



**HAL**  
open science

## Prevalence of multiple sclerosis in France in 2021: Data from the French health insurance database

C. Pierret, Marie Mainguy, Emmanuelle Leray

### ► To cite this version:

C. Pierret, Marie Mainguy, Emmanuelle Leray. Prevalence of multiple sclerosis in France in 2021: Data from the French health insurance database. *Revue Neurologique*, 2024, 180 (5), pp.429-437. 10.1016/j.neurol.2023.12.007 . hal-04487926

**HAL Id: hal-04487926**

**<https://ehesp.hal.science/hal-04487926v1>**

Submitted on 29 May 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution - NonCommercial 4.0 International License

# Prevalence of multiple sclerosis in France in 2021: data from the French health insurance database

Chloé Pierret\*<sup>1</sup>, Marie Mainguy<sup>1</sup>, Emmanuelle Leray<sup>1</sup>

<sup>1</sup>Rennes University, EHESP, CNRS, Inserm, ARENES UMR 6051, RSMS U 1309, Rennes, France

**Corresponding author\*:**

Chloé PIERRET

15 Av. du Professeur Léon Bernard,

35000 Rennes,

France

+33 6 65 60 30 92

[chloe.pierret@ehesp.fr](mailto:chloe.pierret@ehesp.fr)

## **Abstract**

### **Background**

France is among the countries with high prevalence of multiple sclerosis (MS). The most recent estimates are from 2012 and need to be updated because MS prevalence has increased worldwide.

### **Objective**

To estimate MS prevalence in France on December 31, 2021 and to describe the characteristics of the French MS population using data from the French national health insurance database (SNDS).

### **Material and Methods**

Persons with MS (PwMS) were identified in the SNDS database (99% of national coverage) using an algorithm with three criteria: long-term disease status, hospitalizations, and MS-specific drug reimbursements. Crude and sex- and age-stratified prevalence rates were calculated with their 95% confidence intervals as well as the standardized prevalence stratified on the region of residence.

### **Results**

In total, 134,062 PwMS were identified (71.8% of women, median age  $53.0 \pm 14.8$  years) yielding a prevalence of 197.6 per 100,000 (95% CI: [196.5, 198.7]). Prevalence rates in women and men were respectively 274.9 (95% CI [273.2, 276.6]) and 115.2 (95% CI [114.0; 116.4]). In metropolitan France, the highest prevalence rates were observed in the northeastern regions (e.g. >230 PwMS per 100,000 in Grand Est and Hauts-de-France), and the lowest rates in the southwestern regions (~180 PwMS per 100,000 in Nouvelle-Aquitaine and Occitanie). Overall, 32.1% of PwMS had another long-term disease and 51.8% received at least one MS-specific drug in 2021.

### **Conclusion**

MS prevalence in France has increased by ~30% in the last 10 years. This increase is probably linked to population ageing, longer survival of PwMS, and the long observation period. The part attributable to a possible increase in MS risk remains to be determined with incidence studies.

**Keywords** – Epidemiology, Prevalence, France, Multiple Sclerosis, Administrative Claims

## **1. Introduction**

Multiple sclerosis (MS), a demyelinating autoimmune disorder of the central nervous system, is estimated to affect 2.8 million individuals worldwide [1], particularly women. It is often diagnosed between the age of 25 and 35 years [2]. MS has no known cure and leads to progressive cognitive, neurological and physical impairment over the lifetime [3]. As MS reduces life expectancy only marginally, patients with MS (PwMS) live with the disease for many decades and this is associated with increasing and complex healthcare needs [4,5]. The prevalence of MS is influenced by many factors, and shows wide geographical variations, even within the same country, meaning that some regions will have a higher disease burden, with different healthcare needs [6,7].

The third edition of the Atlas of MS by the MS International Federation reported an increase in MS prevalence by 35% in Europe and by 16% in the world between 2013 and 2020 [1]. As the last prevalence estimate for France (151.2 PwMS/100,000; n=99,123) is from 2012 [8], it needs to be updated to identify potential changes and trends and also to inform key decision-makers about the range and scope of the healthcare needs of PwMS.

Since 2009, France has integrated multiple databases from hospitals (private and public), in- and out-patient care clinics, and data on prescribed drug reimbursements into the French national health insurance database (Système national des données en santé; (SNDS)). This database covers approximately 66 million inhabitants (i.e. ~99% of the French population) and has been increasingly used for epidemiological studies [9]. The SNDS database was also used for estimating MS prevalence in France in 2012 [8].

