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The regional distribution of in-hospital fatality among Acute Miocardial Infarction events in Italy

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Abstract

Aim of this paper is to investigate into the differences in the first treatment of Acute Myocardial Infarction (AMI) among Italian regional health care systems, by focusing on the regional distribution of in-hospital deaths. Starting from the theoretical care pathway (from the onset of the illness to hospitalization and recovery or possible death), the in-hospital deaths in each region are decomposed into the contributions of the attack rate, hospitalization and in-hospital fatality. The discrepancies in regional behaviour are investigated, in the aim to assess whether they can be attributed to different performances among Italian regions. The study is based on two data sources: hospital discharges, based on Diagnosis Related Groups (DRG) and provided by the Ministry of Health; death and population data by regions of residence, provided by the National Institute of Statistics.

keywords: Acute Myocardial Infarction, Fatality rates, Attack rates, Hospitalization rates.

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1. Introduction

Among the coronary heart diseases, Acute Myocardial Infarction (AMI, ICD9: 410) is characterized by high fatality level associated with a fast course of the disease. Consequently timeliness and appropriateness of the first treatment are fundamental for a positive recovery of the hospitalized patients. In Italy, Acute Myocardial Infarction is among the main causes of death in the resident population aged 45 and over (ISTAT, 2002, 2004). Many evidences have demonstrated that in Italy risk factors associated with the diffusion and severity of AMI have a geographical connotation: Giampaoli and Vannuzzo (1999), Celentano *et al.* (1999), Giampaoli, Panico *et al.* (2001). On the other hand the quality of first care treatments provided by the Italian National Health System should be homogeneously distributed.

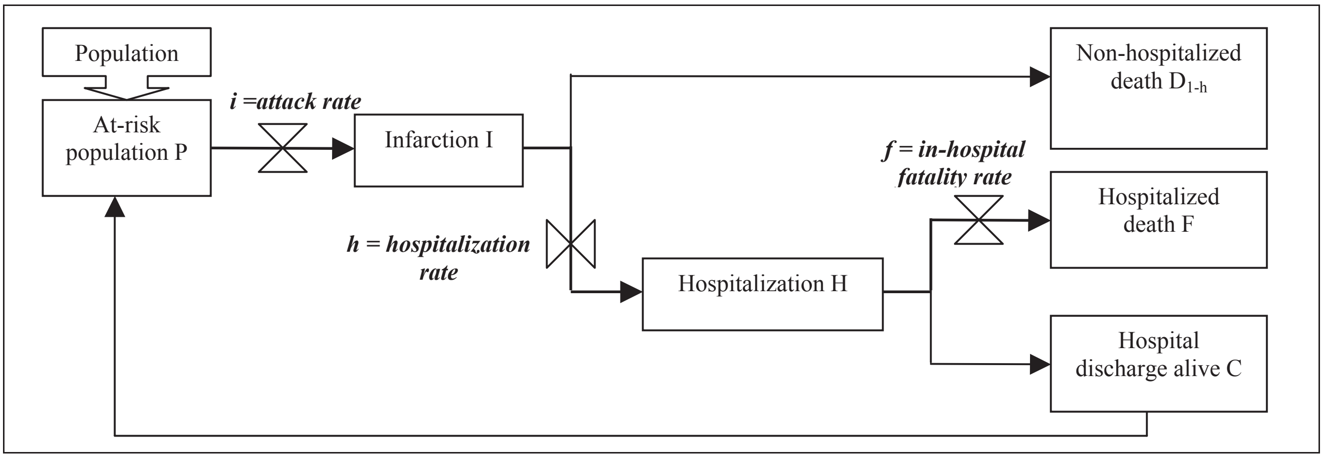
Aim of this paper is to investigate into the possible differences among Italian regional health care systems in the first treatment of AMI, starting from a theoretical care pathway: from the onset of the illness to hospitalization and recovery or possible death (in or out of hospital). In particular we investigate the geographical distribution of in-hospital fatality rate (defined as the ratio between the number of AMI fatal cases occurred in hospital and the total number of AMI hospitalizations) trying to assess whether the observed discrepancies can be attributed to different regional performances. The study is based on two data sources: hospital discharges, based on Diagnosis Related Groups (DRG) and provided by the Ministry of Health; death and population data by regions of residence, provided by the National Institute of Statistics.

The paper is structured as follows: section 2 illustrates the data main features and defines the indicators which will be used throughout the paper; section 3 presents the methods implemented to investigate the regional differences in the in-hospital fatality rate and to attribute the deviations of the in-hospital deaths from the Italian average to different components of the care pathway (morbidity, hospitalization, fatality); section 4 illustrates the main results of the decomposition method; and finally section 5 is devoted to the discussion and further developments.

2. Materials

Diagram 1 describes the pathway from infarction to hospitalization to recovery or death. It constitutes the frame of the decomposition method proposed in this paper.

Diagram 1: Acute Myocardial Infarction pathway



The National Institute of Statistics provides the number of deaths due to myocardial infarction occurred in Italy during the years 1999 and 2000 and the corresponding Italian population at January 1st 2000. Deaths and population data are stratified by sex, region (region of death and region of residence) and age group. The age groups considered for the analysis are: 45-64, 65-74, 75+ and 45+ years, being the number of myocardial infarctions occurring in young women and men below age 45 negligible.

