Relevance of statistical techniques when using administrative health data: gender inequality in mortality from cardio-vascular disease

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INTRODUCTION

In most health care systems, data are routinely collected at hospitals for financing purposes. In particular, the worldwide use of prospective *per case* financing schemes requires information on patients' characteristics to determine reimbursement levels (Busse et al., 2006). These data are of primary interest for researchers. They are routinely collected for all patients in all hospitals; the data collection is most often compulsory; hospitals have strong incentives to commit to a high-quality coding in order to get an adequate payment. Hence, large and exhaustive databases are available for in-patient discharges in several countries. However, these databases are not designed for research purposes but to quickly reveal the hospital profile without generating too much excess work. As a consequence, they cannot be compared to observational studies or clinical trials. There is thus a trade-off between using large but incomplete databases *versus* using detailed but small and often poorly representative ones.

The main difficulty of using administrative data for research is the insufficient information about patients' clinical characteristics. In the present paper, we examine the specific case of gender differences in in-patient mortality from cardio-vascular disease. We postulate that limitations of administrative databases can be overcome through a better understanding of how insufficient data bias results and can be compensated through appropriate statistical techniques. To do so, we rely on a large administrative database including all discharges for cardio-vascular diseases at all NHS Portuguese hospitals during the 2000-2006 period. Results from our dataset are compared to those obtained in the literature over the last 10 years in studies using detailed surveys and administrative data.

RATIONALE

Methodological issue

Suppose one seeks to estimate the impact of revascularization, either percutaneous coronary intervention – here-below PCI – or bypass surgery, on in-patient mortality. According to the literature, candidates for intervention are chosen based on a series of patients' characteristics. Let us quote, among others, age, ST-segment elevation on initial echocardiogram, medical history (previous diagnoses and interventions), severity on admission, and time from the onset of symptoms to hospital arrival (Vaccarino et al., 2005). However, administrative data are generally limited to the patient's age, sex, and primary and secondary diagnoses, which define the patient's Diagnosis Related Group (DRG) used to set payments. Hence, severity of disease – and, more generally, heterogeneity among patients – is imperfectly accounted for, leading to biased results. In addition, physicians' decisions depend on expected outcomes. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines indicate for example that, among AMI patients, PCI is appropriate when performed on patients with low mortality risk (<0.5%), and inappropriate when the risk is high (>=1%) (Epstein et al., 2003). In turn, mortality risk is related to severity of disease which is poorly observed in administrative databases.

Unless one succeeds in controlling for severity differences, two statistical problems occur which likely bias results on the impact of treatment on mortality: (i) selection bias due to treated and untreated patients experiencing different unobservable characteristics; (ii) endogeneity due to treatment decision being based on expected outcome related to unobserved characteristics. We are thus confronted to a classical problem of selection, but aggravated on the one hand by the treatment decision being endogenous to expected outcome, and the criteria to select into treatment being partially non-observable. If gender and unobserved severity are correlated, then the measurement bias will also affect the estimate of gender differences in mortality and treatment use.

Gender inequality in treatment and mortality

Over the last ten years, several studies have been produced to measure gender differences in treatment use for cardio-vascular disease and mortality. The Table 1 summarizes the result of a systematic survey on these topics for the 2000-2010 period. Studies are classified in two categories according to the population they consider (with or without AMI) and the risk-adjustors they include (detailed clinical factors, medical history, age and comorbidities).

Our search included studies that measured gender differences in in-patient mortality (several of them also measured gender differences in treatment). All selected studies were published in English in peer-reviewed journals in the year 2000 or after. We excluded the studies that constituted their cohorts based on interventions, restricting our search to cohorts based on disease (CHD and/or AMI). The search covered the PUBMED bibliographic databases. The following

terms were used in the search equation: ‘gender diff*’, ‘gender dispar*’, ‘sex diff*’, ‘gender bias’, ‘sex dispar*’, ‘cardio’, ‘coro*’, ‘myocardial’, ‘treatment’, ‘death, ‘mortality’. Finally, we also followed a snowball search, including references from the 10 most recent studies.