The main objective of this study was to estimate MS prevalence in France on December 31, 2021 and to describe the French MS population in terms of age, sex and geographical location using the SNDS database.

## **2. Material and Methods**

### **2.1 Data source**

The SNDS database contains data from hospitalization records (in- and out-patient care) and all prescribed drug reimbursements. The hospital entry and exit dates are recorded, as well as the ICD-10 diagnosis codes at discharge [9].

Sociodemographic data also are available, such as date of birth, sex, insurance scheme and city of residence. Each city of residence is associated with an ecological deprivation index called FDep. This social deprivation index classifies cities in five quintiles of deprivation (from 5 = most deprived, to 1 = least deprived) based on four socioeconomic indicators (e.g. median household income, proportion of high school graduates, proportion of blue-collar workers, and the unemployment rate) [10]. Moreover, French residents with low income have the right to a specific insurance scheme called Couverture Medicale Universelle (CMU) based on their income and household size. Conversely, information on individual behaviors, such as tobacco, recreational drug and alcohol consumption, is not available. As SNDS primary goal is to measure healthcare expenditures, reports from consultations with clinicians and laboratory reports are not available and identification algorithms have to be used to identify diseases. Every year, the *Caisse National d'Assurance Maladie* (CNAM) releases reports on a list of 58 common diseases using SNDS data [11].

Since 1945, a long-term disease (LTD) status is used in France for 30 chronic diseases (e.g. MS, diabetes, cancer) with expensive and/or long treatments. For patients with this status, 100% of the healthcare costs are covered by the French national security system and no upfront payment is needed on all medical care related to that disease. The declaration of this status, present in the SNDS, is not mandatory and is done at the patient's and general practitioner's discretion. As MS has no cure, the LTD status for this disease does not have an expiration date.

This study was conducted at the French School of Public Health (EHESP), which has permanent access to the SNDS database in application of the provisions of Articles R. 1461–11 to R. 1461-17 of the French Public Health Code and the French data protection authority decision CNIL-2016-316. As permanent users of the SNDS, the authors declared the study to the EHESP's SNDS registry and were exempted from Institutional Review Board approval.

## 2.2 Study population

### 2.2.1 MS identification

The aim of this cross-sectional study was to quantify and describe the MS population in France on December 31, 2021. MS was identified based on the presence of at least one of the following criteria: i) LTD status for MS (MS-LTD), ii) hospitalization for MS, and iii) MS-specific drug reimbursement (beta-interferon, cladribine, dimethyl fumarate, fingolimod,

glatiramer acetate, natalizumab, ocrelizumab, ponesimod, and teriflunomide). The identification period for hospitalization records and drug reimbursement data was from January 1, 2009 to December 31, 2021 and was without any minimum date for LTD status (up to December 31, 2021).

LTD status and hospitalizations for MS were identified based on the “G35” ICD-10 code. To ensure the specificity of our case definition, individuals were not included if i) they did not have the MS-LTD status, ii) they had only one hospitalization related to MS, and iii) they did not have any MS-specific drug reimbursement. Similarly, individuals i) without MS-LTD status, ii) without hospitalizations for MS, and iii) with only one MS-specific drug reimbursement during the observation period were not included.

As the clinical similarities between neuromyelitis optica spectrum disorder (NMOSD) and MS can lead to a false-positive MS diagnosis, individuals with at least one NMOSD hospitalization (ICD-10: G36) and without MS-LTD status or MS-specific drug reimbursement also were excluded [12,13].

MS identification date was defined as the earliest available date for hospitalization for MS, MS-LTD status declaration, or MS-specific drug reimbursement. All individuals who met the inclusion criteria and without exclusion criteria and who were alive on December 31, 2021 were included.

### *2.2.2 Descriptive characteristics*

Department of residence, insurance scheme, comorbidities of interest and MS-related characteristics were retrieved for the year 2021. In order to minimize missingness, when information was missing, characteristics from 2020 were retrieved. Patients were defined as having received a specific DMT if they had at least one reimbursement of that drug during the year and patients could be reimbursed for different DMTs.