The Ministry of Health supplies the number of hospital discharges (either dead or alive) with myocardial infarction diagnosis, which are collected for administrative purposes by the hospitals through individual discharge cards and then sent to the Ministry of Health. These data are based on Diagnosis Related Groups (DRG), a prospective payment system for hospital care. Patients hospitalized for myocardial infarction can be assigned to three different DRGs: DRG 121 (AMI without cardiovascular complication, discharged alive); DRG 122 (AMI with cardiovascular complication, discharged alive); DRG 123 (AMI discharged dead). Besides information on the DRG, the discharge card contains variables at individual level concerning demographic aspects (age, sex, residence and marital status of the patient) and clinical aspects (length of hospital stay, diagnosis, therapy and vital status). Hospital discharges subdivided into dead and alive patients with myocardial infarction diagnosis refer to the years 1999 and 2000 and are stratified by sex, region of hospitalization and age group (the same age groups as for deaths and population data). Hospital discharges are collected for administrative purposes, and present some limitations when used in epidemiological studies. To this regard we make the following assumptions:

a) due to the organization of the hospital discharge database, the same event could be counted more than once (multiple discharges). In order to correct for this bias, discharges of one day of length were excluded from the analysis;
b) follow-up information is not included in our data, therefore we count deaths after hospitalization as new cases;
c) data on population refer to population resident in the region, whilst data on hospitalizations and deaths refer to the population present in the region; being AMI an acute illness we suppose that interregional migration is negligible;
d) in-hospital deaths collected by the Ministry of Health are a subset of the total deaths collected by ISTAT, i.e. the reporting delay is negligible;
e) there are no regional differences in the data collection and recording;
f) silent events, intended as non-diagnosed non-severe infarctions, are not relevant for the evaluation of the quality and the timeliness of medical care assistance, therefore are ignored in our analysis.

The following indicators are particularly relevant to our study: the population mortality rate m is defined as the ratio of the total deaths by infarction over the relevant population; the attack rate i, is the ratio between the infarction cases (obtained as the sum of the hospitalized cases discharged alive and the total deaths) and the relevant population; the hospitalization rate h is the ratio between the number of hospitalized cases and the infarction cases; the in-hospital fatality rate f describes the mortality among the hospitalized infarction cases, i.e. the ratio between the deaths by infarction and the hospitalized cases. They can be computed as:

$$m = \frac{D}{P} \qquad i = \frac{(C+D)}{P} = \frac{I}{P} \qquad h = \frac{(C+F)}{(C+D)} = \frac{H}{I} \qquad f = \frac{F}{(C+F)} = \frac{F}{H} \tag{1}$$

where P is the relevant population (here the Italian residents aged 45+); $D=F+D_{1-h}$ is the total number of deaths by infarction, which includes the deaths inside the hospitals (F), and those outside (D_{1-h}); H is the number of hospitalizations by AMI. The number of infarction events I occurred in a population in a time period is estimated as the sum of the total number of deaths by infarction D and the number of hospital discharges (alive) by infarction C.

Table 1 provides the absolute figures and the age distribution of in-hospital deaths by infarction, derived from the DRG system and total deaths by infarction, provided by the National Institute of Statistics.

Table 1: Age distribution of deaths by AMI in Italy by sex and age. Years 1999-2000

	Males				Females			
age	in-hospital deaths	(%)	total deaths	(%)	in-hospital deaths	(%)	total deaths	(%)
45-64	564	*(13)*	4675	*(23)*	174	*(4)*	991	*(7)*
65-74	1135	*(27)*	6212	*(31)*	665	*(16)*	2739	*(19)*
75+	2512	*(60)*	9366	*(46)*	3372	*(80)*	10761	*(74)*
45+	**4211**	*(100)*	**20253**	*(100)*	**4211**	*(100)*	**14491**	*(100)*

Different indicators provide different insights into the phenomenon: in the years 1999-2000 every 10,000 males of age 45 and over (here indicated as 45+) there were about 54 AMI events, of which 40 were hospitalized, 4 died in hospital and 13 out of hospital; in the same period every 10,000 women there were about 25 AMI events, of which 17 were hospitalized, 3 died in hospital and 7 out of hospital. Tables 2 and 3 describe in more details the relevant regional rates, which are standardized by age.

Table 2: Age-adjusted attack (i) and mortality (m) rates x 10,000 by sex and Italian regions.

Year 1999-2000; age 45+

	Males		Females	
Italian regions	i	m	i	m
Piemonte & Val d'Aosta	44	16	21	10
Lombardia	51	18	26	11
Trentino Alto Adige	65	27	32	14
Veneto	53	20	28	12
Friuli Venezia Giulia	56	18	29	12
Liguria	56	18	25	10
Emilia Romagna	58	19	27	11
Toscana	54	15	26	9
Umbria	57	19	29	12
Marche	56	16	25	10
Lazio	54	19	24	11
Abruzzo	58	17	25	10
Molise	56	21	24	11
Campania	64	20	27	12
Puglia	46	15	22	9
Basilicata	42	17	19	9
Calabria	52	15	21	9
Sicilia	58	18	25	10
Sardegna	51	19	21	10
ITALIA	**54**	**18**	**25**	**11**