We observe on Table 1 that over the last ten years, most studies using detailed risk-adjustors do not find significant differences between men and women. Shaw et al. (2008) observe however a significant difference against women in patients with stable angina, Jneid et al. (2008) in patients with STEMI, and Reina et al. (2007) in patients with AMI. Note also that when age groups are distinguished, younger women experience worse outcome than younger men (Vaccarino et al., 1999, 2009, Simon et al., 2006).

Fewer studies have been carried using administrative data. Four in seven studies found that women have an excess risk of death and one found that this excess is limited to younger women. However the number of studies is quite small, precluding the possibility to draw robust conclusions, studies using administrative data seem more prone to find significant gender differences than do studies using detailed clinical data.

METHODS AND DATA

Formally, the problem can be set as follows. We model the probability of death from cardio-vascular disease, m_i, as a function of receiving treatment, t_i, the patient’s gender, g_i, and other individual characteristics denoted by x_i, as a probit model:

$$m_i^* = \alpha_0 + \alpha_1 t_i + \alpha_2 g_i + \alpha_3 x_i + \varepsilon_i \quad (1)$$

m_i = 1 if $m_i^* > 0$

= 0 otherwise

The probability of receiving treatment is also a binary dependent variable that can also be modeled as a probit model:

$$t_i^* = \beta_0 + \beta_1 t_i + \beta_2 g_i + \beta_3 x_i + \mu_i \quad (2)$$

t_i = 1 if $t_i^* > 0$

= 0 otherwise

This has been the classical way to deal with this issue, i.e., treating both equations as separate (generally assuming a logistic instead of a normal distribution). The presence of endogeneity would however imply that error terms are correlated, which we do assuming a joint distribution of error terms, i.e. $(\varepsilon_i, \mu_i) \sim \mathrm{N}(0, \Omega)$. This boils down to adopting a bivariate probit modeling approach.

This model differs from the traditional one in that the treatment variable appears in the first equation, which renders the model recursive. However, the model

cannot be assimilated to a simultaneous-equation model because otherwise we would have mortality appearing as explanatory variable in equation (2). This is not the case because obviously treatment is not influenced by mortality, but well by unobservable factors that influence the probability of death and also that of treatment (e.g. the risk factors identified in the ACC/AHA guidelines). As noted by Jones et al. (2006) in a different context, we face an unobservable heterogeneity bias rather than a simultaneous equations bias. Following these authors, this allows us to adopt a type II approach appropriate to the use of a recursive model – treatment influences mortality and not the mortality-based propensity to be treated. The following method is thus inspired on Jones et al. (2006).

The complete model is one where error terms of equations (1) and (2) depend on unobservable factors:

$$\varepsilon_i = \rho_1 \nu_i + \delta_{i1}$$

and

$$\mu_i = \rho_2 \nu_i + \delta_{2i}$$

This model is estimated using a Full Information Maximum Likelihood (FIML) estimator (see Jones, 2000). If we denote by ρ the correlation coefficient between ε_i and μ_i, then the statistical significance of ρ will allow detect the presence of endogeneity.

We studied patients admitted for cardio-vascular disease at NHS hospitals in Portugal for the 2000-2006 period. Data were provided by the Central Authority for Health Services ("Autoridade Central de Serviços de Saúde", ACSS), a state agency that collects data on in-patient discharges from medical records for administrative purposes. Since cardio-vascular diseases are mostly treated at NHS hospitals, this offers us an exhaustive data set representative of national patterns of treatment.

The following principal diagnosis were selected (using codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification*, ICD-9-CM): AMI (410.xx), stable (411.1x) or unstable angina (413.0x, 413.1x and 413.9x), chronic ischemic heart disease (414.xx), congestive heart failure (428.xx), hypertensive heart disease with congestive heart failure (402.91) and chest pain (786.5x). Transfers to another acute care facility and patients admitted at hospitals not equipped to perform high-technology procedures are excluded, since we cannot follow patients across admissions. Our final sample includes 255,953 discharges from 59 hospitals (40.0 percent women, 60.0 percent men). We also analyse two sub-samples, including patient with the highest severity of disease (acute myocardial infarction, 64,546 discharges) and the lowest severity of disease (stable angina, 17,600 discharges).