## **3. Statistical analysis**

### **3.1 Study population characteristics**

The data of the study population were described using medians and interquartile ranges for continuous variables and crude numbers and percentages for categorical variables. Sociodemographic characteristics, comorbidities of interest, and MS-related characteristics were reported.

## 3.2 Prevalence

MS prevalence was defined as the number of PwMS identified on December 31, 2021 divided by the French population on January 1, 2022 (i.e. the reference population) [14]. The age and sex-stratified MS prevalence rates also were reported. To facilitate comparison with previous French and international studies, prevalence was standardized by sex and age to the 1976, 2013 and 2021 European populations as well as to the 2013 and 2021 world populations.

Statistical analyses were performed with SAS v.8.3.7 and R v.4.1.2.

## 4. Results

### 4.1 Population characteristics

We identified 134,062 PwMS in France on December 31, 2021. Among these PwMS, 76.9% met at least two of the three selection criteria. The most frequent identification criterion was LTD status (92.6%). The Venn diagram showing the distribution of the three criteria is in Figure 1. The PwMS mean age was  $52.9 \pm 14.8$  years, without difference between sexes, and 494 PwMS were 18 or younger; the age distribution by sex is shown in Figure 2. Overall, 71.8% of PwMS were women. The median time from the LTD declaration date to 2021 was 12 years (IQR [5; 19]) and the mean age at LTD declaration was  $40.0 \pm 12.2$  years, without difference between sexes. The population characteristics are summarized in Table 1.

The MS population had a complex clinical profile: 32.1% of PwMS had at least one LTD status for another disease, 41.5% had been hospitalized at least once (in- or out-patient stay, related or not related to MS), and 27.4% had been hospitalized at least once for an MS-related pathology in 2021. Approximately a third of the population had a psychiatric disorder or was taking a psychotropic treatment.

Most PwMS were covered by the general insurance scheme and were living in cities that were evenly distributed in the five FDep index levels. In 2021, 51.7% of PwMS had been treated at least once with a DMT; teriflunomide, dimethyl fumarate and fingolimod were the most frequent. These patients were, on average, 12 years younger than patients who did not receive disease-modifying treatments (47 vs 59), without difference between sexes.

Between 2009 and 2021, we identified 14,159 PwMS deaths and their mean age at death was 68 years (F: 69, M: 66).

We excluded 11,653 persons because they only had one hospitalization for MS and no MS-LTD status or MS-specific drug reimbursement, 1,200 persons who had only one MS-specific drug reimbursement but no MS-LTD status or hospitalization, and 364 persons with at least one NMOSD hospitalization and no MS-LTD status or MS-specific treatment.

## 4.2 Prevalence

On December 31, 2021, the French national crude prevalence of MS was 197.6 per 100,000 inhabitants (95% CI: [196.5, 198.7]). Prevalence in women was 2.3-fold higher than in men (274.9, 95% CI [273.2, 276.6] vs 115.2, 95% CI [114.0, 116.4], respectively). The age- and sex-stratified prevalence rates are shown in Table 2, with a peak in the 55 to 59-year-old group for both men and women. Prevalence rates standardized to the 1976, 2013 and 2021 European populations and the 2013 and 2021 world populations are presented in Table 3.

The standardized prevalence rates for each region are presented in Table 4 and for each 'department' in Figure 3 and Supplemental Table 1. The percentage of prevalence increase compared with the 2012 regional rates are also shown in Table 4. MS prevalence rates varied among regions, with a 1.4-fold difference between the regions with the highest and lowest prevalence. The highest prevalence rates were in the northeastern regions (e.g. Grand Est and Hauts-de-France had rates >230 PwMS per 100,000) and the lowest rates in the southwestern regions (e.g. Nouvelle-Aquitaine and Occitanie had rates ~180 PwMS per 100,000).

Prevalence was substantially lower in the overseas regions (50.1, 95% CI: [47.0; 53.2]).

## 5. Discussion

We estimated an overall crude MS prevalence of 197.6 per 100,000 inhabitants (95% CI: [196.5, 198.7]), which corresponded to a 30% increase compared with the 2012 estimate [8]. When comparing standardized rates between 2012 and 2021, the increase ranged between 20% (1976-European population) and 36% (2013-World population). This increase is consistent with the 35% increase in MS prevalence in Europe between 2013 and 2020 [1]. Depending on the region, the increase ranged between 19.6% (Picardie) and 45.5% (Corse), without differences between men and women. We also confirmed the previously described North-East to South-West gradient [15]. The information on residence is from the year 2021 and may differ from their residence at the time of diagnosis, which was not reported in this study. Although we standardized on age and sex, we were unable to adjust for other



determinants of MS incidence such as sun exposure, country of birth or smoking behavior as well as other important factors such as mortality, availability of care and diagnostic practices.

