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Prevalence of severe cardiovascular disease in patients with schizophrenia

La prévalence des maladies cardiovasculaires sévères nécessitant une hospitalisation chez les patients hospitalisés pour schizophrénie ou trouble psychotique en France

Jean-Christophe Marche¹*, Aurélie Bannay², Sylvain Baillot², Valérie Dauriac-Le Masson³, Philippe Leveque⁴, Christophe Schmitt⁵, Vincent Laprévote⁶, Raymund Schwan⁶, Daniela Dobre⁷

¹ Psychiatry and Clinical Psychology Service (G06), Psychotherapeutic Center of Nancy, 1 Rue Dr Archambault, 54520 Laxou, France

² Department of Evaluation and Medical Informatics, CHRU-Nancy, 29 Avenue du Maréchal de Lattre de Tassigny, 54035 Nancy, France

³ Department of Medical Informatics, GHU Paris "Psychiatrie & Neurosciences", 1 Rue Cabanis, 75014 Paris, France

⁴ Department of Medical Informatics, Ravenel Hospital Center, 1115 Avenue René Porterat, 88500 Mirecourt, France

⁵ Department of Medical Informatics, Jury Hospital Center, Centre Hospitalier de Jury - BP 75088 - 57073 Metz cedex 3, France

⁶ "Grand Nancy" Hospital-university Center for Adult Psychiatry and Addictology, Psychotherapeutic Center of Nancy, 1 Rue Dr Archambault, 54520 Laxou, France; Inserm U1114, France; University of Lorraine, France

⁷ Department of Medical Informatics and Clinical Research and Investigation Unit, Psychotherapeutic Center of Nancy, 1 Rue Dr Archambault, 54520 Laxou, France

* Corresponding author: Jean-Christophe Marche

Psychiatry and Clinical Psychology Service (G06), Psychotherapeutic Center of Nancy, 1 rue

du Docteur Archambault, 54520 Laxou, France

E-mail : jeanchristophe.marche@cpn-laxou.com

Abstract

Objectives: We assessed the prevalence of severe cardiovascular (CV) disease requiring hospitalization among patients with schizophrenia in France. Method: We included patients hospitalized with schizophrenia or psychotic disorder during 2015, in five French psychiatric hospitals. Patients with CV disease were defined as those with a correspondent ICD-10 code during a hospital stay in any general hospital, five years before or three years after the psychiatric hospitalization. CV disease included myocardial infarction (MI), stroke, heart failure (HF), coronary artery disease (CAD) or peripheral artery disease. Risk factors such as hypertension, obesity and diabetes were recorded. Results: In total, 4424 patients with schizophrenia were included. Overall, 203 (4,6%) patients were diagnosed with CV disease, 93 (2.1%) with CAD, 86 (1.9%) with HF and 49 (1.1%) with stroke. The prevalence of hypertension, obesity and diabetes was 11.3%, 9.7% and 7.8%. The median (interquartile range) age of patients with MI and diabetes was 57 (49-70) and 56 (48-66) years. **Conclusion:** Patients with schizophrenia develop severe CV disease requiring hospitalization at an early age. These severe events are associated with a high prevalence of risk factors. Early screening and treatment of CV disease and risk factors is important to improve life expectancy and quality of life of these patients.

Key words: schizophrenia, psychotic disorder, cardiovascular disease, cardiovascular risk factors, France

