Original Research

Spatial distribution of in- and out-of-hospital mortality one year after acute myocardial infarction in France

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ABSTRACT

Objective: To describe the spatial distribution of acute myocardial infarction (AMI) mortality in France in association with the socio-economic characteristics of the patient's place of residence.
Methods: In this population-based study, we included patients hospitalized for AMI identified according to ICD-10 codes, using data from the national health insurance database from January 1, 2013 to December 31, 2014. In- and out-of-hospital deaths were identified over a period of 1 year following the first hospital stay for AMI.
An exploratory analysis was performed to classify area profiles. The spatial analysis of AMI mortality was performed using a principal component analysis followed by an ascending hierarchical classification taking into account socio-economic data, access-time by road to coronary angiography, standardized in-hospital prevalence, and 1 year mortality.
Results: Over the 2 years, 115,418 patients were hospitalized with a diagnosis of AMI. Patients were a mean of 68 ± 15 years and most were men (68.5%). The overall mortality rate was 12.2% after 1 year. More than half of patients (65.5%) underwent an early revascularization procedure. The map of standardized 1 year mortality showed a geographic area of high mortality extending diagonally from north-east to south-west France. We identified 6 different area profiles with standardized mortality varying from 15.9 to 54.4 per 100,000 inhabitants. The spatial distribution of higher mortality was associated with lower socioeconomic levels. These findings were not associated with a lower access to coronary angiography.
Conclusion: There are considerable geographical differences in the prevalence of AMI and 1 year mortality. The spatial distribution of lower healthcare indicators follows the distribution of social inequalities. This study highlights the importance of focusing national policies on universally accessible prevention programs such as the promotion cardiac rehabilitation and healthy lifestyles.

1. Introduction

Ischemic heart disease is presently the primary cause of death in the developed world [1–3]. However, the management and prognosis of acute myocardial infarction (AMI) has improved considerably over the past two decades [4–6]. The reduction in mortality can be explained by improvements in the management of AMI, including more frequent use of revascularization procedures and better access to

angioplasty, better use of recommended drug treatments, and also changes in patient population characteristics [7]. Patients with ST-segment elevation myocardial infarction (STEMI) have a higher early mortality risk than patients with non-ST-segment elevation myocardial infarction (NSTEMI) [8]. STEMI outcomes are improved by a shorter access time to proper treatment [9,10]. As recommended by current European guidelines, time from first medical contact to balloon inflation should be less than to 2 h in any case and less than 90 min in

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patients presenting early (less than 2 h after symptom onset) with large infarct and low bleeding risk [11].

In this context, it is crucial for national healthcare systems to ensure optimal time and equal access to treatment. However, the uneven use of percutaneous coronary interventions (PCI) cannot be entirely explained by the location of facilities and service supply [12,13], and socioeconomic variables have been shown to influence patient access to PCI [14]. Previous studies have shown that income, education level and employment status have a direct effect on AMI mortality rates [15–19]. In particular, the decline in AMI mortality rate was lesser in low-income populations [20]. To our knowledge, these associations have not been studied in France on a national scale.

The objective of this study was thus to describe the spatial distribution of AMI mortality in France in relation to socio-economic status and the patient's place of residence.

2. Methods

2.1. Study population

2.1.1. Source of data

Data were extracted from the French National Health Data System (*Système National des Données de Santé*; SNDS). It contains data for all individuals covered by the French national health insurance system and can be used for epidemiological and public health purposes [21]. This database includes basic demographic data, visits to physicians, drugs dispensed in retail pharmacies, and date of death (in-hospital and overall). It also contains discharge abstracts (which capture administrative, clinical and demographic information on hospital discharge) from all public and private hospitals (*Programme de Médicalisation des Systèmes d'Information*; PMSI) including main and associated diagnoses encoded using the International Classification of Diseases (ICD-10) and procedures using the common classification system for medical procedures (CCAM). The quality of this database has previously been established [22], and it has been used to conduct epidemiological studies using the data of hospitalized patients in France [23–27].

2.1.2. Inclusion and exclusion criteria

All the hospital stays for patients presenting with a diagnosis of AMI recorded in the national SNDS databases in 2013 and 2014, whatever their age, were included. To avoid counting the same patient twice, only the first stay was included in our analysis. We excluded patients with a "transfer" admission, that is to say patients who stayed first in one establishment and then moved to a second establishment with a main diagnosis of AMI. We also excluded patients with a main diagnosis of AMI in the year before the inclusion in order to retain only incident cases.

2.1.3. Ethics

This study was approved by the National Committee for data protection (registration number 1889989) and the National health data institute (registration number 144) and therefore was conducted in accordance with the Declaration of Helsinki. Written consent was not needed for this study. The SNDS data were transmitted by the National Health Insurance Fund (*Caisse nationale d'assurance maladie*).

2.2. Collection of subject information

AMI was defined as an increase in serum troponin I and clinical symptoms of ischemia or characteristic ECG signs. AMI was selected with ICD-10 codes I21, I22 and I23. To avoid iatrogenic AMI, we selected patients with a main diagnosis of AMI. This approach was taken to specifically focus on patients who were hospitalized for acute myocardial ischemia and not those with AMI secondary to surgery, hypotension or other events after admission. For patients who were transferred during their management, the complete duration of the hospital stay was taken into account [28,29]. We also retrieved any information related to

STEMI, atrial fibrillation, revascularization, percutaneous coronary interventions (including transluminal angioplasty) and coronary artery bypass grafts that occurred during the AMI stay. Comorbidities were assessed with the Elixhauser or Charlson comorbidity index. We considered as severe AMI patients those with anterior infarction, cardiogenic shock, heart failure, or age older than 70 years.

In- and out-of-hospital deaths were identified over a period of 1 year following the first hospital stay for AMI. Our primary endpoint was overall mortality at one-year.

Access to angiography was dependent on the driving time to the closest healthcare facility providing coronary angioplasty. In France, percutaneous coronary intervention is regulated by the public authorities in order to ensure good training for emergency angioplasty and is only done in centers which are able to perform more than 350 angioplasty procedures per year [30,31].

We identified the patients' place of residence according to the PMSI geographic code registered in the SNDS data, which corresponds to their residential zip code. We categorized the PMSI geographic codes according to the typology established by the *Institut National de la Statistique et des Etudes Economiques* (INSEE), which is the French national census institute [28,32]. The INSEE classifies urban areas according to their level of urbanization and the number of jobs held in the area. We aggregated municipality data for the PMSI geographic codes and retained 4 categories: major urban centers, the suburbs of major urban centers, small and mid-sized centers and rural areas.

2.3. Ascertainment of death

We have detailed ascertainment of death in a previous paper [33]. France has an official registration of civil status that is held by municipalities and centralized within a national register where a national personal identity number is given at birth. All deaths have to be registered. For each death, the physician's certificate comprises two separable parts: one part which records the fact that the person has died, with nominative identification but no information on the cause of death; the second part is anonymous and bears the medical information. This medical part of the death certificate is transmitted to the relevant departmental administration of the Health Ministry, and then to the INSERM Epidemiology Centre for Causes of Death (CépiDC). The process of coding the causes of death includes verifying the information provided by the physician, coding it, and selecting the initial cause of death. This circuit guarantees the reliability of the data [34–36].

2.4. Statistical analyses

2.4.1. Patient characteristics

Patient characteristics were described and then compared between patients who were alive or not using Student's t-tests for quantitative variables and Chi2 tests for qualitative variables.