Several potential mechanisms could explain this prevalence increase. First, it could be due to a decrease in mortality. Compared with 2012, the peak in prevalence by age group moved from the 50-54 years group to the 55-59 years group. Moreover, the prevalence increase was higher in the older age groups. For example, the percentage of >60-year-old PwMS increased from 26.3% to 30.6%. This aging trend in PwMS is in accordance with a potential decrease in mortality. Second, the criteria for MS diagnosis changed over time, becoming more sensitive. This could partly explain the prevalence increase, although it should be matched with an increase in the observed incidence [16]. Third, it could be linked to an increase in incidence; however, recent studies mostly observed a decrease or stabilization in MS incidence since 2010, arguing against this explanation [17–21]. Fourth, it could be due to a more sensitive identification algorithm; indeed, our observation period was 12 years for hospitalizations and MS-specific drug reimbursements and unlimited for LTD status and this allowed identifying persons with milder and less active MS whereas Foulon et. al. only had a 2-year observation period for DMTs and a 5 year observation period for hospitalizations

Every year, CNAM releases reports on the prevalence of some diseases in France, including MS, using data from the SNDS database. In 2021, it reported 122,800 active MS cases. This means that we identified approximately 9% more cases [22]. The CNAM population and our MS population shared the same age and sex characteristics. Therefore, the prevalence difference could be explained by a difference in selection algorithms. Our identification algorithm was based on the algorithm used by Foulon et al in 2012 [8] and updated in collaboration with neurologists and SNDS experts. LTD status is requested by the patient's general practitioner with the patient's approval and is then validated by an independent healthcare professional from the health insurance system. Hospitalization records are coded by clinicians and ICD-10 codes are mandatory because they will determine the cost of each hospital stay. Coding is regularly controlled by the paying bodies to ensure its validity. Finally, drug reimbursement is an automated process linked to the drug barcode. Moreover, due to the high price of MS-specific drugs, it is unlikely that patients would not request reimbursement.

Although the CNAM used the same three identification criteria, our observation period was longer (from 2009 to 2021 in our study vs 2017 to 2021 for hospitalizations and LTD status and only 2021 for MS-specific drugs in the CNAM population). The longer observation

period allowed identifying PwMS who are not treated anymore or who were not recently hospitalized for an MS-related reason. Moreover, CNAM required at least two reimbursements of MS-specific drugs in 2021. However, in 2021, a PwMS could have had only one reimbursement for MS-specific drugs, for example if this patient switched from a MS-specific to a non-specific drug, or if MS progressed to the progressive form (for which there is no treatment approved), or if the patient decided to stop treatment (e.g. side effects, contraindication, years of disease inactivity, pregnancy, personal convenience).

The higher sensitivity of our identification algorithm raises the question of whether false positives were included in our estimates [23]. To minimize this risk, we adapted the identification algorithm from 2012 to render it more specific by adding the following exclusion criteria : we excluded i) individuals with a single MS-specific drug reimbursement, no MS-LTD status and no hospitalizations as well as ii) individuals with a single hospitalization for MS, no drug reimbursement and no MS-LTD status. In addition, as NMOSD can sometimes lead to a false diagnosis of MS, we did not include individuals with one or multiple MS hospitalizations, but no MS-LTD status or MS-specific drug reimbursement if they also had at least one hospitalization for NMOSD. Also, unlike Foulon et. al, we did not use MS-dedicated pensions. Finally, we could not identify PwMS if they did not have MS-LTD status and had not been hospitalized or treated between 2009 and 2021. This means that we might have missed some benign cases as well as some 2021 incident cases who had not received MS-related care yet. Indeed, we could not measure MS incidence because we used healthcare consumption data.