Résumé

Objectif : Les maladies cardiovasculaires (CV) sont fréquentes chez les patients atteints d'une schizophrénie ou d'un trouble psychotique, mais le taux de patients hospitalisés pour une maladie CV a été peu étudié dans cette population en France. Nous avons souhaité évaluer la prévalence des maladies CV sévères nécessitant une hospitalisation parmi les patients qui ont été hospitalisés pour une schizophrénie ou un trouble psychotique en France. Méthode : En utilisant les ressource du PMSI (Programme de Médicalisation des Système d'Information), nous avons effectué une étude rétrospective sur les patients hospitalisés pour schizophrénie ou trouble psychotique durant l'année 2015 dans cinq hôpitaux psychiatriques français. Les patients atteints d'une maladie CV étaient définis comme ceux ayant été hospitalisé au moins une fois avec un diagnostic CIM-10 principal ou associé de maladie CV dans un hôpital général en France, cinq ans avant ou trois ans après l'hospitalisation de référence dans l'hôpital psychiatrique en 2015 (pour au total huit années de suivi). Les maladies CV étaient définies par l'occurrence soit d'un infarctus du myocarde, d'un accident vasculaire cérébral, d'une insuffisance cardiaque, d'une maladie coronarienne ou d'une maladie artérielle périphérique. Les facteurs de risque CV tel que l'hypertension, l'obésité et le diabète sucré ont également été évalués. Enfin, les données issues de ces cinq hôpitaux psychiatriques ont été comparées avec celles issues de l'ensemble des hôpitaux psychiatriques de la France métropolitaine en utilisant la même méthodologie. Résultats : Nous avons inclus un total de 4 424 patients atteints de schizophrénie ou d'un trouble psychotique. Globalement, sur l'ensemble des 8 années de suivi, 203 (4.6%) des patients avaient été hospitalisé au moins une fois dans le cadre d'une maladie CV. Parmi ces patients, 93 (2.1%) présentaient une maladie coronarienne, 86 (1.9%) présentaient une insuffisance cardiaque, 49 (1.1%) présentaient un accident vasculaire cérébral et 27 (0.6%) présentaient un infarctus du myocarde. La prévalence de l'hypertension, de l'obésité et du diabète était respectivement de 11.3%, 9.7% et 7.8%. L'âge médian (écart interquartile) des patients hospitalisés pour une maladie CV était de 60 (51-72) ans. L'âge médian des patients présentant un infarctus du

myocarde était de 57 (49-70) ans, et celui des patients présentant un diabète était de 56 (48-66) ans. Nous n'avons pas retrouvé de différence majeure de prévalence des maladies CV parmi les cinq hôpitaux évalués et l'ensemble de la France métropolitaine. **Conclusion :** Notre étude montre que les maladies CV sévères nécessitant une prise en charge hospitalière et les facteurs de risque CV sont non seulement fréquents chez les patients atteints de schizophrénie ou de trouble psychotique, mais surviennent également à un âge beaucoup plus précoce en comparaison avec la population générale française (environ 10 ans plus tôt). Ainsi, le dépistage et le traitement précoce des maladies et facteurs de risque CV sont importants pour améliorer l'espérance et la qualité de vie des patients atteints de schizophrénie ou de trouble psychotique.

Mots-clés : schizophrénie, trouble psychotique, maladie cardiovasculaire, facteurs de risque cardiovasculaire, France

Introduction

Schizophrenia is a severe chronic disease requiring costly medical care and psychosocial measures [1,2]. The societal impact of the disease is also important as it occurs in young adults and concerns around 600 000 patients in France [3–5].

Despite considerable treatment improvement during the last decades [6], the disease remains associated with reduced life expectancy compared to the general population [7–11]. Overall, patients with schizophrenia have 2 to 3-fold increased mortality rate [12–15], and this is to a small extent related to suicide [16]. Despite the increased risk, many patients have limited access to general health care compared to non-psychiatric population [7,17]. The quality of life of these patients is also severely affected, due to debilitating disease symptoms, social withdrawal and cognitive impairment, but also because of other severe co-morbidities, such as cardiovascular (CV) disease, pulmonary disease or cancer [18,19]. On the other hand, with the progress of psychiatric treatment and social measures, it is estimated that more patients with schizophrenia will reach older ages, which in turn will be associated to a higher burden of co-morbidities. It is estimated that the number of elderly patients with schizophrenia will double by the year 2050 [20].

To date, several studies showed that CV disease is frequent in patients with schizophrenia or psychotic disorder [21,22], and represents the most important natural cause

of death in this population [23]. Some studies reported the onset of CV disease in patients with schizophrenia at a mean age of 46 years [24]. However, little is known in France about the prevalence of severe CV disease and the socio-demographic characteristics of patients with schizophrenia requiring hospitalization for a CV event.