Table 3: Age-adjusted hospitalization (h) and in-hospital fatality (f) rates x 100 by sex and Italian regions. Years 1999-2000; age 45+

	Males		Females	
Italian regions	h	f	h	f
Piemonte & Val d'Aosta	72	10	67	19
Lombardia	73	10	70	17
Trentino Alto Adige	68	12	72	22
Veneto	73	12	72	20
Friuli Venezia Giulia	75	9	72	18
Liguria	78	12	76	23
Emilia Romagna	77	12	74	22
Toscana	79	9	79	17
Umbria	73	10	71	17
Marche	78	9	76	19
Lazio	73	12	69	21
Abruzzo	75	9	72	17
Molise	65	7	62	14
Campania	71	6	61	12
Puglia	71	6	65	11
Basilicata	63	6	54	6
Calabria	74	6	66	13
Sicilia	71	5	63	8
Sardegna	69	8	65	18
ITALIA	**74**	**9**	**70**	**18**

Looking at the regional distribution of these indicators some interesting features are apparent: among people of age 45+ (Table 2), as well as among people of age 75+ (Fig. 1 and 2) there are regional differences in mortality and attack rates but no specific regional trends; on the other hand the regional distribution of in-hospital fatality rates among people of age 45+ (Table 3) ranges from 5% in Sicilia to 12% in Trentino Alto Adige, Veneto, Liguria, Emilia Romagna and Lazio, among men; and from 6% in Basilicata to 23% in Liguria, among women, revealing a South-North gradient. This pattern requires further investigation.

Fig. 1: Attack rate x 10,000 in Italian regions. Years 1999-2000; age 75+

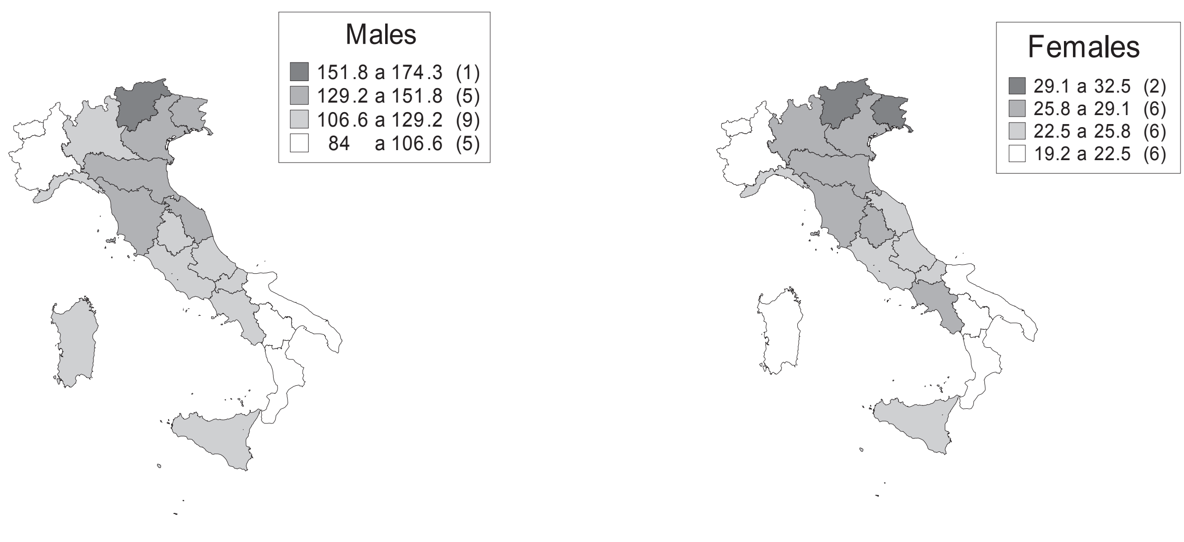
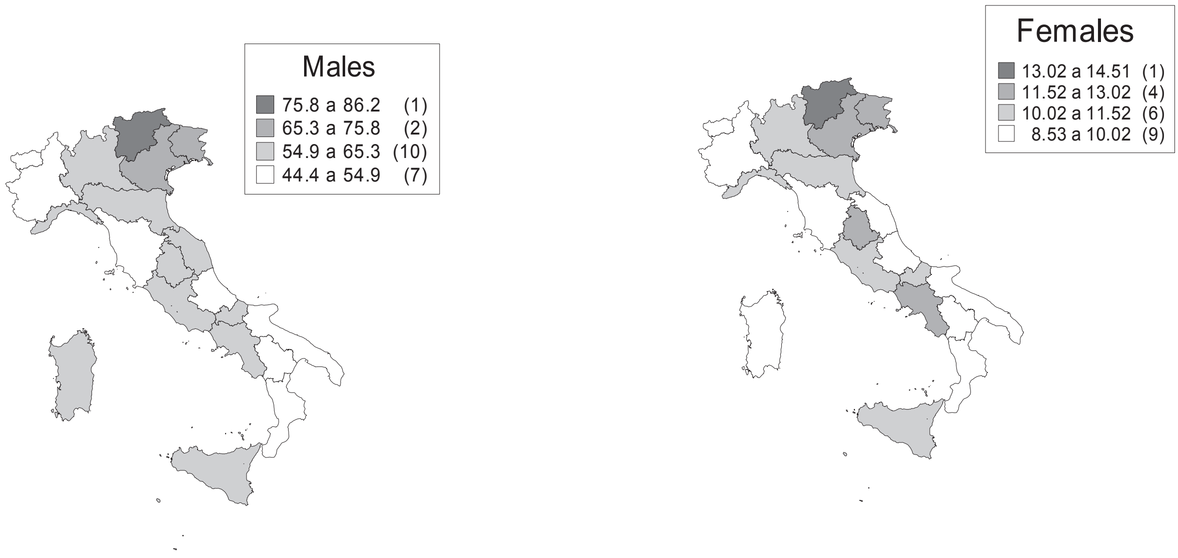