Regarding psychiatric comorbidities, we observed estimates comparable to the existing literature with 33% of our population with an LTD, a hospitalization or more than 3 drug reimbursements related to a mental health disorder and 29% having received either antidepressants or anxiolytics in the year 2021 [24-27]. Our population had slightly higher than previously described estimates of prevalence for comorbidities associated with age such as diabetes and cancer, most probably due to differing age structures [28-30]. One limitation of our study is that the main purpose of the database is to manage healthcare reimbursement to patients and hospitals. Therefore, it does not include important information, such as income, smoking and alcohol drinking status, or immigration status, to better describe our population. We used proxy variables, such as the CMU status and the FDep index, to estimate the socioeconomic status of our population and did not observe a difference with the general population [31]. Moreover, as the SNDS database does not collect clinical information, the

type of MS, severity of symptoms and disability remained unknown as well as the date of diagnosis certified by a neurologist. In addition, mitoxantrone, a drug proposed only to patients with highly active MS, cannot be identified in the SNDS database. This might have resulted in missing a small number of PwMS.

## **6. Conclusion**

To conclude, we estimated MS prevalence in France on December 31, 2021: 197.6 PwMS per 100,000 inhabitants (95% CI: [196.5, 198.7]). This represents roughly an increase by 30% from the previous estimate in 2012, as observed in other European countries. It remains unclear whether this prevalence increase can be explained solely by longer PwMS survival, and better case identification with our algorithm, or if it reflects an increase in incidence. Incidence studies are needed to understand the underlying mechanisms behind this increase.

## **Funding**

This work was supported by the *EDMUS-ARSEP Foundation* and the *Institut des Neurosciences Cliniques de Rennes*.

## **Declaration of competing interest**

Chloé Pierret and Marie Mainguy have no conflicts of interest.

Emmanuelle Leray reports consulting and lecture fees or travel grants from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi, not related to the submitted work.

## References

- [1] Walton C, King R, Rechtman L, Kaye W, Leray E, Marrie RA, et al. Rising prevalence of multiple sclerosis worldwide: Insights from the Atlas of MS, third edition. *Mult Scler J* 2020;26:1816–21. <https://doi.org/10.1177/1352458520970841>.
- [2] Leray E, Moreau T, Fromont A, Edan G. Epidemiology of multiple sclerosis. *Rev Neurol (Paris)* 2016;172:3–13. <https://doi.org/10.1016/j.neurol.2015.10.006>.
- [3] Thompson AJ, Baranzini SE, Geurts J, Hemmer B, Ciccarelli O. Multiple sclerosis. *Lancet Lond Engl* 2018;391:1622–36. [https://doi.org/10.1016/S0140-6736\(18\)30481-1](https://doi.org/10.1016/S0140-6736(18)30481-1).
- [4] Scalfari A, Knappertz V, Cutter G, Goodin DS, Ashton R, Ebers GC. Mortality in patients with multiple sclerosis. *Neurology* 2013;81:184–92. <https://doi.org/10.1212/WNL.0b013e31829a3388>.
- [5] Kobelt G, Thompson A, Berg J, Gannedahl M, Eriksson J, MSCOI Study Group, et al. New insights into the burden and costs of multiple sclerosis in Europe. *Mult Scler Houndmills Basingstoke Engl* 2017;23:1123–36. <https://doi.org/10.1177/1352458517694432>.
- [6] Llorca J, Guerrero P, Prieto-Salceda D, Dierssen-Sotos T. Mortality of multiple sclerosis in Spain: demonstration of a north-South gradient. *Neuroepidemiology* 2005;24:135–40. <https://doi.org/10.1159/000083296>.
- [7] Forouhari A, Taheri G, Salari M, Moosazadeh M, Etemadifar M. Multiple sclerosis epidemiology in Asia and Oceania; A systematic review and meta-analysis. *Mult Scler Relat Disord* 2021;54:103119. <https://doi.org/10.1016/j.msard.2021.103119>.
- [8] Foulon S, Maura G, Dalichampt M, Alla F, Debouverie M, Moreau T, et al. Prevalence and mortality of patients with multiple sclerosis in France in 2012: a study based on French health insurance data. *J Neurol* 2017;264:1185–92. <https://doi.org/10.1007/s00415-017-8513-0>.
- [9] 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* 2017;65:S149–67. <https://doi.org/10.1016/j.respe.2017.05.004>.
- [10] Rey G, Jouglu 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 Public Health* 2009;9:33. <https://doi.org/10.1186/1471-2458-9-33>.
- [11] Rachas A, Gastaldi-Ménager C, Denis P, Barthélémy P, Constantinou P, Drouin J, et al. The Economic Burden of Disease in France From the National Health Insurance Perspective: The Healthcare Expenditures and Conditions Mapping Used to Prepare the French Social Security Funding Act and the Public Health Act. *Med Care* 2022;60:655. <https://doi.org/10.1097/MLR.0000000000001745>.
- [12] Winter A, Chwalisz B. MRI Characteristics of NMO, MOG and MS Related Optic Neuritis. *Semin Ophthalmol* 2020;35:333–42. <https://doi.org/10.1080/08820538.2020.1866027>.
- [13] Cree BAC, Goodin DS, Hauser SL. Neuromyelitis optica. *Semin Neurol* 2002;22:105–22. <https://doi.org/10.1055/s-2002-36534>.
- [14] Estimation de la population au 1<sup>er</sup> janvier 2023 | Insee n.d. <https://www.insee.fr/fr/statistiques/1893198> (accessed September 21, 2023).
- [15] Fromont A, Biquet C, Sauleau EA, Fournel I, Bellisario A, Adnet J, et al. Geographic variations of multiple sclerosis in France. *Brain J Neurol* 2010;133:1889–99. <https://doi.org/10.1093/brain/awq134>.