In this study, we aimed to assess the prevalence of severe CV disease requiring hospitalization and CV risk factors among patients hospitalized for schizophrenia or psychotic disorder in France.

Methods

We performed a retrospective observational study in the national PMSI database. The PMSI database is the French Hospital Discharge database [Programme de Médicalisation des Systèmes d'Information (PMSI)] based on the Diagnosis-Related Group used for hospital's billing. It contains discharge diagnoses (with ICD-10 codes) and medical procedures performed during each hospital stay [25]. First, we identified patients hospitalized during 2015 (full-time hospitalization) with a diagnosis of schizophrenia or psychotic disorder, in five French psychiatric hospitals: Hospital Center of Ravenel at Mirecourt, Psychotherapeutic Center of Nancy at Laxou, Northern Alsace Public Establishment of Health at Brumath, Hospital Center of Jury at Jury and Hospital Center of Saint-Anne in Paris. Multiple hospitalizations were excluded, patients were selected if they had at least one hospitalization during 2015. Four of those psychiatric hospitals were chosen based on their location in the Great East region of France while the fifth one (Saint-Anne, in Paris) was chosen for comparison outside the region. All five hospitals are specialized large mental health hospitals with a capacity ranging from 222 to 464 beds.

Inclusion criteria for patients hospitalized in psychiatric hospitals were ICD-10 diagnosis codes of schizophrenia, psychotic or delusional disorders (F 20-21-22-23-25-28-

29). Second, from this cohort, we identified patients hospitalized with a principal or an associated diagnosis of CV disease (full-time hospitalization), in any general hospital in France, five years before or three years after the index hospitalization in the psychiatric hospital. Cardiovascular disease was defined by the occurrence of at least one of the following diseases: myocardial infarction (MI), stroke, heart failure (HF), coronary artery disease (CAD) or peripheral artery disease (PAD). Inclusion criteria for CV disease were ICD-10 diagnostic codes of MI (I 21-23), stroke (I 60-64), HF (I 50 and I 110), CAD (I 25) or PAD (I77). The age of CV disease onset was the age of the patients at the moment of hospitalization in the general hospital.

Cardiovascular risk factors such as hypertension, obesity and diabetes mellitus, were also recorded in the same timeframe window (five years before and three years after the psychiatric stay) using ICD-10 diagnostic codes I 10 (hypertension), E 66 (obesity) and E 10-14 (diabetes). In the results section, hospitals were anonymized.

To validate our findings in a larger sample size, we assessed by using the same methodology the prevalence of CV disease in patients hospitalized during 2015 for schizophrenia or psychotic disorder in any metropolitan France psychiatric hospitals. Both CV diseases and risk factors were assessed in the same timeframe window (five years before and three years after the psychiatric stay).

Statistical analysis

Data extraction from the national PMSI database was realized in an aggregated format by using the SAS program version 9.4. Continuous variables in the study were described as median (25th-75th percentiles), and categorical variables as frequencies (percentages).

Results Study population

We included a total of 4 424 patients hospitalized in five psychiatric hospitals. Table 1 summarizes the socio-demographic characteristics of patients and their repartition in the five hospitals. Overall, the median (25th, 75th percentiles) age of patients was of 43 (32-55) years. Patients from one hospital (H4) were in average five years older than those from two other hospitals, H1 and H5 (median age 46 (36-57) versus 41 (29-52) and 41 (30-53) years). The majority of patients included in the study were men (61%). The entire metropolitan France group included 96 100 patients. Our study population had a similar age and sex ratio distribution as the metropolitan France group.

CV diseases

The percentage of patients with CV disease and the socio-demographic characteristics of patients with CV disorders are summarized in Table 2a.

In the whole study population, during 8 years of follow-up (five years before or three years after the index hospitalization in psychiatry), 203 (4,6%) patients had at least one hospitalization documenting the occurrence of CV disease. The median (25th, 75th percentiles) age of patients with CV disease was of 60 (51-72) years and 53% were male. The most frequent CV diseases were CAD with 93 (2,1%) patients, HF with 86 (1,9%) patients and stroke with 49 (1,1%) patients. The median (25th, 75th percentiles) age of patients with CAD, stroke and HF was 59 (50-73), 62 (54-73) and 62 (54-73) years, respectively. Importantly, 27 (0.6%) patients had a MI, and the median (25th, 75th percentiles) age of these patients was 57 (49-70) years.