Fig. 2: Mortality rate x 10,000 in Italian regions. Years 1999-2000; age 75+



3. Methods

We use here a statistical method, the Statistical Process Control (SPC), which was proposed in the 1930's by the physicist Walter A. Shewhart (1931), and much more recently adapted to healthcare evaluation. In Shewhart approach variation is categorized according to the action needed to reduce it: common-cause variation, which is intrinsic to the process, and special-cause variation, which is the result of factors extrinsic to the process. To discriminate between the two sources of variation a simple graphical method -the control chart- is developed: the mean of the process is plotted together with the upper and lower control limits; if the corresponding data point lies within the limits it is accepted, but if it falls outside the control limits, a special-cause variation is suggested and further investigation is required. The value proposed by Shewhart for the control limits is +/- 3 σ, where σ is a variability measure - an empirical adaptation of the large sample Normal approximation.

We assume that i) the reference in-hospital fatality rate is the Italian one; ii) the regional in-hospital deaths are binomial outcomes with probability f of realization in H_r hospitalizations. Then for each region r σ_r is:

$$\sigma_r = \frac{f \times (1 - f)}{H_r}$$

Figures 3a and 3b illustrate the situation for males and females, where the vertical bars represent the +/- 3 σ_r control limits. We observe that some Northern and Central regions (Trentino Alto Adige, Veneto, Liguria, Emilia Romagna and Lazio – and also Lombardia for men) are above the upper control limit, while some Southern regions (Sicilia, Calabria, Campania and Puglia – and also Basilicata for women) are below the lower control limit.

Fig. 3a: Regional distribution of in-hospital fatality (%).
Years 1999-2000; age 45+; Males