We first model the impact of gender on in-patient mortality using a probit multivariate model, following equation (1). The treatment variable, t_i, is represented by revascularization procedures, i.e PCI and stents (ICD-9-CM procedure codes 36.01, 36.02, 36.05 and 36.06), and coronary artery bypass

graft (ICD-9-CM procedure codes 36.03, 36.1, 36.2). The other patient characteristics, x_i, are represented by a series of risk factors, including age, comorbidities, and year of admission. Then in-patient mortality is modeled using a bivariate probit modeling approach, estimating jointly equations (1) and (2). Treatment is modeled in equation (2) as a function of gender and other patient characteristics that are the same as those used in equation (1). In order to avoid identification problems, we include hospital dummies in the treatment equation (equation (2)). Estimations are performed first for the complete sample, and then separately for patient with AMI and stable angina.

RESULTS

On Table 2, we observe that women are more likely to die and less likely to be treated. They are older on average and more prone to suffer from all comorbidities but malignancy. Using the probit model, we observe no significant gender differences in in-patient mortality for the whole sample (Table 3) and stable angina (Table 5). By contrast, women are more likely to die after AMI (Table 4). Using the bivariate model, men are now significantly more likely to die than women, for the all sample and for women with stable angina. For patients with AMI, gender differences are no more significant. The use of the bivariate model shows that, when accounting for unobserved heterogeneity, outcomes are less favorable for men.

For all samples, we observe that the impact of treatment in reducing mortality risk is much smaller in magnitude using the probit model than using the bivariate model. The correlation coefficient ρ is positive significant, which indicates the presence of endogeneity. On average, treatment is more provided to high risks, hence the impact of treatment is under-estimated using the probit model. When accounting for selection, revascularization reveals more effective. As women are on average more severely affected than women, accounting for selection also reduces (resp. increases) the pro-men (resp. pro-women) gender gap.

The Table 6 displays the predicted mortality rates for men and women using the different models, with all other variables set at their mean value. For all patient types, we observe that women experience higher death rates in the unadjusted and probit models, and a lower death rate when using the bivariate model.

DISCUSSION

The use of administrative data on in-patient discharges is widespread in various domains of research on health services and health systems, and to design health policies. In particular, they have been increasingly used to build performance indicators, which are in turn used for benchmarking and design financing incentives (many examples are provided in Iezzoni, 2003). This obliges us to think carefully about the limitations of such databases in order to avoid biased conclusions with significant effects on practice. In particular, it is crucial to be aware of the insufficient information on individual characteristics. Iezzoni (2003) largely discusses this difficulty, how it may influence results and the methods to

reduce potential biases. This study presents an alternative strategy, based on econometric methods, and applies it to the study of gender differences in in-patient mortality from cardio-vascular disease.

Treatment decision is influenced by the mortality risk, which is itself affected by unobservable factors in administrative health data, namely detailed clinical information from diagnosis procedures. Selection into treatment and endogeneity, both related to unobserved heterogeneity, produce biased estimates. Indeed, our study indicates that results substantially differ according to whether controls for unobserved heterogeneity or not. As compared to the classical approach, controlling for unobserved heterogeneity dramatically increases the positive impact of treatment. Also, the women's excess mortality disappears, with a gender gap becoming unfavorable to men or non significant.

Treatment is more provided to those more at risk, hence the effect of treatment is under-estimated if one fails to appropriately measure risk or severity. As women are more severely affected than men at admission, the women excess mortality is over-estimated. The higher women's severity on admission has already been investigated, with several explanations, in particular related to a lower referral at earlier stages of disease. Women's disease is detected later, for several reasons mainly related to providers' views over cardiovascular disease in women and interpretation of symptoms (Schulman et al., 1999 and Arber et al., 2006). Other authors also argue that women have a different way to present their symptoms and a higher reluctance to undergo invasive procedures, although these hypothesis have not received empirical validation (Saha et al., 1999, Schecter et al., 1996). Finally, women are more severely affected when admitted because men are more likely to die before hospitalization (…).

As regards gender differences in mortality, relevant policy implications can be drawn. First, several authors justify the lower treatment of women due to their lower resistance to treatment (Vaccarino et al., 2003, Guru et al., 2006). This statement could be considered as valid had we not controlled for unobserved heterogeneity. This indicates one very concrete consequence of not dealing adequately with bias of administrative health data. Second, other authors state that women are discriminated either at earlier stages of disease through lower referral (McKinlay., 1996) or during admission through lower treatment. Our analysis does not reject any of these statements, as women appear as more severely affected at admission (hence more likely to die) and however less treated even controlling for unobserved heterogeneity.

TABLES

Table 1. Published studies 1999-2009 on gender differences in in-patient or short-term (<=30 days) death.

Authors	Population[1]	Gender differences[2]
Detailed risk-adjustment[3]		
Alfredsson, 2009	NSTEMI	None
Berger, 2009	STEMI	None
	NSTEMI	None
	Unstable angina	Men+
Vaccarino, 2009	AMI	None for age>=55 Women+ for age<55
Zimmermann, 2009	STEMI	None
Jneid, 2008	AMI	None
	STEMI	Women+
Moriel, 2008	ACS	None
Setoguchi, 2008	MI	Men+
Shaw, 2008	Stable angina	Women+
	ACS	None
Alfredsson, 2007	NSTEMI	None
Radovanovic, 2007	ACS	None
Reina, 2007	AMI	Women+
Koek, 2006	AMI	None
Simon, 2006	AMI	None for age>=67 Women+ for age<67
Martinez-Salles, 2005	AMI	None
Vaccarino, 2005	MI	None
De Gevigney, 2001	AMI	None
Barakat, 2000	AMI	None
Bowker, 2000	ACS	None
Gan, 2000	AMI	None
Hochman, 1999	STEMI	None
	NSTEMI	None
	Unstable angina	Men+
Scirica, 1999	Unstable angina	None
Vaccarino, 1999	AMI	None for age>=75 Women+ for age<75
Non-detailed risk-adjustment[3]		

Fang, 2006	AMI	Women+
Hollenbeak, 2006	AMI	None
Milcent, 2006	AMI	Women+
Perers, 2005	ACS	Women+
Nicolau, 2004	AMI	None
Canto, 2002	AMI	Women+
MacIntyre, 2001	AMI	None for age>=75 Women+ if age<75

[1]ACS: Acute Coronary Syndrome, including Non-ST Elevation Myocardial Infarction (NSTEMI) or unstable angina and ST Elevation Myocardial Infarction (STEMI).

[2]"Women+": women are significantly more likely to die; "men+" : men are significantly more likely to die; "none": no significant differences between men and women.

[3]Detailed risk-adjustment means that gender differences are risk-adjusted for detailed clinical factors from NIT (Q-waves, ST-segment elevation) or CATH (location and extent of disease - percentage diameter stenosis - , ejection fraction, number of affected vessels), and/or medical history (diabetes, hypertension, prior myocardial infarction, hypercholesterolemia, angina, previous PCI or CABG, smoking habit).

Non-detailed risk-adjustment means that gender differences are risk-adjusted for factors commonly available in administrative data: comorbidities (congestive heart failure, pulmonary edema, shock, malignancy, cardiac dysrhythmia, acute or chronic renal insufficiency, or Charlson comorbidity index), socio-economic status (insurance status or education, and ethnicity or race), age.

Table 2. Patient characteristics

	Men, % (n=153,759)	Women, % (n=102,374)
In-patient mortality	7.41 (11,376)	11.88 (12,086)
Revascularization	28.43 (43,659)	13.65 (13,979)
Age (Mean, SD)	66.14 (12.60)	73.48 (11.68)
Comorbidities		
Congestive heart failure	7.23 (142,475)	9.03 (9,242)
Cardiac dysrhytmias	17.42 (26,755)	25.85 (26,464)
Cerebrovascular disease	4.20 (6,451)	5.45 (5,579)
Pulmonary edema	0.40 (615)	0.61 (622)
Diabetes with complication	3.92 (6,027)	6.13 (6,280)
Chronic renal failure	5.10 (7,829)	5.99 (6,130)
Acute renal failure	2.51 (3,850)	3.34 (3,420)
Malignancy	1.73 (2,651)	1.24 (1,268)
Shock	0.93 (1,422)	1.22 (1,248)

Table 3. Adjusted marginal effects for in-hospital death and revascularization use among patients – all sample[1].