There were no major differences in the percentage of CV disease among the five hospitals. However, few differences are to be mentioned concerning the occurrence of MI and stroke.

The percentage of patients with MI was slightly lower at H1 (0.3%) compared to H2 and H3 (0.8% and 0.7%), but importantly, patients at H1 were younger at the age of MI occurrence (median age of 47 (44-49) years versus 54 (47-64) and 60 (41-76) years).

The percentage of patients with stroke was much lower at H2 (0.2%) and at H1 (0.7%) compared to H3 (1.6%) and H5 (1.5%). Very important also, patients from the later hospitals were younger at the age of stroke occurrence compared to patients from the former hospitals (median age 56 (51-60) and 60 (53-73) years versus 80 (80-80) and 69 (62-72) years).

The metropolitan France group, which included a higher sample of patients, only exhibited a slightly higher percentage of patients with MI (0.7%) and stroke (1.3%) with no major differences for the other CV diseases. In contrast, the median (25th, 75th percentiles) age of patients with stroke was 59 (50-69) years compared to 62 (54-73) years in our study group.

CV Risk factors

The percentage of patients with CV risks factors and their characteristics are summarized in Table 2b. In our study population, 500 (11.3%) patients had hypertension, 344 (7.8%) patients had diabetes mellitus and 431 (9.7%) patients had obesity. The median (25th, 75th percentiles) age of patients with hypertension, diabetes mellitus and obesity was of 60 (49-68), 56 (48-66) and 49 (39-59) years, respectively.

There were no major differences in the percentage of patients with obesity among the five hospitals, but few differences on the occurrence of hypertension and diabetes mellitus are to be mentioned. The percentage of patients with hypertension was higher at H2 and H4 (around 14%) compared to H3 and H5 (8.3% and 9.0%), probably in relation with the older age of patients in the former hospitals (62 (49-68) and 61 (51-69) years versus 56 (49-67) and 58 (49-70) years). The percentage of patients with diabetes mellitus was almost double at H4

(10.5%) compared to H1 and H5 (5.7% and 5.4%), but similarly patients with diabetes mellitus were slightly older at H4.

The metropolitan France group exhibited a slightly lower percentage of patients with hypertension (9.5%) and diabetes mellitus (6.7%) with no major difference for obesity. Patients in the metropolitan France group had a similar median age as our overall population, for both hypertension and diabetes mellitus. Sex ratio distribution was also nearly equivalent.

The rate of CV disease in relation to the psychiatric hospitalization

Table 3 summarizes the rate of CV disease and CV risk factors in our study population, five years before and three years after the index psychiatric hospitalization in 2015. In the overall study population, the rate of CV disease was 2.4% (106 patients) five years before, and 2.2% (97 patients) three years after the index hospitalization (new cases of CV events). A similar trend was found in the entire metropolitan France group.

Coronary artery disease and CV risks factors were more frequent before the psychiatric hospitalization. In contrast, stroke and HF were more frequent after the psychiatric hospitalization, probably in relation with the advanced age of patients.

Principal diagnosis and associated diagnosis

Table 4 shows the repartition between principal and associated diagnosis of CV disease in the overall study population and the metropolitan France. Certain CV diseases, such as MI and stroke, were around 80% coded as a principal diagnosis. For HF, 40% of cases were coded as principal diagnosis. For CAD, PAD and diabetes mellitus most patients were coded as an associated CV diagnosis. The other CV risk factors, such as hypertension and obesity, were almost entirely coded as associated diagnosis. Similar results were observed in the metropolitan France group.