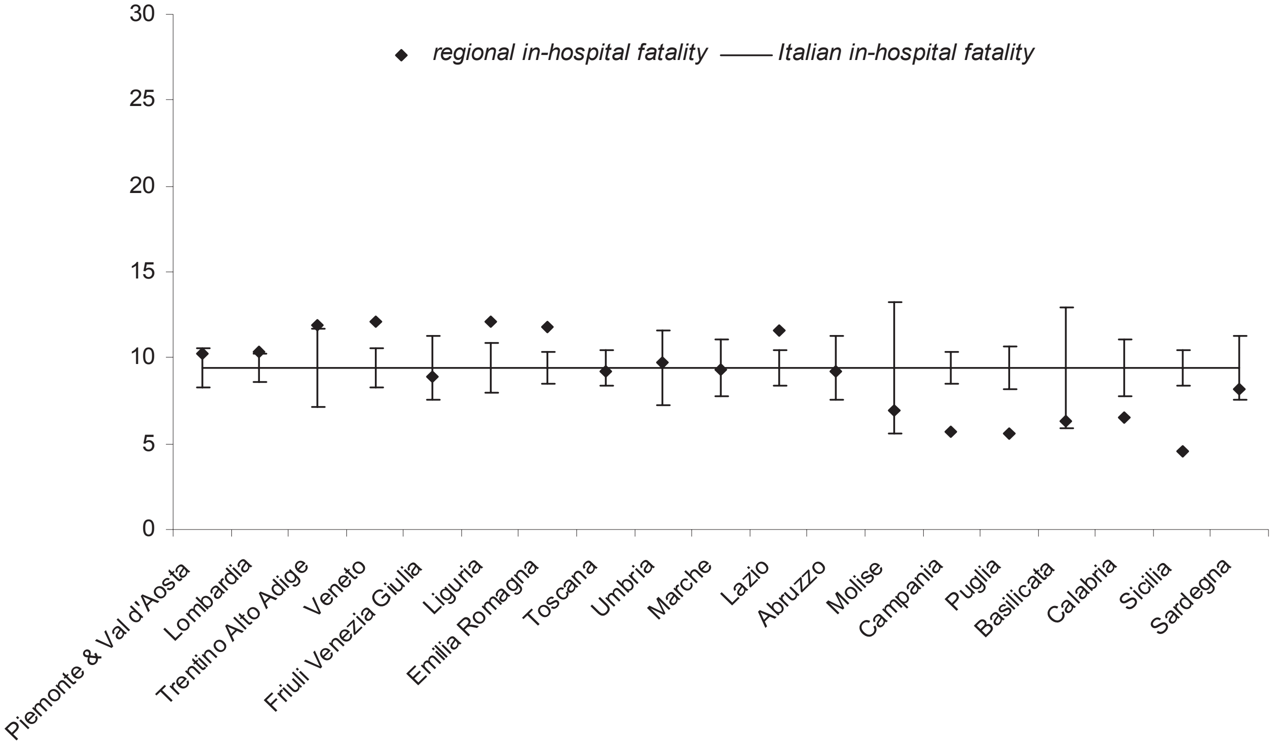
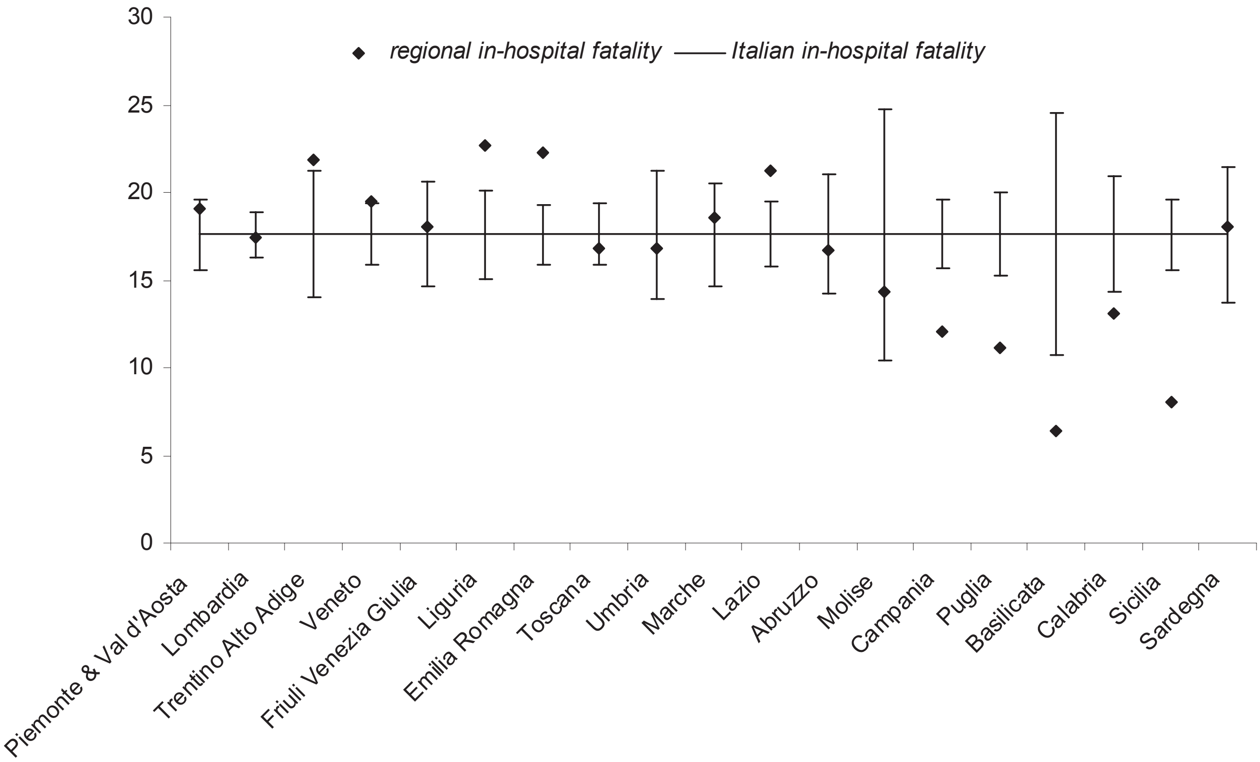


Fig. 3b: Regional distribution of in-hospital fatality (%).
Years 1999-2000; age 45+; Females



This geographical trend could be related to regional discrepancies in the process of the disease occurrence (from risk factors exposure to in-hospital death). The process approach illustrated in Diagram 1 allows us to decompose the in-hospital deaths F into the product of three conditional probabilities:

$$F = P \times \Pr(Infarction \mid population) \times \Pr(Hospitalization \mid Infarction) \times \Pr(Inhospital.death \mid hospitalization) \qquad (2)$$

By using the definitions (1) we apply (2) to region *r* and obtain a decomposition of the in-hospital deaths F_r for each Italian region:

$$F_r = P_r \times i_r \times h_r \times f_r .$$

In order to obtain the standardized number of deaths by infarction in the hospitals of region r $\left(\overline{F_r}\right)$, we substitute the regional rates with the corresponding average Italian rates:

$$\overline{F_r} = P_r \times \bar{i} \times \bar{h} \times \bar{f} .$$

Thus, we are able to compare the regional performances in terms of the deviation of the in-hospital deaths in region r from the corresponding standardized value:

$$F_r - \overline{F_r} = P_r \times \left(i_r \times h_r \times f_r - \bar{i} \times \bar{h} \times \bar{f}\right). \qquad (3)$$

By setting

$$i_r = \bar{i} + \Delta i_r \qquad h_r = \bar{h} + \Delta h_r \qquad f_r = \bar{f} + \Delta f_r$$

(3) becomes:

$$F_r - \overline{F_r} = P_r \times \left\{\left(\bar{i} + \Delta i_r\right) \times \left(\bar{h} + \Delta h_r\right) \times \left(\bar{f} + \Delta f_r\right) - \left(\bar{i} \times \bar{h} \times \bar{f}\right)\right\}. \qquad (4)$$

After developing the inner products, the deviation of the regional in-hospital deaths from the corresponding standardized value decomposes into a series of 'single' and 'mixed' contributions, as shown in Table 4, whereby 'single' contribution means the contribution of a single regional gap in a specific rate (i.e. hospitalization rate) while the other two rates (i.e. attack rate and in-hospital fatality rate) are supposed equal to the Italian average; 'mixed' contribution means the contribution of two or three regional rates at the same time.