2.4.2. Mortality rates

The mortality rate included all deaths (in- and out-of-hospital) over a period of 1 year following the first hospital stay for AMI. We first calculated one-year mortality as the number of deaths/number of subjects included. We then calculated standardized mortality rates (SMR) at one year, adjusted on age and gender according to the structure of the population for each geographic code of France, per 100,000 inhabitants. It was standardized for age and gender according to the direct method using 2013 French census data from the INSEE as a reference.

2.4.3. Exploratory analysis: typology of the territories according to their socioeconomic and demographic structures related to mortality

The exploratory analysis consisted of a principal components analysis (PCA) followed by an ascending hierarchical classification (AHC) using Ward's step method bearing on several variables of interest at the scale of the 5637 PMSI geographic codes. The aim of AHC is to identify groups of

comparable individuals, or to partition individuals into several groups based on common traits. The AHC, conventionally used in other medical specialties, maximizes homogeneity among the clusters produced by classification and maximizes the heterogeneity between them. Applying an AHC to the PCA results can lead to more stable groups. Thus, the AHC, in this study, consisted of a gradual aggregation of the geographic codes according to their similarity. This allowed us to predict the cluster of geographic codes according to the values taken by the predictive variables: proportion of each occupational category, of unemployed individuals, and of retired or pre-retired individuals aged 15–64 in the active population; proportion of the whole population aged less than 20 years, aged from 20 to 59 years and aged more than 60 years; travel time to the closest healthcare facility performing angioplasty; standardized rate of AMI mortality at one year and in-hospital prevalence of AMI per 100,000 inhabitants.

2.4.4. Multilevel analysis

To examine the association of travel-time to revascularization facility and overall mortality at one year, we performed a 2-level hierarchical model to account for socio-demographic factors and their variation among geographic codes. The first level concerned individual variables, and the second level took into account variables related to geographic codes. For the second level, we considered ecological indicators collected according to geographic code: a deprivation index (French Deprivation Index [Fdep]) built from some of the variables used in the spatial analysis to estimate socioeconomic status [37], and a spatial accessibility indicator (Local Potential Accessibility [LPA]) to account for the multiple dimensions of access to general practitioners, nurses, and pharmacists [38]. Due to numerous correlations, the adjustment was done on gender, atrial fibrillation, percutaneous transluminal angioplasty, coronary artery bypass graft, STEMI, severe AMI, Fdep and LPA.

SAS 9.4 software was used for all analyses. GIS (Geographic Information System) MapInfo 11.0 was used for the cartography.

3. Results

3.1. Characteristics of the study population

The characteristics of the patients admitted for AMI in 2013 and 2014 in France are presented in Table 1. Over the 2 years studied, 115,418 patients were hospitalized with a diagnosis of AMI. Among them, 86,817 (76.1%) were STEMI. The mean age of patients with AMI was 68 ± 15 years, and most were men [79,112 (68.5%)]. The overall mortality rate was 12.2% (in-hospital mortality: 11.5%) within 1 year (Fig. 1), and most deaths (70.6%) occurred within 30 days of AMI. More than half of the population (65.5%) underwent early revascularization, consisting of 74,636 (64.7%) percutaneous coronary interventions (including transluminal angioplasty) and 1007 (0.9%) coronary artery bypass grafts. Nearly 45% of patients had several comorbidities, with an Elixhauser comorbidity index or Charlson comorbidity index equal or greater than 2.

Compared with patients alive one year after AMI (Table 1), deceased patients were older and more likely to be STEMI, to have had severe AMI, comorbidities or atrial fibrillation (p < 0.01 for all). They also lived more in small and mid-sized centers or in rural areas. On the contrary, they had less revascularization and were less likely to be men (p < 0.01 for all). Access to coronary angiography (Table 2) was a little bit higher for patients who died than for surviving patients (average of 31 min vs 29 min, p < 0.01).

3.2. Spatial characteristics of AMI

Spatial analyses were conducted among patients living in metropolitan France (European France including Corsica but excluding overseas territories), and the 3102 (2.7%) patients living in overseas French territories were excluded. Most AMI patients live in major urban centers (63,188; 56.3%) and the suburbs of those major centers (24,321; 21.7%).

Table 1

Description and comparison of the characteristics of patients admitted for acute myocardial infarction from 2013 to 2014 in France (n = 115,418).

	Population	Deceased at one year	Alive at one year	p-value
	N = 115,418	N = 14,032 (12.2%)	N = 101,386	
	mean±SD	mean±SD	mean±SD	
Age	68±15	79±12	66±15	<0.01
	n (%)	n (%)	n (%)	
Men	79,112 (68.5%)	7687 (54.8%)	71,425 (70.5%)	<0.01
STEMI	86,817 (76.1%)	11,404 (83.1%)	75,413 (75.1%)	<0.01
Atrial fibrillation	13,505 (11.7%)	3066 (21.9%)	10,439 (10.3%)	<0.01
Severe AMI	75,954 (65.8%)	12,946 (92.3%)	63,008 (62.2%)	<0.01
Percutaneous transluminal angioplasty	67,183 (58.2%)	4579 (32.6%)	62,604 (61.8%)	<0.01
Coronary artery bypass graft	1007 (0.9%)	101 (0.7%)	906 (0.9%)	0.04
Other percutaneous coronary intervention	7453 (6.5%)	733 (5.2%)	6720 (6.6%)	<0.01
Charlson comorbidity index				<0.01
0-1	61,071 (52.9%)	4661 (33.2%)	56,410 (55.6%)	
2	29,448 (25.5%	3892 (27.7%)	25,556 (25.2%)	
3	12,514 (10.8%)	2178 (15.5%)	10,336 (10.2%)	
≥4	12,385 (10.7%)	3301 (23.5%)	9084 (9.0%)	
Elixhauser comorbidity index				<0.01
0	31,704 (27.5%	2485 (17.7%)	29,219 (28.8%)	
1	30,741 (26.6%)	2669 (19.0%)	28,072 (27.7%)	
2	23,547 (20.4%)	2770 (19.7%)	20,777 (20.5%)	
3	14,458 (12.5%)	2417 (17.2%)	12,041 (11.9%)	
≥4	14,968 (13.0%)	3691 (26.3%)	11,277 (11.1%)	
Areas				<0.01
Major urban centres[a]	63,188 (56.3%)	7454 (54.3%)	55,734 (56.7%)	
Suburbs of major centres[a]	24,321 (21.7%)	2871 (20.9%)	21,450 (21.8%)	
Small and mid-sized centres[a]	10,801 (9.6%)	1493 (10.9%)	9308 (9.5%)	
Rural areas[a]	13,759 (12.3%)	1922 (14.0%)	11,837 (12.0%)	

[a] Among metropolitan France (N = 112,496); Missing data = 247 (0.2%).

At the scale of geographic codes (Fig. 2), the map of standardized in-hospital prevalence of AMI revealed clusters with higher prevalence, notably a geographic diagonal following a north-east/south-west axis. Similarly, the spatial distribution of the standardized mortality rate shows higher mortality on a north-east/south-west diagonal line. Higher mortality was also found in the south of Normandy. A lower mortality rate after AMI was observed in the southeastern part of France (Fig. 2).

Spatial distribution of higher overall mortality did not differ for only severe AMI (patients with anterior infarction or cardiogenic shock or heart failure or age older than 70 years) and only STEMI.