Discussion

In this study, we assessed the prevalence of CV diseases and CV risk factors, as documented during a hospitalization in a general hospital, among patients hospitalized for schizophrenia or a psychotic disorder, in five French psychiatric hospitals. We found that during the eight years follow-up (five years before and three years after the index hospitalization in the psychiatric hospital), 203 (4.6%) patients had at least one hospitalization documenting the occurrence of a CV disease. Among these patients, 93 (2.1%) had CAD, 86 (1.9%) had HF, 49 (1.1%) had stroke and 27 (0.6%) had MI. Importantly, the median age of patients hospitalized for CV disease was of 60 (51-72) years and 57 (49-70) years for MI. The percentage of patients with hypertension, obesity and diabetes mellitus was of 11.3%, 9.7% and 7.8%, respectively. The median age of patients diagnosed with diabetes was of 56 (48-66) years. No major differences in the prevalence of CV disease was identified in the metropolitan France sample, but patients with stroke were in average 3 years younger in this sample compared to our five hospitals study group.

To our knowledge, this is the first French study assessing the prevalence and the age onset of severe CV disease requiring hospitalization in patients with schizophrenia or psychotic disorder.

Comparison with the data from the literature

When compared to the literature, the rate of CV disease in the general French population, in both hospital and ambulatory setting, is of 6.51 % [26] as compared to 4.6% in our study, which included only hospitalized cases. Importantly also, the mean age of patients with CV disease in the general French population is of 70.6 years [26] as opposed to a median of 60 (51-72) years in our study. In this regard, our findings are in line with previous studies showing that patients with schizophrenia and psychotic disorder are at least 10 years younger at CV disease onset, even for severe CV events requiring hospitalization [24,27].

Importantly however, certain severe CV diseases not only occur at a younger age but are also more frequent in patients with psychotic disorder than in the general population [26]. For instance, the rate of MI was 0.6% in our study as opposed to 0.1% in the general population, while the median age of patients with MI was of 57 (49-70) years in our study compared to a mean age of 67.7 years in the general population. Also, probably in relation with the high prevalence and the early occurrence of MI and diabetes, the rate of HF is almost twice as high as in the general population (1.9% versus 1.07%), while patients are in average 15 years younger (median age of 62 (54-73) years versus a mean age of 77.6 years in the general population). The prevalence of stroke is slightly lower in our study (1.1%) than that reported in general population (1.15%), but importantly stroke occurs in average 8 years earlier in our study population (median age 62 (54-73) versus mean age of 70.2 years in the general population). The early life occurrence of MI and stroke as well as HF in this population is particularly worrying, as these severe CV events are associated with disability, impaired quality of life and reduced life expectancy.

Regarding the prevalence of CV risk factors, it is of note the high rate of diabetes mellitus in our study population (7.8%), which is almost double than the rate reported in the general French population (4.7%) [28], despite the younger age of patients (median 56 (48-66) years versus mean 65 years in the general population) [28].

Regarding hypertension and obesity, the rate of these CV risk factors, although high, was lower in our study than in the general population (11.3% and 9.7% versus 32.3% and around 15%), but occurred at a much younger age compared to the general population [29–31]. The lower rates of hypertension and obesity in our study might be explained by the fact that these risk factors are not always registered, as they are generally coded as associated diagnosis. In contrast, in studies designed to assess these risk factors, most of them performed in ambulatory setting, data are rigorously recorded according to strict criteria. The rate of

CAD (excepting MI), and the rate of PAD, are also probably better registered in ambulatory setting than in the hospitalized setting, where these diseases are often coded as an associated diagnosis. A recent comprehensive meta-analysis, including 3 211 768 patients from 27 studies, found a pooled CV disease prevalence of 9.9% in severe mental disease patients with 11.8% in patients with schizophrenia and 8.4% in those with bipolar disorder [27]. Nevertheless, in some of these studies, the definition of CV disease was broadened to the occurrence of atrial fibrillation and pulmonary embolism. Also, this meta-analysis included all patients diagnosed with a CV disease, and not only those diagnosed in hospital setting.