Table 4: Components of the regional deviations from standardized in-hospital fatality

Single	Attack	$\Delta i_r \times \overline{h} \times \overline{f}$
	Hospitalization	$\overline{i} \times \Delta h_r \times \overline{f}$
	In-hospital Fatality	$\overline{i} \times \overline{h} \times \Delta f_r$
Mixed	Attack & Hospitalization	$\Delta i_r \times \Delta h_r \times \overline{f}$
	Attack & In-hospital Fatality	$\Delta i_r \times \overline{h} \times \Delta f_r$
	Hospitalization & In-hospital Fatality	$\overline{i} \times \Delta h_r \times \Delta f_r$
	Attack & Hospitalization & In-hospital Fatality	$\Delta i_r \times \Delta h_r \times \Delta f_r$

Let us define $\left(F_r - \overline{F_r}\right)_{(h)}$ the deviation (due to hospitalization (DDH)) of the in-hospital deaths from the standardized counterpart, when the regional attack and in-hospital fatality rates are supposed equal to the Italian rates. Equation (4) becomes:

$$(F_r - \overline{F}_r)_{(h)} = P_r \times \left\{\overline{i} \times \overline{f} \times (\overline{h} + \Delta h) - (\overline{i} \times \overline{f} \times \overline{h})\right\} = P_r \times \overline{i} \times \overline{f} \times (h - \overline{h}) . \qquad (5)$$

We can similarly proceed for the other two: deviation due to in-hospital fatality (DDF) as $\left(F_r - \overline{F_r}\right)_{(f)}$ and deviation due to attack (DDI) as $\left(F_r - \overline{F_r}\right)_{(i)}$.

4. Results

Fig. 4a and fig 4b illustrate, separately for men and women, how the difference between observed and expected in-hospital deaths in region *r* decomposes into the contributions due to attack, hospitalization and in-hospital fatality rates (here expected is used with the same meaning as standardized). The three bars represent the % contribution of each deviation, obtained as:

$$\%DDI = \frac{\left(F_r - \overline{F_r}\right)_{(i)}}{\overline{F_r}} \times 100$$

$$\%DDH = \frac{\left(F_r - \overline{F_r}\right)_{(h)}}{\overline{F_r}} \times 100$$

$$\%DDF = \frac{\left(F_r - \overline{F_r}\right)_{(f)}}{\overline{F_r}} \times 100$$

The numbers near the region names represent the total difference as obtained in (4). The % contributions can either be positive, if the regional rate is higher than the standardized one, or negative, vice versa. When the three contributions have the same sign the effects add up, and reinforce each other. When their signs are different the effects may cancel out, and the combined contribution becomes more difficult to evaluate.

In Northern and Central regions there is an excess of observed in-hospital deaths compared to the expected values, while in Southern regions the observed in-hospital deaths are fewer than the expected ones; the only exception being Piemonte & Valle d'Aosta, which behave like the Southern regions.

A closer look to the regions, which were found out of statistical process control, as highlighted in Fig.3a and 3b, reveals some common patterns and some exceptions. In particular in most of the Northern regions of interest (Trentino Alto Adige, Veneto, Liguria, Emilia Romagna) the excess of observed in-hospital deaths is a combination of excess due to attack rate, hospitalization and in-hospital fatality: more people are ill, more people go to hospital, more people die in hospital (and also outside). In Lombardia (males) and Lazio (both sexes) the excess of in-hospital deaths is due to an excess of in-hospital fatality only, while the other two components give a null or negative contribution: in spite of a lower number of people who become ill, and a lower number who are hospitalized, more people die in hospital (and also outside). In most of the Southern regions of interest (Puglia and Calabria both sexes, Basilicata and Sicilia females) there is an overall lack of observed in-hospital deaths, which is a combination of a lack due to attack rate, hospitalization and in-hospital fatality: less people become ill, less people are hospitalized, less people die in hospital (and also outside). Exceptions are Campania and Sicilia (males), where the lack of observed in-hospital deaths is a combination of negative contributions due to fatality and hospitalization and positive contribution due to attack rate: although more people become ill and die, less people are hospitalized and die in hospital.

Fig. 4a: Decomposition of difference between observed and expected in-hospital deaths. Years 1999-2000; age 45+; Males