	In-patient death		Revascularization use	
	Probit model	Bivariate model	Probit model	Bivariate model
Revascularization	-0.048*	-0.192**	.	.
Female	0.001	-0.023**	-0.084**	-0.014
Congestive heart failure	0.034**	0.014**	-0.083**	0.069**
Cardiac dysrhytmias	0.034**	0.008**	-0.102**	0.369**
Cerebrovascular disease	0.064**	0.053**	-0.057**	0.108**
Pulmonary edema	0.049**	0.028**	-0.084**	-0.036
Diabetes with complication	0.025**	0.011**	-0.050**	0.037
Chronic renal failure	0.034**	0.009**	-0.097**	0.026
Acute renal failure	0.133**	0.105**	-0.109**	0.517**
Malignancy	0.066**	0.027**	-0.124**	0.140**
Shock	0.662**	0.608**	-0.050**	1.649**
Pseudo-R2	0.186	(id)	0.127	(id)
rho	.	0.827**	.	(id)

Notes: [1]All regressions include 11 dummies for age groups and 5 dummies for year, which are not reported. *p-value<0.10**p-value<0.05.

Table 4. Adjusted marginal effects for in-hospital death and revascularization use among patients with acute myocardial infarction[1].

	In-patient death		Revascularization use	
	Probit model	Bivariate model	Probit model	Bivariate model
Revascularization	-0.082*	-0.277**	.	.
Female	0.010**	-0.003	-0.050**	-0.050**
Congestive heart failure	0.051**	0.016**	-0.125**	-0.129**
Cardiac dysrhytmias	0.098**	0.092**	-0.026**	-0.034**
Cerebrovascular disease	0.060**	0.025**	-0.113**	-0.116**
Pulmonary edema	0.016	-0.008	-0.094**	-0.100**
Diabetes with complication	0.036**	0.008	-0.090**	-0.090**
Chronic renal failure	0.023**	0.006	-0.066**	-0.072**
Acute renal failure	0.158**	0.144**	-0.040**	-0.047**
Malignancy	0.078**	0.033**	-0.126**	-0.126**
Shock	0.646**	0.568**	-0.002	-0.011
Pseudo-R2	0.229	(id)	0.126	(id)
rho	.	0.792**	.	(id)

Notes: [1]All regressions include 11 dummies for age groups and 5 dummies for year, which are not reported. *p-value<0.10**p-value<0.05.

Table 5. Adjusted marginal effects for in-hospital death and revascularization use – patients with stable angina[1].

	In-patient death		Revascularization use	
	Probit model	Bivariate model	Probit model	Bivariate model
Revascularization	-0.006**	-0.087**	.	.
Female	0.001	-0.011**	-0.067**	-0.067**
Congestive heart failure	0.011**	0.005	-0.079**	-0.082**
Cardiac dysrhytmias	0.022**	0.197**	-0.079**	-0.082**
Cerebrovascular disease	0.026**	0.037**	-0.039**	-0.042**
Pulmonary edema	0.015	0.024	-0.023	-0.021
Diabetes with complication	-0.001	-0.013*	-0.051**	-0.052**
Chronic renal failure	0.013**	<0.001	-0.097**	-0.097**
Acute renal failure	0.047**	0.056**	-0.082**	-0.086**
Malignancy	0.022**	0.013	-0.098**	-0.100**
Shock	0.585**	0.567**	-0.004	0.099
Pseudo-R2	0.230	(id)	0.081	(id)
rho	.	0.907**	.	(id)

Notes: [1]All regressions include 11 dummies for age groups and 5 dummies for year, which are not reported. *p-value<0.10**p-value<0.05.

Table 6. Adjusted in-hospital death rates.

	Men	Women	Difference
All sample			
Unadjusted model	7.41	11.81	4.4
Probit Model	5.85	5.95	0.10
Bivariate model	16.63	13.64	-2.99
AMI			
Unadjusted model	11.07	18.83	7.76
Probit Model	8.78	9.81	1.03
Bivariate model	13.87	13.57	-0.3
Stable angina			
Unadjusted model	1.74	2.66	0.92
Probit Model	0.87	0.94	0.07
Bivariate model	4.84	3.72	-1.12

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