Comparison among the five hospitals

Our study revealed few differences among the five hospitals concerning the occurrence of severe CV events. Some of these differences, such as a lower percentage of patients with MI at H1, could be explained by the younger age of the baseline population. However, the higher percentage of stroke at H3, occurring at a considerable younger age of patients, is difficult to explain. Certainly, differences exist among hospitals and primary/ambulatory care services regarding the methods of prevention, early detection and hospitalization of patients with severe CV events. Finally, the majority of our patients with severe CV disease (excepting HF) were men, which seems consistent with the higher reported CV risk in younger men, but also with the known underdiagnosis of some CV diseases in women [32]. It must also be noted that our baseline population was composed of around 60% of men which might also explain these sex differences.

The etiology of CV disease in patients with schizophrenia or psychotic disorder is multifactorial and includes genetical predisposition, lifestyle factors [33–35], and risk factors [36], but it is also favored by treatment with certain atypical neuroleptics which may induce weight gain, worsen metabolic conditions [37,38], and be associated with a higher CV risk [39]. As schizophrenia and psychotic disorders are chronic diseases requiring many years of

neuroleptic treatment [40,41], a balance between the CV risk and the psychiatric disease stabilization has to be found to assure the well-being and to increase the life expectancy of these patients.

Important clinical findings of our study

Patients with schizophrenia or psychotic disorder develop severe CV diseases requiring hospitalization at an early age (around ten years earlier than in the general population) and some diseases more frequently than the general population. The high rate and the early occurrence of diabetes mellitus also underlines the risk for CV disease and other complications in a population that is frequently engaged in unhealthy lifestyle [33–35].

Finally, psychiatric medication may also increase the risk of CV disease. For patients on neuroleptic treatment, French health authorities guidelines, based on several studies, recommend a close monitoring of body mass index, glycemia, blood pressure and lipid profile [42,43]. The same guidelines also recall that the second generation neuroleptics, especially Olanzapine and Clozapine, are more likely to cause or worsen cardiometabolic conditions when compared to first generation neuroleptics.

To reduce the risk of CV disease, several measures must be undertaken. First, the risk factors for CV disease, such as hypertension, obesity, diabetes mellitus, smoking but also other factors, such as social isolation must be identified and rigorously addressed. It is very important as CV diseases can be prevented by treating frequent risk factors, such as hypertension and diabetes mellitus [36]. Also, patients with an established CV disease must be early identified and rigorously treated. Psychiatrists and generalists need to work together to identify the best preventive measures according to patient profile. This includes also a strict surveillance of treatment, with preference for neuroleptics that do not increase the risk of overweight, diabetes mellitus and CV risk overall [37–39].

Study strength and limitations

The main strength of our study relies on the accuracy of data regarding the occurrence of severe CV disease requiring hospitalization. The French PMSI is a national database in which the trajectory of hospitalized patients can be accurately followed, from psychiatric to general hospital setting. The coding of diagnosis in general hospitals in France is also comprehensive and reliable. Second, data regarding the occurrence of severe CV disease were provided for five major French psychiatric hospitals and for the entire metropolitan France psychiatric hospitals, which included a sample of almost 100 000 patients.

Our study has also limitations. We included only hospitalized patients and not those diagnosed in ambulatory setting as the actual PMSI system does not allow the extraction of general hospital ambulatory data for patients hospitalized in psychiatry. In this regard, we probably underestimated the rate of some severe CV diseases and especially of some CV risk factors, such as hypertension, which are mainly diagnosed and treated in ambulatory setting. Also, we included patients diagnosed with a CV disease five years before or three years after the index hospitalization in psychiatry (for a total of 8 years follow-up), which may also have underestimated the prevalence of CV disease in the general hospital setting. On the other hand, the coding of the diagnosis is probably more precise in this timeframe window as we know that the accuracy of data and the coding practices change over time.

Conclusion

Our study shows that patients with schizophrenia or psychotic disorder develop severe CV disease, such as MI and stroke, at an early age, around ten years earlier than the general population. This early life event rate has a major impact on quality of life and life expectancy of these patients, as well as on health care costs. Importantly, these severe CV events are associated with a high percentage of preventable and treatable risk factors, such as hypertension and diabetes. Psychiatrists and generalists, as well as other health care providers need to work together to assure an appropriate prevention and treatment of CV disease in this

vulnerable population.

The authors have no conflicts of interest.