- [16] Cree BAC, Oksenberg JR, Hauser SL. Multiple sclerosis: two decades of progress. *Lancet Neurol* 2022;21:211–4. [https://doi.org/10.1016/S1474-4422\(22\)00040-0](https://doi.org/10.1016/S1474-4422(22)00040-0).
- [17] Faraji F, Ahmadi F, Mohaghegh P, Talaie A. Temporal Incidence and Prevalence Trends of Multiple Sclerosis in Markazi Province, Iran. *Mult Scler Relat Disord* 2022;60:103691. <https://doi.org/10.1016/j.msard.2022.103691>.
- [18] Wnuk M, Maluchnik M, Perwieniec J, Podwojcic K, Szelag M, Walkiewicz D, et al. Multiple sclerosis incidence and prevalence in Poland: Data from administrative health claims. *Mult Scler Relat Disord* 2021;55:103162. <https://doi.org/10.1016/j.msard.2021.103162>.
- [19] Koch-Henriksen N, Magyari M. Apparent changes in the epidemiology and severity of multiple sclerosis. *Nat Rev Neurol* 2021;17:676–88. <https://doi.org/10.1038/s41582-021-00556-y>.
- [20] Costa-Arpín E, Ares B, González-Quintela A, Prieto-González J. Temporal trends in the incidence and prevalence of Multiple Sclerosis in the Northwest of Spain. *Mult Scler Relat Disord* 2021;52:102979. <https://doi.org/10.1016/j.msard.2021.102979>.
- [21] Gbaguidi B, Guillemin F, Soudant M, Debouverie M, Mathey G, Epstein J. Age-period-cohort analysis of the incidence of multiple sclerosis over twenty years in Lorraine, France. *Sci Rep* 2022;12:1001. <https://doi.org/10.1038/s41598-022-04836-5>
- [22] CNAM, DSES, DEPP. Fiche pathologie : Personnes prises en charge pour sclérose en plaques (SEP) en 2021 2023.
- [23] Ducatel P, Debouverie M, Soudant M, Guillemin F, Mathey G, Epstein J. Performance of administrative databases for identifying individuals with multiple sclerosis. *Sci Rep* 2023;13:18310. <https://doi.org/10.1038/s41598-023-45384-w>.
- [24] Marrie RA, Fisk JD, Tremlett H, Wolfson C, Warren S, Tennakoon A, et al. Differences in the burden of psychiatric comorbidity in MS vs the general population. *Neurology* 2015;85:1972–9. <https://doi.org/10.1212/WNL.0000000000002174>.
- [25] Marrie RA, Horwitz R, Cutter G, Tyry T, Campagnolo D, Vollmer T. The burden of mental comorbidity in multiple sclerosis: frequent, underdiagnosed, and undertreated. *Mult Scler Houndmills Basingstoke Engl* 2009;15:385–92. <https://doi.org/10.1177/1352458508099477>.
- [26] Marrie RA, Cohen J, Stuve O, Trojano M, Sørensen PS, