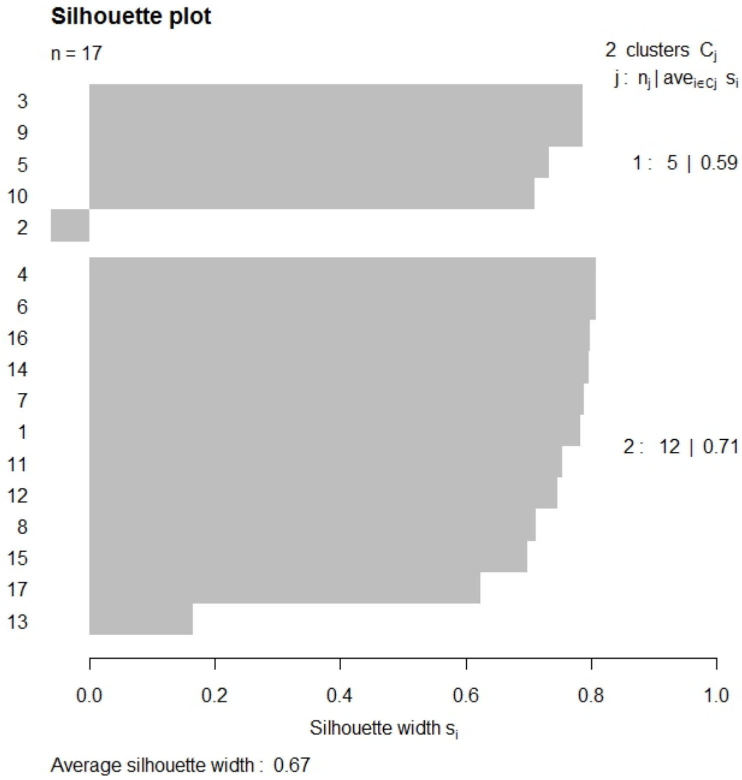

Figure 2: Silhouette plot

(3) We fit a non parametric GLMM, with the selected covariates of the GLMM model and with two mass points, according to the previous optimal choice (K=2). Figures 3 and 4 show the estimated survival probabilities corresponding to the two mass points, in case of less and more severe infarction, respectively. Starting from this step, we classify an hospital as "Bad" or "Good" according to the arg-max of the posterior probabilities of each structure estimated for the two masses, i.e. we assigned each hospital to the group whose estimated posterior probability was greater. In this case hospital $2, 3, 5, 9, 10, 13$ are clustered in the lower level, and this procedure is in total agreement with the one described in point (1).

Table 2: Hospital classification using SSR index, GLMM and NPLM.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
SSR	+	−	−	+	−	+	+	+	−	−	+	+	−	+	+	+	+
GLMM	+	−	−	+	−	+	+	+	−	−	+	+	+	+	+	+	+
NPLM	+	−	−	+	−	+	+	+	−	−	+	+	−	+	+	+	+

Following these three clustering procedures we obtain the same clustering structure except for one structure (hospital 13) which is classified as "Bad" following the procedure (1) and (3) and as "Good" following the procedure

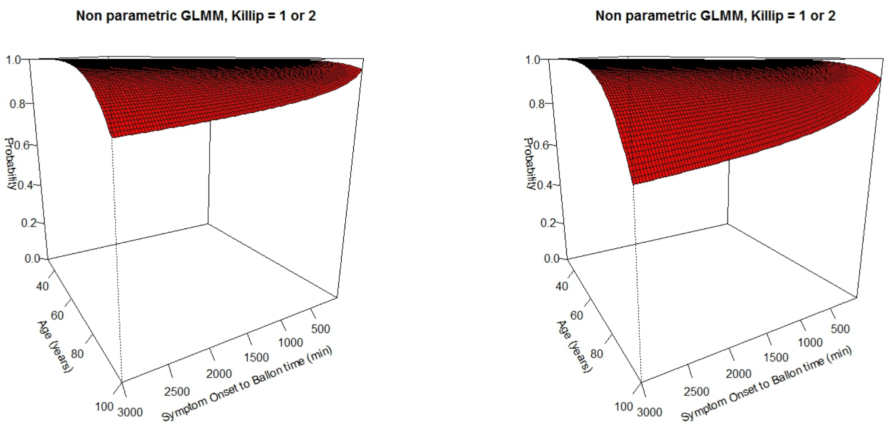

Figure 3: Left panel: Estimated survival probability surface for less severe class of Killip: *bad* hospital. Right panel: Estimated survival probability surface for less severe class of Killip: *good* hospital.

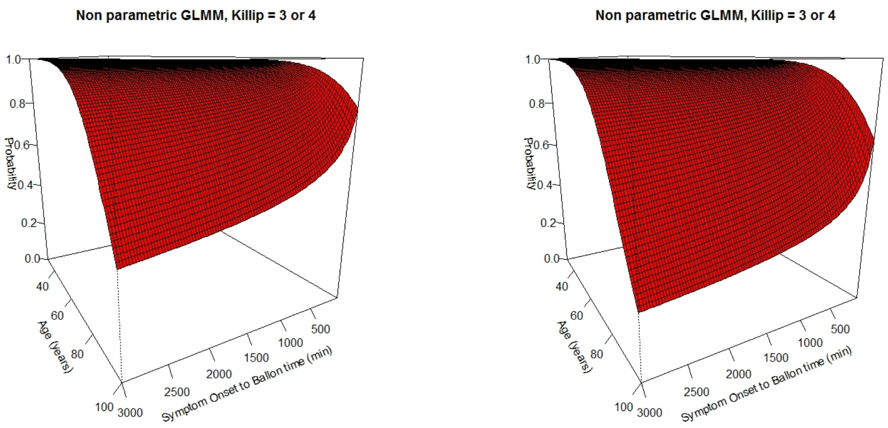

Figure 4: Estimated survival probability surface for more severe class of Killip: *bad* hospital". Right panel: Estimated survival probability surface for more severe class of Killip: *good* hospital.

(2). We can resume results obtained with different classification techniques comparing their performances as shown in Table 2. The quite global agreement in classification of the 3 methods support the idea that a real strong classification structure in two groups exists.

7 Conclusions and Open Problems

Provider profiling involves comparison of health care provider's structure, processes of care or outcomes to a normative or community standards. In this paper we have shown how different modelling techniques can be employed in provider profiling.

The results of this study support the idea of using performance indicators for comparing institutional offers of care. Performance indicators measuring is strainghtforward and relatively easy to define, but their relationship to actual health outcomes is often difficult to quantify. For this reason, the role of statistician in explaining outcomes by means of suitable predictors and performance indicators becomes crucial. We have shown relatively simple and effective methods for gaining these goals, and we believe that this approach could be taken into account by people concerned with health-care governance in order to support decisions in clinical context.

Since substantial agreement among three methods has emerged (100% of agreement between SSR and NPLM methods, 94.11% between these two and GLMM), it is difficult to us to rank them in some way. In general, the choice of classifying method is straightforward once a model for describing problem has been chosen. In our case, GLMM and NPLM methods of estimation are more suitable since they enable the statistician to take into account overdispersion of outcome induced by grouped nature of data, so GLMM and NPLM classification criteria could be preferred. On the other side, SSR criterion is easier to compute and its interpretation results more manageable, expecially when interactions with audience coming from different backround and knowhow are requested.

Finally, future developments of this work we are now working on are comparisons of our results with those arising from bayesian classification setting (Guglielmi *et al.* 2010) and on validation of these results on more complex and wider database, arising from integration of clinical registers and administrative databases, as is the case of STEMI Archive and Publich Health Database of Lombardia Region (Barbieri *et al.* 2010).

References

[1] Aitkin, M. (1999) A general maximum likelihood analysis of variance components in generalized linear models, *Biometrics*, **55**, 117128.