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Hospital /	H1	H2	H3	H4	Н5	Overall	Metropolitan
characteristics						hospitals	France
Number of patients	597	508	617	1405	1306	4424	96100
Age, median (IQR)	41 (29-52)	43 (33-55)	42 (33-53)	46 (36-57)	41 (30-53)	43 (32-55)	43 (32-54)
Sex, men, n (%)	375 (63)	301 (59)	399 (65)	863 (61)	749 (57)	2680 (61)	58709 (61)

 Table 1. Socio-demographic characteristics of patients with schizophrenia or psychotic

 disorder included in the study

*IQR – interquartile range, H1 – Hospital 1, H2 – Hospital 2, H3 – Hospital 3, H4 – Hospital 4, H5 – Hospital 5

	H1	H2	H3	H4	H5	Overall	Metropolitan
	(N=597)	(N=508)	(N=617) (N	(N=1405)	(N=1405) (N=1306)	hospitals (N=4424)	France (N=96100)
CV diseases, n (%)	22 (3,7)	19 (3,7)	29 (4,7)	79 (5,6)	54 (4,1)	203 (4,6)	4518 (4,7)
Age, median (IQR)	58 (50-71)	60 (49-68)	56 (49-60)	64 (53-77)	61 (51-71)	60 (51-72)	60 (50-70)
Sex, men, n (%)	14 (64)	13 (68)	15 (52)	37 (47)	28 (52)	107 (53)	2623 (58)
MI	2 (0,3)	4 (0,8)	4 (0,7)	9 (0,6)	8 (0,6)	27 (0,6)	686 (0,7)
Age, median (IQR)	47 (44-49)	54 (47-64)	60 (41-76)	60 (56-71)	56 (49-71)	57 (49-70)	57 (48-66)
Sex, men, n (%)	2 (100)	3 (75)	2 (50)	7 (78)	4 (50)	18 (67)	482 (70)
Stroke	4 (0,7)	1 (0,2)	10 (1,6)	14 (1,0)	19 (1,5)	49 (1,1)	1279 (1,3)
Age, median (IQR)	69 (62-72)	80 (80-80)	56 (51-60)	67 (53-75)	60 (53-73)	62 (54-73)	59 (50-69)
Sex, men, n (%)	1 (25)	0 (0)	5 (50)	7 (50)	9 (47)	22 (45)	718 (56)
HF	9 (1,5)	8 (1,6)	11 (1,8)	38 (2,7)	20 (1,5)	86 (1,9)	1915 (2,0)
Age, median (IQR)	70 (61-79)	59 (53-69)	58 (47-73)	63 (53-77)	65 (55-74)	62 (54-73)	62 (52-73)
Sex, men, n (%)	6 (67)	5 (63)	4 (36)	13 (34)	6 (30)	34 (40)	975 (51)
CAD	11 (1,8)	10 (2,0)	8 (1,3)	35 (2,5)	29 (2,2)	93 (2,1)	1849 (1,9)
Age, median (IQR)	50 (47-58)	59 (49-65)	58 (47-65)	65 (54-81)	58 (50-70)	59 (50-73)	60 (51-69)
Sex, men, n (%)	9 (82)	8 (80)	5 (63)	21 (60)	18 (62)	61 (66)	1244 (67)
PAD	0 (0)	0 (0)	1 (0,2)	0 (0)	3 (0,2)	4 (0,1)	114 (0,1)
Age, median (IQR)			26 (26-26)		62 (58-73)	60 (42-68)	53 (41-62)
Sex, men, n (%)			1 (100)		2 (67)	3 (75)	58 (51)

Table 2a. Percentage of patients with CV disease and socio-demographic characteristics of patients with CV disorders

*CV – Cardiovascular, MI – myocardial infarction, HF – Heart Failure, CAD – Coronary Artery Disease, PAD – Peripheral Artery Disease, IQR - interquartile range, H1 - Hospital 1, H2 - Hospital 2, H3 - Hospital 3, H4 - Hospital 4, H5 - Hospital 5

patients								
	H1 (N=597)	H2 (N=508)	H3 (N=617)	H4 H5 7) (N=1405) (N=130	H5 (N=1306)	Overall (N=4424)	Metropolitan France (N=96100)	
Hypertension	55 (9,2)	75 (14,8)	51 (8,3)	193 (13,7)	118 (9,0)	500 (11,3)	9165 (9,5)	
Age, median (IOR)	58 (47-67)	62 (49-68)	56 (49-67)	61 (51-69)	58 (49-70)	60 (49-68)	60 (51-69)	