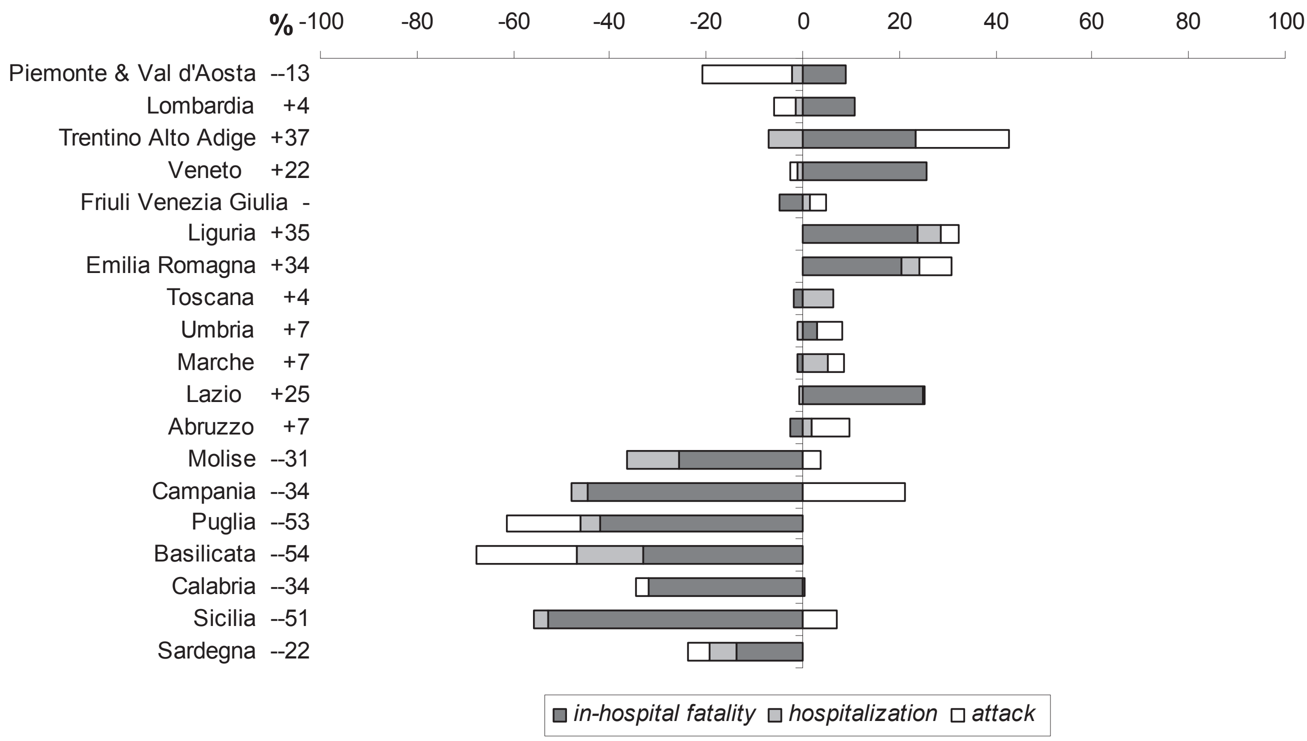
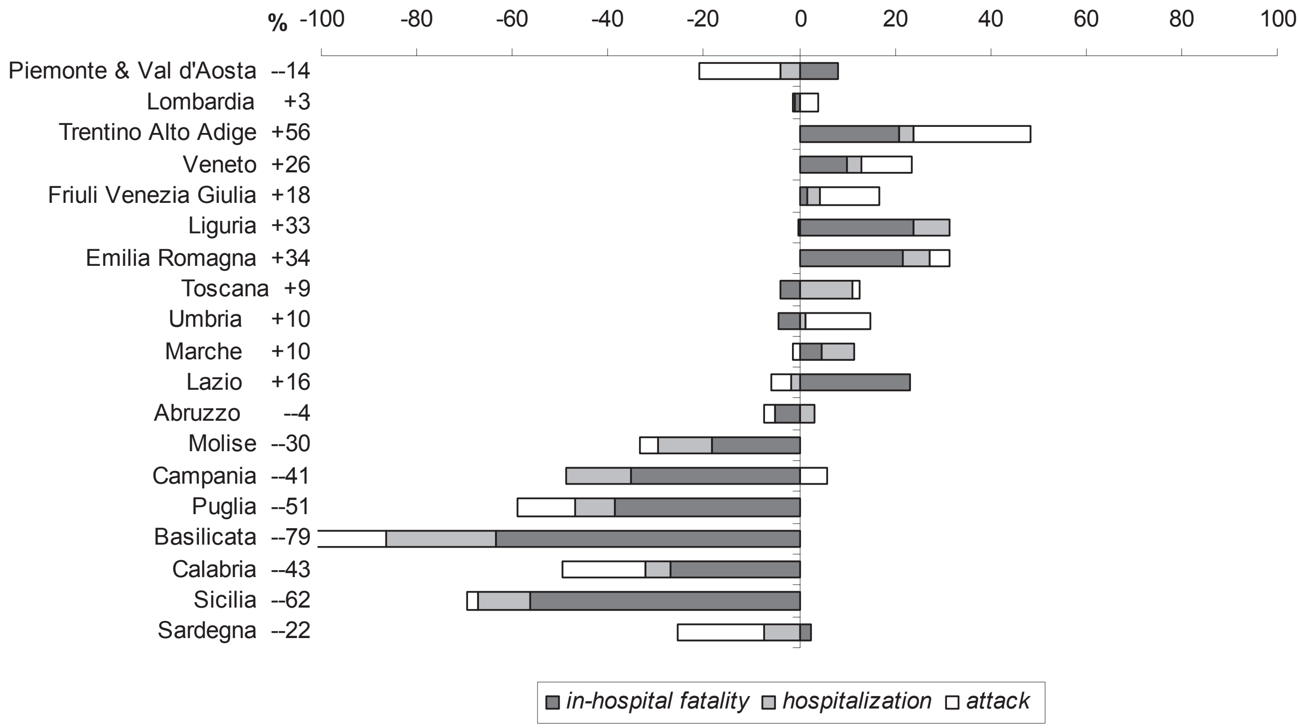