The overall mean travel time to the closest facility offering angioplasty was under 30 min. Patients living in small and mid-sized centers as well as rural areas had longer access times with a mean of nearly 60 min.
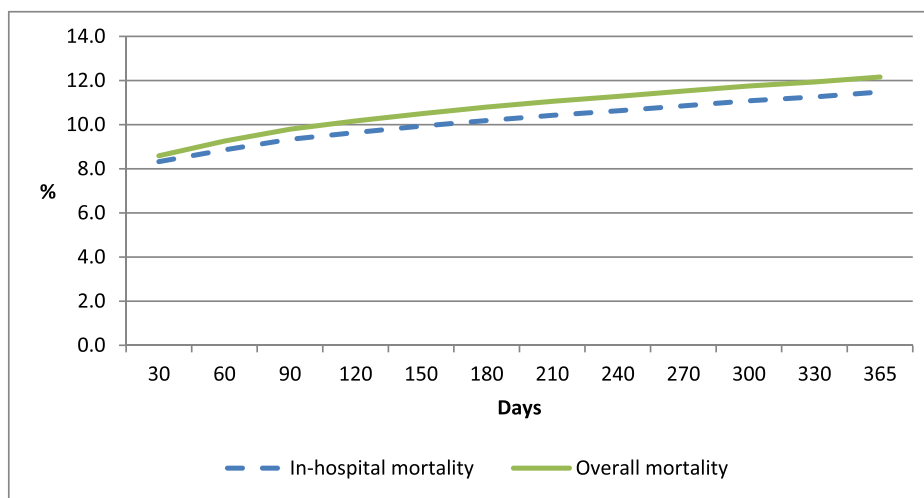
Fig. 1. Cumulative rate of in-hospital mortality and overall mortality (in- and out-patient death) at one-year following acute myocardial infarction, 2013–2014.

Table 2
Description and comparison of access to coronary angiography for patients admitted for acute myocardial infarction from 2013 to 2014 in metropolitan France (n = 112,496).

	Population	Deceased at one year	Alive at one year	p-value
	N = 112,079	N = 13,740	N = 98,339	
Mean±SD	29±26	31±27	29±26	<0.01
Median [Q1-Q3]	21 [6–46]	25 [7–49]	21 [6–45]	
By quartile*				<0.01
Lowest quartile	29,088 (25.9%)	3360 (24.4%)	25,728 (26.2%)	
Second quartile	26,987 (24.1%)	3048 (22.2%)	23,939 (24.3%)	
Third quartile	28,703 (25.6%)	3585 (26.1%)	25,118 (25.5%)	
Highest quartile	27,301 (24.4%)	3747 (27.3%)	23,554 (24.0%)	
Dummy variable				
>21 min	56,004 (50.0%)	7332 (53.4%)	48,672 (49.5%)	<0.01
>90 min	3132 (2.8%)	435 (3.2%)	2697 (2.7%)	<0.01

Missing data = 247 (0.2%); * Lowest quartile: [0–6], Second quartile:]6–21], Third quartile:]21–46], Highest quartile:]46–163].

The access time in most French territories was less than 90 min except for some mountainous areas (Alps, Pyrenees, Massif Central and Jura), western Normandy and the north-eastern regions (Fig. 3).

3.3. Socio-residential and spatial analysis of AMI mortality

Table 3 presents the results of the ascending hierarchical classification using PMSI geographic codes and the characteristics of each cluster. The spatial distribution of each cluster is presented on the map in Fig. 4.

Cluster 1 represents main cities and the nearby urban areas which benefit from the economic dynamism of the large cities. This cluster is mostly characteristic of large urban conglomerations. Mean in-hospital prevalence of AMI is the lowest (161.2 per 100,000 inhabitants) and mean AMI mortality is among the lowest (17.5 per 100,000 inhabitants); the proportion of over 60-year-olds and retired persons is low (23.9% and 21.3%). This population has the fastest access to angioplasty (20.2 min) and high socioeconomic status with the highest proportion of managers and professional occupations (21.0%) and a low proportion of employees (25.5%), skilled workers (17.3%) and unemployed individuals (9.3%).

Cluster 2 is also major urban centers contiguous to cluster 1. The proportion of over 60-year-olds and retired persons is low (24.0% and 21.7%) The mean AMI prevalence and mortality are low (161.9 and 15.9 per 100,000 inhabitants). Unlike cluster 1, the unemployment rate is high 14.8%. The proportion of low-income occupations (31.4%) is comparatively higher than the proportion of managers or professional occupations (10%).

Cluster 3 represents active rural areas and the suburbs of major centers mostly located in the northern part of France. Mean AMI mortality and prevalence are low (17.8 and 163.8 per 100,000 inhabitants, respectively), and the proportion of over 60-year-olds (24.4%) and retired persons (22.7%) is low. A large proportion of the population is skilled workers (32.9%). Access to angioplasty is slightly longer (48.4 min).

Cluster 4 represents rural areas in the southern part of France. The population is older with one of the highest proportions of over 60-year-olds and retired persons (36.5 and 33.5%). The proportion of farmers (11.2%) is the highest in France. However, AMI prevalence is moderately lower than the national mean and AMI mortality is also low (192.4 and 16.9 per 100,000 inhabitants, respectively). Moreover, the population in this cluster has the longest access time to angioplasty (67.9 min).

Territories in cluster 5 are urban areas mostly situated along the Mediterranean coast in Provence, Alps, Pyrenees and Corsica. It is characterized by the most aged population among the clusters with 37.4% of over 60-year-olds and 34.0% of retired persons, and a high level of unemployment (15.9%), associated to a high in-hospital prevalence and AMI mortality rate (264.3 and 36.4 per 100,000 inhabitants).

Cluster 6 is distributed along a geographic diagonal axis following a north-east to south-west course, as shown previously (Fig. 2). This area contains many small and mid-sized cities. The population tends to have more low-income professions (28.5% employees and 29.0% skilled workers). The AMI in-hospital prevalence and AMI mortality rate are considerably higher than national mean (291.6 and 54.4 per 100,000 inhabitants). Access time to angioplasty is also longer (50.5 min).

The spatial distribution of each cluster did not differ when considering only severe AMI and only STEMI.