[2] Antman, E.M., Hand, M., Amstrong, P.W., Bates, E.R., Green L.A. & al. (2008) Update of the ACC/AHA 2004 Guidelines for the Management of Patients with ST Elevation Myocardial Infarction, *Circulation*, **117**, 269-329.

[3] Barbieri, P., Grieco, N., Ieva, F., Paganoni, A.M., Secchi, P. (2010) Exploitation, integration and statistical analysis of Public Health Database and STEMI archive in Lombardia Region *Mox Report n. 02/2010*, Dipartimento di Matematica, Politecnico di Milano. [Online] http://mox.polimi.it/it/progetti/pubblicazioni/quaderni/02-2010.pdf In presso on collective book "Complex data modeling and computationally intensive statistical methods", Contribution to Statistics, Springer.

[4] Bates, D. & Maechler, M. (2010) lme4: Linear mixed-effects models using S4 classes. [Online] http://CRAN.R-project.org/package=lme4

[5] Cannon, C.P., Gibson, C.M., Lambrew, C.T., Shoultz, D.A., Levy, D., French, W.J., Gore, J.M., Weaver, W.D., Rogers, W.J., Tiefenbrunn A.J. (2000) Relationship of Symptom-Onset-to-Balloon Time and Door-to-Balloon Time with Mortality in Patients undergoing Angioplasty for Acute Myocardial Infarction, *Journal of American Medical Association* **283**, 22, 2941-2947.

[6] Dalby, M., Bouzamondo, A., Lechat, P. & Montalescot, G. (2003) Transfer for Primary Angioplasty versus Immediate Thrombolysis in AMI: a Meta-Analysis, *Circulation*, 1809-1814.

[7] Direzione Generale Sanità – Regione Lombardia (2005) Patologie cardiocerebrovascolari: Interventi di Prevenzione, Diagnosi e Cura, *Decreto N° 20592, 11/02/2005.*

[8] Einbeck, J., Darnell, R. & Hinde, J. (2009) npmlreg: Nonparametric maximum likelihood estimation for random effect models. [Online] http://CRAN.R-project.org/package=npmlreg

[9] Guglielmi, A., Ieva, F., Paganoni, A.M., & Ruggeri, F. (2010) A Bayesian random-effects model for survival probabilities after acute myocardial infarction *Mox Report n. 17/2010*, Dipartimento di Matematica, Politecnico di Milano. [Online] http://mox.polimi.it/it/progetti/pubblicazioni/quaderni/17-2010.pdf

[10] Goldstein, H. (2003) *Multilevel Statistical Models*, Arnolds, London.

[11] Grieco, N., Corrada, E., Sesana, G., Fontana, G., Lombardi, F., Ieva, F., Paganoni, A.M., Marzegalli, M. (2008) Predictors of reduction of treatment time for ST-segment elevation myocardial infarction in a complex urban reality. The MOMI^2 survey *Mox Report n. 10/2008*, Dipartimento di Matematica, Politecnico di Milano. [Online] http://mox.polimi.it/it/progetti/pubblicazioni/quaderni/10-2008.pdf

[12] Hartigan, J.A. & Wong, M.A. (1979) A K-means clustering algorithm, *Applied Statistics*, **28**, 100-108. 1979.

[13] Hasday, D., Behar, S., Wallentin, L. & al. (2002) A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin. the euro heart survey of acute coronary syndromes (euro heart survey acs), *European Heart Journal*, **23**, 1190-1210.

[14] Ieva, F. (2008) Modelli statistici per lo studio dei tempi di intervento nell'infarto miocardico acuto, *Master Thesis* Dipartimento di Matematica, Politecnico di Milano. [Online] http://mox.polimi.it/it/progetti/pubblicazioni/tesi/ieva.pdf

[15] Ieva, F. & Paganoni, A.M. (2009) A case study on treatment times in patients with ST–Segment Elevation Myocardial Infarction *Mox Report n. 05/2009*, Dipartimento di Matematica, Politecnico di Milano. [Online] http://mox.polimi.it/it/progetti/pubblicazioni/quaderni/05-2009.pdf

[16] Ieva, F. & Paganoni, A.M. (2010) Multilevel models for clinical registers concerning STEMI patients in a complex urban reality: a statistical analysis of MOMI^2 survey, *Communications in Applied and Industrial Mathematics*. In press.