Fig. 4b: Decomposition of difference between observed and expected in-hospital deaths.
Years 1999-2000; age 45+; Females



5. Discussion

Several epidemiological studies have been conducted in the world involving patients with AMI: the largest and most relevant being the MONICA (Monitoring Trends and Determinants in Cardiovascular Disease) Project: data were produced from across the world with the scope of assessing the contribution of incidence, case fatality, trends in risk factors and advancement in coronary care towards the decline of mortality, which has been apparent since the late 70's. (Tunstall-Pedoe *et al*., 1999). Other large studies include OASIS (Yusuf *et al.,* 1998), the ENACT study (Fox *et al*., 2000), and the GRACE registry (Fox, 2000). More recently an attempt to define monitoring indicators and standardized methods for future data collection in the European Union has been established by the EUROCISS project (2003).

In Italy most epidemiological studies aim at investigating the causes and reducing the risk factors related to cardiovascular diseases: see, for example, Giampaoli and Vannuzzo (1999), Giampaoli, Panico *et al.* (2001); other works use the findings of the MONICA project to estimate the incidence and prevalence of major coronary events, including IMA: Ferrario *et al*. (2001), Giampaoli, Palmieri *et al*. (2001). A project aimed at establishing a national surveillance system for acute coronary and cerebrovascular events was initiated at the end of the 90's and the first results were available in the Italian Atlas of Cardiovascular Diseases: Giampaoli and Vannuzzo (2003), Giampaoli, Vannuzzo, *et al*. (2004); the Atlas contains estimates of fatal and nonfatal coronary events in 7 areas of the country, surveying about 4.5 million people for the years 1998 and 1999.

Our contribution is aimed at providing a tool for the evaluation of possible regional differences in Italy in the quality of care for AMI patients, by using information on in-hospital fatality. We found a South-North trend in the in-hospital fatality rates and tried to identify those regions "out of control" in terms of the Statistical Process Control (SPC) - a method that has received increasing interest in the healthcare community and is used to help improve clinical and administrative processes (Carey, 2003), to measure the variability of a process over time (Shahian *et al*., 1996), to compare performances, such as mortality rates, among different hospitals (Mohammed *et al*., 2001). Furthermore we tried to understand the causes for the different regional performances by looking at the entire care pathway from infarction to death (in or out of hospital) or recovery and proposed a method to attribute the in-hospital deaths to different causes: attack, hospitalization or in-hospital fatality rates.

Different conditions influence the survival and recovery of an AMI patient: the severity and suddenness of the event, where and when the heart attack occurs, the availability of assistance facilities nearby, the time lag between medical intervention and transportation to the hospital, and the prompt and correct routing at the hospital acceptance. Some of these factors have been estimated directly (hospitalization and attack rate), others have been neglected (severity of the illness and promptness of the intervention) because our data did not contain the relevant information (for example on risk factors). Therefore in drawing conclusions one must be cautious about various confounding factors, first of all the severity of the disease.

The use of DRG data in epidemiology has its advantages and disadvantages: administrative data are readily available, inexpensive to acquire, computer readable and typically encompass large populations (Iezzoni, 1997); on the other hand the DRG system can be prone to opportunistic features aimed to increase the reimbursement level of the hospital and this may cause incompleteness and inaccuracy of the data and misclassification of diagnoses (Mahonen *et al*., 2000).

Bearing these limits in mind, we have attained some general conclusions: in those Northern and Central regions where the observed in-hospital fatality is out of the upper control limit, the decomposition suggests a more frequent and severe illness, generally accompanied by a higher availability of hospitals. Exceptions are Lombardia and Lazio, where the combination of excess of in-hospital deaths and lack of infarction events and hospitalizations seems to suggest some inefficiencies in the hospital system. In most Southern regions where the number of in-hospital deaths is out of the lower control limit, the decomposition confirms a less frequent and less severe illness. Exceptions are Campania and Sicilia where, in spite of higher incidence and mortality rates, fewer people reach the hospital and fewer die in hospital, thus suggesting a selection of cases: only the less severe ones reach the hospital and then recover, the others die before reaching the hospital.

From the gender perspective the situation of the women is far worse: the in-hospital fatality is more than double that of the men. This result is consistent with the findings of several studies: in general males and females have different natural histories regarding AMI, the female's being a more aggressive form with a high mortality rate: Pimenta *et al.* (2001), Tofler *et al*. (1987), Greenland *et al*. (1991).

An interesting development of this work is the study of the correlation between in-hospital deaths and the distribution of emergency care departments, such as Coronary Care Units (CCU) and first care ambulances. The more reliable data regarding CCU refer to a survey carried out in the year 2000 among the Italian hospitals (Federazione Italiana di Cardiologia, 2003) about the availability of emergency structures. However the data refer to the availability of beds and not to their effective use and would allow only a rough comparison: more detailed information on their actual use and their geographical location (taking into account also the morphological differences in the territory) are needed in order to gather a wider and better picture. Moreover, the availability of the geographical distribution of the main risk factors, as a proxy of the severity of the disease, would allow us to better identify the influence of the quality of care on the outcome of the disease.

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