3.4. Multilevel analysis

After adjustments (on gender, atrial fibrillation, percutaneous transluminal angioplasty, coronary artery bypass craft, STEMI, severe AMI, Fdep and LPA), we no longer found an association between time to revascularization facility and overall mortality at one year, whether by taking the variable continuously, by quartile, or by dummy variables (Table 4).
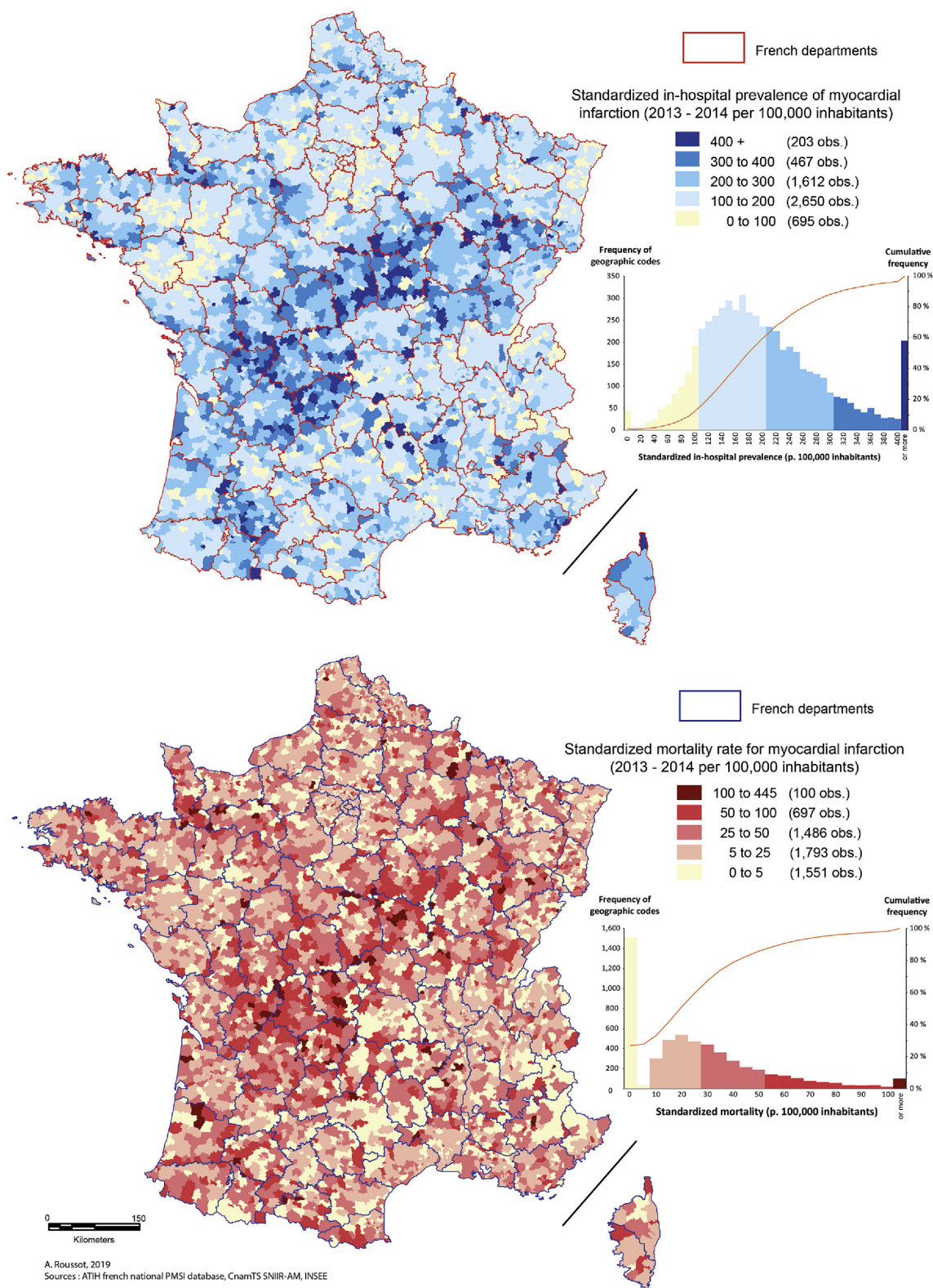
Fig. 2. Standardized in-hospital prevalence and standardized rate of mortality at one year following acute myocardial infarction at the level of PMSI geographic codes, 2013–2014.

4. Discussion

We identified 115,418 patients admitted for AMI in France over the 2-year study period (57,279 in 2013 and 58,139 in 2014), with an overall mortality rate at one year of 12.2%. Nevertheless, the prevalence of AMI and 1 year mortality varied considerably throughout the country. We identified 6 different area profiles (using geographic codes) with standardized mortality varying from 15.9 to 54.4 per 100.000 inhabitants. We also found that the longest travel time to revascularization facility was recorded for rural dwellers. However, this access to coronary
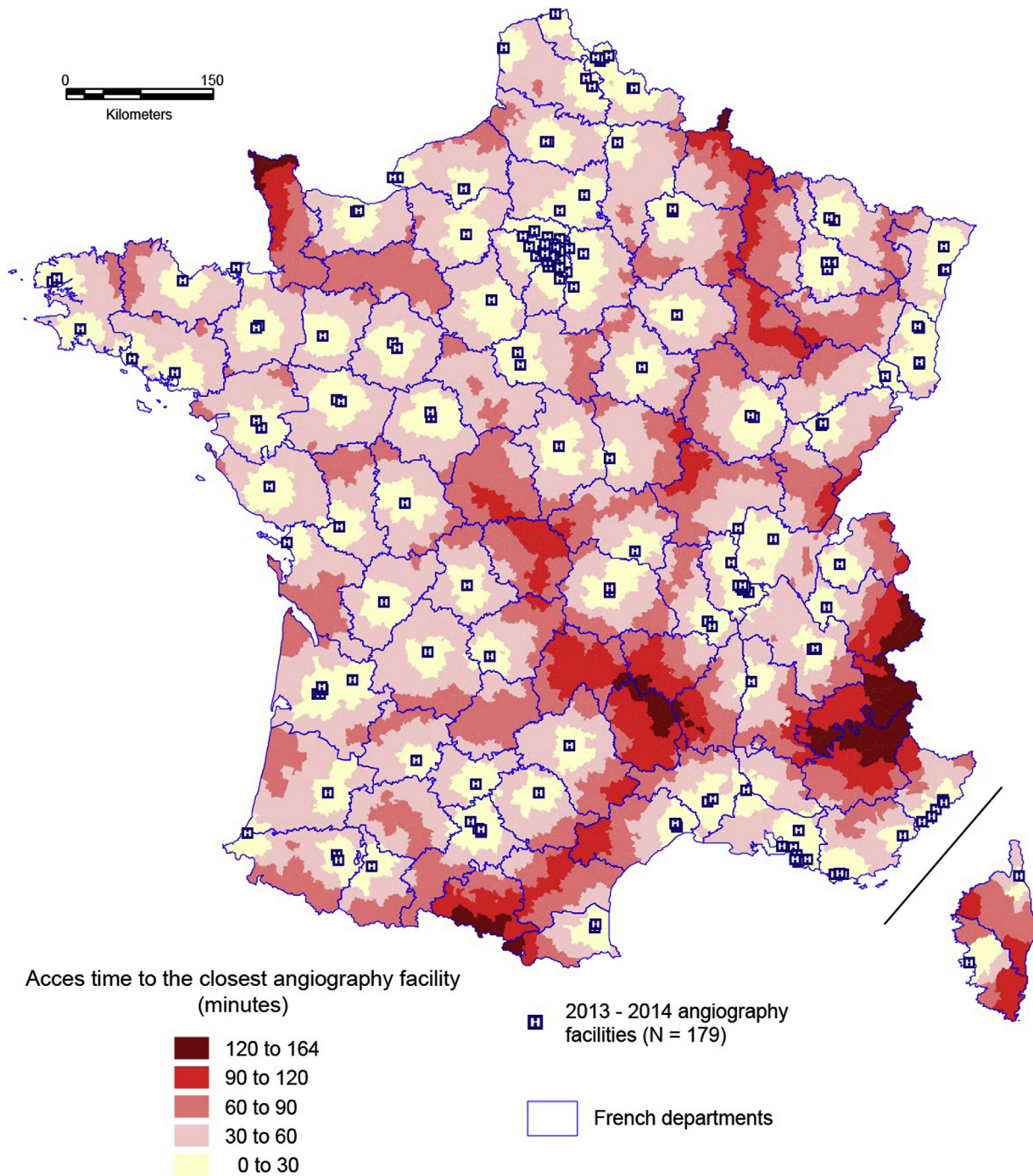
Acces time to the closest angiography facility (minutes)

	120 to 164
	90 to 120
	60 to 90
	30 to 60
	0 to 30

2013 - 2014 angiography facilities (N = 179)

French departments

Areas	mean	SD	median	minimum	maximum
Major urban centres	17	22	7	1	140
Suburbs of major centres	33	20	28	3	133
Small and mid-sized centres	52	22	47	1	159
Rural areas	58	23	55	1	163
Overall	29	27	21	0	163

Among metropolitan France; Missing data=247 (0.2%)

A. Roussot, 2018
Sources : ATIH french national PMSI database, IGN

Fig. 3. Spatial distribution of facilities performing angiography and access time to the closest facility in minutes, 2013–2014.