Table 2b. Percentage of patients with CV risk factors and socio-demographic characteristics of

						(N=4424)	(11-90100)
Hypertension	55 (9,2)	75 (14,8)	51 (8,3)	193 (13,7)	118 (9,0)	500 (11,3)	9165 (9,5)
Age, median (IQR)	58 (47-67)	62 (49-68)	56 (49-67)	61 (51-69)	58 (49-70)	60 (49-68)	60 (51-69)
Sex, men, n (%)	25 (45)	31 (41)	26 (51)	99 (51)	57 (48)	241 (48)	4336 (47)
Diabetes	34 (5,7)	44 (8,7)	45 (7,3)	147 (10,5)	71 (5,4)	344 (7,8)	6441 (6,7)
Age, median (IQR)	57 (47-67)	58 (49-69)	55 (45-62)	57 (49-69)	55 (47-61)	56 (48-66)	56 (47-64)
Sex, men, n (%)	14 (41)	25 (57)	23 (51)	75 (51)	38 (54)	176 (51)	3249 (50)

Obesity	65 (10,9)	48 (9,5)	68 (11,0)	126 (9,0)	111 (8,5)	431 (9,7)	9098 (9,5)
Age, median (IQR)	47 (36-56)	48 (40-59)	50 (42-59)	53 (45-62)	45 (35-58)	49 (39-59)	48 (38-58)
Sex, men, n (%)	26 (40)	22 (46)	34 (50)	54 (43)	50 (45)	190 (44)	3 861 (42)

*IQR – interquartile range, H1 – Hospital 1, H2 – Hospital 2, H3 – Hospital 3, H4 – Hospital 4, H5 – Hospital 5

	Five hos (N=44	-	Metropolitan France (N=96100)		
	5 years before	3 years after	5 years before	3 years after	
CV diseases, n (%)	106 (2,4)	97 (2,2)	2666 (2,8)	1852 (1,9)	
MI	13 (0,3)	14 (0,3)	392 (0,4)	294 (0,3)	
Stroke	23 (0,5)	26 (0,6)	692 (0,7)	587 (0,6)	
HF	39 (0,9)	47 (1,1)	1005 (1,1)	910 (1,0)	
CAD	54 (1,2)	39 (0,9)	1163 (1,2)	686 (0,7)	
PAD	2 (0,1)	2 (0,1)	85 (0,1)	29 (0,0)	
Risk factors, n (%)					
Hypertension	350 (7,9)	150 (3,4)	6161 (6,4)	3004 (3,1)	
Diabetes	255 (5,8)	89 (2,0)	4613 (4,8)	1828 (1,9)	
Obesity	275 (6,2)	156 (3,5)	5775 (6,0)	3323 (3,5)	

Table 3. The rate of CV disease and risk factors before and after the index psychiatric hospitalization

*CV – Cardiovascular, MI – myocardial infarction, HF – Heart Failure, CAD – Coronary Artery Disease, PAD – Peripheral Artery Disease

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	Principal diagnosis	Associated diagnosis			
CV diseases, n (%)	109 (54)	94 (46)			
MI	21 (78)	6 (22)			
Stroke	39 (80)	10 (20)			
Heart failure	32 (37)	54 (63)			
CAD	25 (27)	68 (73)			
PAD	1 (25)	3 (75)			
Risk factors, n (%)					
Hypertension	10 (2)	490 (98)			
Diabetes	83 (24)	261 (76)			
Obesity	33 (8)	398 (92)			

Table 4. Principal and associated diagnosis repartition for the overall study population

*CV – Cardiovascular, MI – myocardial infarction, HF – Heart Failure, CAD – Coronary Artery Disease, PAD – Peripheral Artery

Disease