[17] Mc Cullagh, P. & Nelder, J.A. (2000) *Generalized Linear Models*, Chapman & Hall/CRC

[18] Oltrona, L., Mafrici, A., Marzegalli, M., Fiorentini, C., Pirola, R., Vincenti, A. (2005) La gestione della fase iperacuta dellinfarto miocardico con sopraslivellamento del tratto ST nella Regione Lombardia (GestIMA), *Italian Heart Journal*, **6**, 489-497.

[19] Pinheiro,C. & Bates, D.M. (2000) *Mixed-Effects Models in S and S-Plus*, Springer.

[20] R Development Core Team (2009) R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. [Online] http://www.R-project.org

[21] Rathore, S.S., Curtis, J.P. & Chen, U.J. (2009) Association of door to balloon time and mortality in patients admitted to hospital with ST-elevation myocardial infarction: national cohort study, *British Medical Journal,* **338**

[22] Racz, J. & Sedransk, J. (2010) Bayesian and Frequentist Methods for Provider Profiling Using Risk-Adjusted Assessments of Medical Outcomes, *Journal of the American Statistical Association* **105**, 489, 48–58.

[23] Saia, F., Marzocchi, A., Manari, G., Guastaroba, P., Vignali, L., Varani, E. & al. (2009) Patient selection to enhance the long-term benefit of first generation drug-eluting stents for coronary revascularization procedures: insights from a large multicenter registry, *Eurointervention*, **5**, 1, 57-66.

[24] Struyf, A., Hubert, M. & Rousseeuw, P.J. (1996) Clustering in an Object-Oriented Environment, *Journal of Statistical Software*, **1**.

[25] Ting, H.H., Krumholtz, H.M., Bradley, E.H., Cone, D.C., Curtis J.P. & al. (2008) Implementation and Integration of Prehospital ECGs into System of Care for Acute Coronary Sindrome, *Circulation* online publication, August 13th. [Online] http://circ.ahajournals.org

MOX Technical Reports, last issues

Dipartimento di Matematica "F. Brioschi",
Politecnico di Milano, Via Bonardi 9 - 20133 Milano (Italy)

21/2010 Niccolo' Grieco, Francesca Ieva, Anna Maria paganoni:
Provider Profiling Using Mixed Effects Models on a Case Study concerning STEMI Patients

20/2010 Fabio Nobile, Alfio Quarteroni, Ricardo Ruiz Baier:
Numerical solution of an active strain formulation for the electro-mechanical activity in the heart

19/2010 Loredana Gaudio, Alfio Quarteroni:
hN-adaptive spectral element discretization of optimal control problems for environmental applications

18/2010 Paola F. Antonietti, Nur Aiman Fadel, Marco Verani:
Modelling and numerical simulation of the polymeric extrusion process in textile products

17/2010 Alessandra Guglielmi, Francesca Ieva, Anna Maria Paganoni, Fabrizio Ruggeri:
A Bayesian random-effects model for survival probabilities after acute myocardial infarction

16/2010 Luca Formaggia, Anna Scotti:
Positivity and conservation properties of some integration schemes for mass action kinetics

15/2010 Alfio Quarteroni, Luca Formaggia:
Domain Decomposition (DD) methods

14/2010 Paola F. Antonietti, Lourenco Beirão da Veiga, Marco Verani:
A Mimetic Discretization of Elliptic Obstacle Problems

13/2010 G.M. Porta, Simona Perotto, F. Ballio:
A Space-Time Adaptation Scheme for Unsteady Shallow Water Problems

12/2010 Riccardo Sacco, Paola Causin, Paolo Zunino, Manuela T. Raimondi:
A multiphysics/multiscale numerical simulation of scaffold-based cartilage regeneration under interstitial perfusion in a bioreactor