Table 3

Characteristics of clusters from the ascending hierarchical classification (at the scale of geographic codes).

Cluster	1	2	3	4	5	6
Demographic structure of geographic codes (mean in each cluster)						
Younger than 20 years (%)	25.0	25.5	26.0	19.0	18.6	22.3
20–60 years old (%)	51.1	50.5	49.5	44.6	44.0	47.2
Older than 60 years (%)	23.9	24.0	24.4	36.5	37.4	30.5
AMI burden (mean in each cluster)						
AMI mortality (per 100,000 inhabitants)	17.5	15.9	17.8	16.9	36.3	54.4
AMI in-hospital prevalence (per 100,000 inhabitants)	161.2	161.9	163.8	192.4	264.3	291.6
Time to the closest angiography facility (minutes)	20.2	32.5	48.4	67.9	42.0	50.5
Socio professional category (mean in each cluster)						
Unemployed (%)	9.3	14.8	9.7	10.9	15.9	12.2
Farmers (%)	1.2	1.5	5.6	11.2	2.1	4.8
Craftsmen storekeepers entrepreneurs (%)	6.9	6.0	6.4	11.4	11.4	7.8
Manager or executive occupations (%)	21.0	10.5	8.1	7.8	12.3	8.7
Intermediate professions-technicians (%)	28.8	24.5	21.6	18.9	23.9	21.5
Employees (%)	25.5	31.4	25.9	26.5	32.7	28.5
Skilled workers (%)	17.3	26.6	32.9	24.6	19.0	29.0
Retired persons (%)	21.3	21.7	22.7	33.5	34.0	28.2

angiography does not seem to be associated with an increase in mortality rates for AMI, contrary to a lower socio-economic level which does appear to be related to higher AMI-related mortality.

Using the French SNDS database, we were able to report the overall number of AMI-related deaths in France for the study period (not only in-hospital deaths). The mortality rates from administrative databases are known to be higher than numbers provided by French registries [5,39]. This disparity can be explained by differences in population seeing as the administrative database includes a broader population that is not routinely admitted to cardiac intensive care units and is therefore not monitored by the registries [22].

We found that the longest travel time to revascularization facility was recorded for rural dwellers (Fig. 3). These areas (clusters 3, 4 and 6) had a more deprived socio-residential context than urban areas. However certain rural territories (clusters 3 and 4) with longer access times to the closest angiography facility had lower in-hospital prevalence and mortality for AMI, suggesting that longer distances to facilities are not systematically related to such health indicators. These results are consistent with a previous American study which concluded that in-hospital mortality for AMI was not related to a rural place of residence [40]. However, rural residents had a higher risk of transfer and 30-day readmission. Moreover, following French health ministry recommendations and in accordance with European guidelines, transport time to angioplasty should be achieved in less than 90 min in most of the territory [41]. Some areas remain isolated with a travel time that is longer than 90 min. These were generally located in less populous mountainous (Alpes, Pyrenees, Massif Central and Jura) and rural regions.

In our study, the road distance to coronary angiography did not appear to increase or to be associated with mortality rates for AMI, as shown by the results obtained with the AHC or after adjustment with the multilevel analysis. This finding is consistent with a Canadian study that found a significant adverse effect of socioeconomic status on 1-year mortality after a first AMI, and which was not explained by lower access to coronary angiography or revascularization [19]. However, other studies showed that access time to facilities combined with individual socio-educational status could have a negative impact on access to specific and recommended practices such as fibrinolysis or coronary angioplasty [42]. In our study, the classification showed that the demographic structure was not the only factor of socio-territorial

organization to affect mortality. Indeed, the areas with the oldest populations (clusters 4–6) are contrasted, with lower (cluster 4) and also higher (cluster 6) mortality rates adjusted on age and gender. Apart from the age of the population, differences in mortality followed the territorial distribution of socio-professional categories.

The second major result is that a lower socio-economic level is related to higher AMI-related mortality. To summarize, the spatial distribution of socio-economic and health indicators appears more favorable in the large urban centers. Young, active populations and tertiary-sector professions are concentrated in larger cities and their suburbs (clusters 1 and 2). Active rural areas associated with urban centers (cluster 3) and rural agricultural areas in the southern part of France (cluster 4) also have favorable health indicators. However, those clusters contrast with large underprivileged areas with less favorable socioeconomic indicators associated with aging populations and higher mortality rates (clusters 5 and 6). These findings are concordant with previous studies [14,19], and they highlight the major adverse effect of socioeconomic status on 1-year mortality after AMI. Moreover, our results suggest that improving access to healthcare is not the only solution for reducing mortality in socially deprived patients. Public health policies should focus on primary and secondary prevention such as encouraging healthy food and lifestyle habits to reduce the incidence of both AMI and complications after AMI [43,44]. Education about the characteristic symptoms of AMI and the importance of seeking medical assistance as soon as possible is also a key factor for better medical management [45,46].

Thirdly, maps of standardized in-hospital prevalence and standardized mortality rates allowed us to illustrate the geographical differences on a national level, notably by identifying areas of high mortality from north-east to south-west France, along the "low population density diagonal". Areas along this diagonal line are characterized by aging communities, but the excess mortality cannot be explained by age differences alone seeing as age-standardized mortality was also higher than elsewhere. This zone, often referred to as the "excess mortality diagonal" in France, has already been highlighted by French geographers, notably in terms of premature death in the population at large [47] and in a previous study describing stroke-related in-hospital mortality [28]. If we consider that patients hospitalized for AMI are hospitalized as close as possible to their homes, given that emergency care facilities are supposed to be nearby, these results may indicate the location of "protective" and "accident-prone" zones on a very fine scale. Local observations could provide a diagnostic tool for decision makers to assess the quality of prevention, to evaluate the efficacy of public healthcare messages, and the burden of risk factors in certain areas [48,49].

4.1. Strengths

This is the first time a study of AMI mortality based on a spatial analysis using zip-codes has been conducted in France. This approach provides more accurate results than those obtained with data obtained by department. Our data showed major disparities in prevalence and mortality, which is difficult to compare to previous epidemiological studies using different a geographical scale [50–54]. However, this result is in line with our previous work concerning stroke, which is a condition that shares a common physiopathology with AMI [28].

Our large national database made it possible to work with a large number of patients, to take into account in- and out-patient deaths, and to report cases that are not usually included in clinical studies. Our figures are concordant with previous epidemiological data [29,55]. In addition, the validity of administrative databases for the description of AMI hospitalization has already been assessed [22,56] and the list of diagnostic codes used to select patients are the same as those used in other French [22,29] and international [16,57,58] studies focused on AMI. This database also allowed us to study the STEMI subgroup, in which we found similar results, using diagnostic codes which appear valid for this population [22]. The rate of STEMI patients was consistent with previous studies carried out in France [5,29,59].
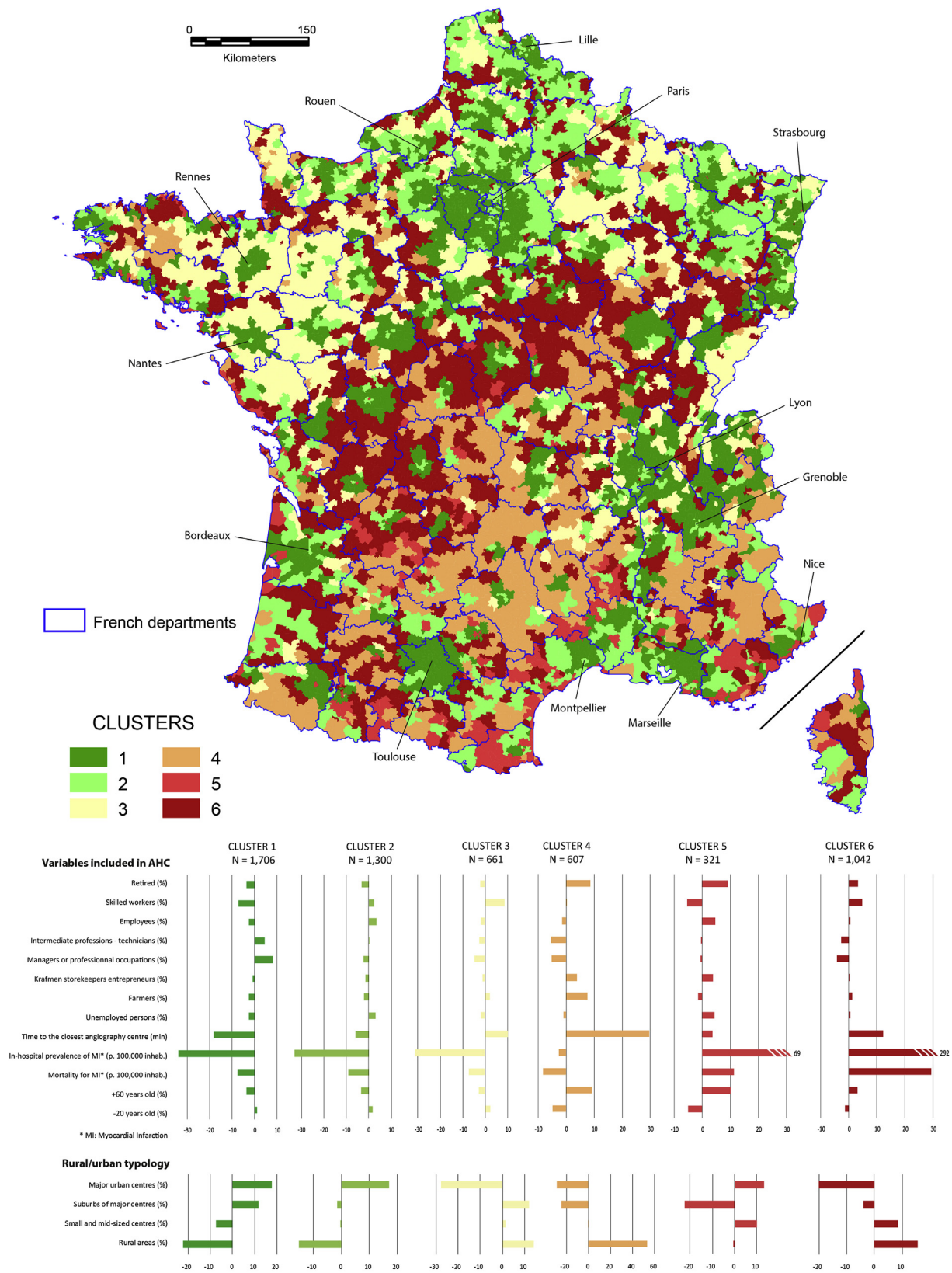
Fig. 4. Spatial distribution of the ascending hierarchical classification results and mean deviation for each cluster characteristics from the ascending hierarchical classification.

Table 4
Multilevel analysis to examine the association of time to revascularization facility and overall mortality at one year (adjustment on gender, atrial fibrillation, percutaneous transluminal angioplasty, coronary artery bypass craft, STEMI, severe AMI, Fdep and LPA).

	Crude OR [CI 95%]	Adjusted OR [CI 95%]	p-value for adjusted OR
Continuously	1.005 [1.004–1.005]	1.000 [0.999–1.001]	0.37
By quartile[a]			0.18
Lowest quartile (ref)	–	–	
Second quartile	1.08 [1.02–1.14]	1.09 [1.03–1.16]	
Third quartile	1.23 [1.17–1.30]	1.06 [0.99–1.13]	
Highest quartile	1.37 [1.30–1.45]	0.98 [0.92–1.05]	
Dummy variable			
>21 min (ref: ≤21 min)	1.25 [1.21–1.30]	0.99 [0.94–1.04]	0.57
>90 min (ref: ≤90 min)	1.30 [1.16–1.45]	1.02 [0.91–1.15]	0.72

Fdep: Deprivation index; LPA: Local Potential Accessibility; OR: odds ratio; CI 95%: Confidence interval 95%.

[a] Lowest quartile: [0–6], Second quartile:]6–21], Third quartile:]21–46], Highest quartile:]46–163].

Our work also showed the interest of associating medical data with socio-residential data from the national census. The use of an ascending hierarchical classification is justified by this geographic aggregation. Clustering techniques and the geographic approach illustrate the interplay between the socioeconomic environment and healthcare issues which include access to health care in France [60,61]. The 6 clusters from the classification divide the territory according to the weight of each variable selected by the AHC. Classification was preferred for this study because it can be used to establish a solid typology that maximizes the similarity between observations (PMSI geographic codes) within the same cluster. Concerning the ageing population in certain areas, the model presented includes the demographic structure of the geographic codes of the place of residence, as well as the smoothed rate of mortality. These variables are treated independently in the classification, which allowed us to contextualize certain high mortality rates.

4.2. Study limitations

Our study has several limitations. The measure of socioeconomic status was not based on individual data but from regional and population data, so we can assume that there is a possible ecological bias in the interpretation of our clustering. The access to angioplasty was based on road travel-time from place of residence to hospital, which may not reflect the actual local healthcare performance in certain areas. The standardization of mortality rates on a fine scale, according to the geographic code of the patient's place of residence, allowed us to reveal local clusters of high mortality. This analysis of local situations, which is more detailed than analyses by department, highlighted geographical differences but cannot replace the results of smaller scale analyses using INSEE codes for communes for example. We intend to continue exploring the impact of healthcare accessibility and the differences of myocardial infarction management on early prognosis.

5. Conclusions

Even in a country like France with a universal healthcare system and a strong egalitarian policy, our results confirm that the prevalence of AMI and 1 year mortality varies considerably in different parts of the country. We identified a north-east to south-west diagonal region characterized by social deprivation associated with high AMI prevalence and mortality. This was not accounted for by age since SMR was also increased. Neither were our findings explained by lower access to coronary angiography or revascularization. This study highlights the importance of focusing national policies on universally accessible prevention programs such as the promotion of cardiac rehabilitation and healthy lifestyles. These types of preventive measures must be improved for the most socially deprived populations.

Author declaration

We wish to confirm that there are no known conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article to disclose.

References

[1] Gbd 2016 Causes of Death Collaborators. Global, regional, and national age-sex specific mortality for 264 causes of death, 1980-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Lond Engl 16 sept 2017;390(10100):1151–210.

[2] Benjamin EJ, Muntner P, Alonso A, Bittencourt MS, Callaway CW, Carson AP, et al. Heart disease and stroke statistics-2019 update: a report from the American heart association. Circulation 05 2019;139(10):e56-528.

[3] Timmis A, Townsend N, Gale C, Grobbee R, Maniadakis N, Flather M, et al. European society of cardiology: cardiovascular disease statistics 2017. Eur Heart J 2018;14(7):508–79. 39.

[4] Danchin N, Puymirat E, Simon T. The (possibly) deceptive figures of decreased coronary heart disease mortality in Europe. Eur Heart J oct 2013;34(39):3014–6.

[5] Puymirat E, Simon T, Cayla G, Cottin Y, Elbaz M, Coste P, et al. Acute myocardial infarction: changes in patient characteristics, management, and 6-month outcomes over a period of 20 Years in the FAST-MI program (French registry of acute ST-elevation or non-ST-elevation myocardial infarction) 1995 to 2015. Circulation 14 nov 2017;136(20):1908–19.

[6] Townsend N, Wilson L, Bhatnagar P, Wickramasinghe K, Rayner M, Nichols M. Cardiovascular disease in Europe: epidemiological update 2016. Eur Heart J 07 2016;37(42):3232–45.

[7] Puymirat E, Simon T, Steg PG, Schiele F, Guéret P, Blanchard D, et al. Association of changes in clinical characteristics and management with improvement in survival among patients with ST-elevation myocardial infarction. J Am Med Assoc 12 sept 2012;308(10):998–1006.

[8] Chan MY, Sun JL, Newby LK, Shaw LK, Lin M, Peterson ED, et al. Long-term mortality of patients undergoing cardiac catheterization for ST-elevation and non-ST-elevation myocardial infarction. Circulation 23 juin 2009;119(24):3110–7.

[9] De Luca G, Suryapranata H, Ottervanger JP, Antman EM. Time delay to treatment and mortality in primary angioplasty for acute myocardial infarction: every minute of delay counts. Circulation 16 mars 2004;109(10):1223–5.

[10] Brodie BR, Webb J, Cox DA, Qureshi M, Kalynych A, Turco M, et al. Impact of time to treatment on myocardial reperfusion and infarct size with primary percutaneous coronary intervention for acute myocardial infarction (from the EMERALD Trial). Am J Cardiol 15 juin 2007;99(12):1680–6.

[11] Ibanez B, James S, Agewall S, Antunes MJ, Bucciarelli-Ducci C, Bueno H, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation: the Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). Eur Heart J 2017;39(2):119–77. 07 2018.

[12] Alter DA, et al. Geography and service supply do not explain socioeconomic gradients in angiography use after acute myocardial infarction. CMAJ (Can Med Assoc J) 2003;168(3):261–4.

[13] Insam C, Paccaud F, Marques-Vidal P. The region makes the difference: disparities in management of acute myocardial infarction within Switzerland. Eur J Prev Cardiol mai 2014;21(5):541–8.

[14] Hagen TP, Häkkinen U, Iversen T, Klitkou ST, Moger TA, EuroHOPE study group. Socio-economic inequality in the use of procedures and mortality among AMI

patients: quantifying the effects along different paths. Health Econ déc 2015; 24(Suppl 2):102–15.

[15] Rørth R, Fosbøl EL, Mogensen UM, Kragholm K, Numé A-K, Gislason GH, et al. Employment status at time of first hospitalization for heart failure is associated with a higher risk of death and rehospitalization for heart failure. Eur J Heart Fail 2018; 20(2):240–7.

[16] Kilpi F, Silventoinen K, Konttinen H, Martikainen P. Disentangling the relative importance of different socioeconomic resources for myocardial infarction incidence and survival: a longitudinal study of over 300,000 Finnish adults. Eur J Publ Health avr 2016;26(2):260–6.

[17] Kilpi F, Silventoinen K, Konttinen H, Martikainen P. Early-life and adult socioeconomic determinants of myocardial infarction incidence and fatality. Soc Sci Med 1982;177:100–9. 2017.

[18] Bergström G, Redfors B, Angerås O, Dworeck C, Shao Y, Haraldsson I, et al. Low socioeconomic status of a patient's residential area is associated with worse prognosis after acute myocardial infarction in Sweden. Int J Cardiol 1 mars 2015; 182:141–7.

[19] Blais C, Hamel D, Rinfret S. Impact of socioeconomic deprivation and area of residence on access to coronary revascularization and mortality after a first acute myocardial infarction in Québec. Can J Cardiol avr 2012;28(2):169–77.

[20] Spatz ES, Beckman AL, Wang Y, Desai NR, Krumholz HM. Geographic variation in trends and disparities in acute myocardial infarction hospitalization and mortality by income levels, 1999-2013. JAMA Cardiol 2016;1(3):255–65. 01.

[21] Tuppin P, Rudant J, Constantinou P, Gastaldi-Ménager C, Rachas A, de Roquefeuil L, et al. Value of a national administrative database to guide public decisions: from the système national d'information interrégimes de l'Assurance Maladie (SNIIRAM) to the système national des données de santé (SNDS) in France. Rev Epidemiol Sante Publique oct 2017;65(Suppl 4):S149–67.

[22] Massoullié G, Wintzer-Wehekind J, Chenaf C, Mulliez A, Pereira B, Authier N, et al. Prognosis and management of myocardial infarction: comparisons between the French FAST-MI 2010 registry and the French public health database. Arch Cardiovasc Dis mai 2016;109(5):303–10.

[23] Pagès P-B, Cottenet J, Mariet A-S, Bernard A, Quantin C. In-hospital mortality following lung cancer resection: nationwide administrative database. Eur Respir J juin 2016;47(6):1809–17.

[24] Goueslard K, Cottenet J, Mariet A-S, Giroud M, Cottin Y, Petit J-M, et al. Early cardiovascular events in women with a history of gestational diabetes mellitus. Cardiovasc Diabetol 27 janv 2016;15:15.

[25] Abdulmalak S, Cottenet J, Beltramo G, Georges M, Camus P, Bonniaud P, et al. Haemoptysis in adults: a 5-year study using the French nationwide hospital administrative database. Eur Respir J août 2015;46(2):503–11.

[26] Luu M, Benzenine E, Doret M, Michiels C, Barkun A, Degand T, et al. Continuous anti-TNFα use throughout pregnancy: possible complications for the mother but not for the fetus. A retrospective cohort on the French national health insurance database (EVASION). Am J Gastroenterol nov 2018;113(11):1669–77.

[27] Zabawa C, Cottenet J, Zeller M, Mercier G, Rodwin VG, Cottin Y, et al. Thirty-day rehospitalizations among elderly patients with acute myocardial infarction: impact of postdischarge ambulatory care. Medicine (Baltim) juin 2018;97(24):e11085.

[28] Roussot A, Cottenet J, Gadreau M, Giroud M, Béjot Y, Quantin C. The use of national administrative data to describe the spatial distribution of in-hospital mortality following stroke in France, 2008-2011. Int J Health Geogr 11 janv 2016; 15:2.

[29] Lorgis L, Cottenet J, Molins G, Benzenine E, Zeller M, Aube H, et al. Outcomes after acute myocardial infarction in HIV-infected patients: analysis of data from a French nationwide hospital medical information database. Circulation 30 avr 2013; 127(17):1767–74.

[30] Meyer P, Barragan P, Blanchard D, Chevalier B, Commeau P, Danchin N, et al. [Recommendations of the French Cardiac Society concerning the education of physicians performing coronarography and angioplasty, organization and equipment of coronarography and coronary angioplasty centers]. Arch Mal Coeur Vaiss févr 2000;93(2):147–58.

[31] French Ministry of Health. [Circular N° DHOS/O4/2009/279 of August 12, 2009 relative to the endovascular interventional procedures performed under medical imagery in cardiology]. http://circulaire.legifrance.gouv.fr/pdf/2009/09/cir_29453.pdf.

[32] Insee. Définition - zonage en aires urbaines/ZAU/ZAU | Insee [Internet]. [cité 19 mai 2020]. Disponible sur: https://www.insee.fr/fr/metadonnees/definiti on/c1435.

[33] Goldberg M, Jougla E, Fassa M, Padieu R, Quantin C. The French public health information system. J Int Assoc Off Stat 2012;28:31–41.

[34] CépiDc-Inserm. Certification et codification des causes médicales de décès. Rev Prat 2012;62(6):759–63.

[35] Pavillon G, Laurent F. Certification et codification des causes médicales de décès. Bull Épidémiol Hebd 2003;30–31:134–8.

[36] ATIH. Le décès dans le PMSI-MCO, validation et précautions d'utilisation - quelques résultats, rapport. 2008. https://www.atih.sante.fr/sites/default/files/public/conte nt/1282/rapport_deces-def.pdf.

[37] Rey G, Jougla E, Fouillet A, Hémon D. Ecological association between a deprivation index and mortality in France over the period 1997 - 2001: variations with spatial

scale, degree of urbanicity, age, gender and cause of death. BMC Publ Health 22 janv 2009;9:33.

[38] Barlet M, Coldefy M, Collin C, et al. L'accessibilité potentielle localisée (APL): une nouvelle mesure de l'accessibilité aux médecins généralistes libéraux [Internet] Étud Résult 2012. Disponible sur: http://www.irdes.fr/Publications/2012/Q es174.pdf.

[39] Seronde MF, Geha R, Puymirat E, Chaib A, Simon T, Berard L, et al. Discharge heart rate and mortality after acute myocardial infarction. Am J Med oct 2014;127(10): 954–62.

[40] Bechtold D, Salvatierra GG, Bulley E, Cypro A, Daratha KB. Geographic variation in treatment and outcomes among patients with AMI: investigating urban-rural differences among hospitalized patients. J Rural Health Off J Am Rural Health Assoc Natl Rural Health Care Assoc 2017;33(2):158–66.

[41] Van de Werf F, Bax J, Betriu A, Blomstrom-Lundqvist C, Crea F, Falk V, et al. Management of acute myocardial infarction in patients presenting with persistent ST-segment elevation: the task force on the management of ST-segment elevation acute myocardial infarction of the European society of cardiology. Eur Heart J déc 2008;29(23):2909–45.

[42] De Luca G, Petrelli A, Landriscina T, Gnavi R, Giammaria M, Costa G. Geographic and socioeconomic differences in access to revascularization following acute myocardial infarction. Eur J Publ Health 2016;26(5):760–5.

[43] Ohm J, Skoglund PH, Discacciati A, Sundström J, Hambraeus K, Jernberg T, et al. Socioeconomic status predicts second cardiovascular event in 29,226 survivors of a first myocardial infarction. Eur J Prev Cardiol 2018;25(9):985–93.

[44] Gaalema DE, Elliott RJ, Morford ZH, Higgins ST, Ades PA. Effect of socioeconomic status on propensity to change risk behaviors following myocardial infarction: implications for healthy lifestyle medicine. Prog Cardiovasc Dis juill 2017;60(1): 159–68.

[45] Dumont F, Lorgis L, Yeguiayan J-M, Touzery C, Zeller M, Avondo A, et al. Impact of diverting general practitioner's after-hour calls to emergency medical dispatch centers in patients with acute myocardial infarction. Eur J Emerg Med Off J Eur Soc Emerg Med juin 2013;20(3):197–204.

[46] Yonemoto N, Kada A, Yokoyama H, Nonogi H. Public awareness of the need to call emergency medical services following the onset of acute myocardial infarction and associated factors in Japan. J Int Med Res mai 2018;46(5):1747–55.

[47] Fainzang S, et al. Atlas de la santé en France, vol.1 : les causes de décès. [compte-rendu]. Sci Soc Santé 2011;19(2):113–5.

[48] Pedigo A, Seaver W, Odoi A. Identifying unique neighborhood characteristics to guide health planning for stroke and heart attack: fuzzy cluster and discriminant analyses approaches. PloS One 2011;6(7):e22693.

[49] Combier E, Charreire H, Le Vaillant M, Michaut F, Ferdynus C, Amat-Roze J-M, et al. Perinatal health inequalities and accessibility of maternity services in a rural French region: closing maternity units in Burgundy. Health Place nov 2013;24: 225–33.

[50] Kim As, Johnston Sc. Global variation in the relative burden of stroke and ischemic heart disease. Circulation 19 juill 2011;124(3):314–23.

[51] Murphy A, Johnson Co, Roth Ga, Forouzanfar Mh, Ng M, Pogosova N, et al. Ischaemic heart disease in the former soviet union 1990-2015 according to the global burden of disease 2015 study. Heart Br Card Soc janv 2018;104(1):58–66.

[52] Zhang G. Burden of ischaemic heart disease and attributable risk factors in China from 1990 to 2015: findings from the global burden of disease 2015 study [internet]. BMC Cardiovasc Disord 2018;18(1):18 [cité 19 mai 2020].

[53] Moran Ae, Forouzanfar Mh, Roth, Ga, Mensah, Ga M, Flaxman A, et al. The global burden of ischemic heart disease in 1990 and 2010: the global burden of disease 2010 study. Circulation 4 août 2014;129(14):1493–501.

[54] Ga Moran Ae, Tzong Ky, Forouzanfar Mh, Rothy Ga, Ezzati M, et al. Variations in ischemic heart disease burden by age, country, and income: the global burden of diseases, injuries, and risk factors 2010 study. Glob Heart Mars 2014;9(1):91–9.

[55] De Peretti C, et al. Personnes hospitalisées pour infarctus du myocarde en France : tendances 2002-2008. Bull Epidémiol Hebd 2012;41:459–65.

[56] McCormick N, Lacaille D, Bhole V, Avina-Zubieta JA. Validity of myocardial infarction diagnoses in administrative databases: a systematic review. PloS One 2014;9(3):e92286.

[57] Patel AB, Quan H, Welsh RC, Deckert-Sookram J, Tymchak W, Sookram S, et al. Validity and utility of ICD-10 administrative health data for identifying ST- and non-ST-elevation myocardial infarction based on physician chart review. CMAJ Open déc 2015;3(4):E413–8.

[58] Metcalfe A, Neudam A, Forde S, Liu M, Drosler S, Quan H, et al. Case definitions for acute myocardial infarction in administrative databases and their impact on in-hospital mortality rates. Health Serv Res févr 2013;48(1):290–318.

[59] Gabet A, Danchin N, Olié V. Infarctus du myocarde chez la femme : évolutions des taux d'hospitalisation et de mortalité, France, 2002-2013. Bull Epidémiol Hebd 2016;(7–8):100–8.

[60] Vigneron E. [Territorial and social healthcare inequalities in France]. Bull Acad Natl Med mai 2012;196(4–5):939–52.

[61] Ouédraogo S, Dabakuyo-Yonli TS, Roussot A, Dialla PO, Pornet C, Poillot M-L, et al. [Breast cancer screening in thirteen French departments]. Bull Cancer (Paris) févr 2015;102(2):126–38.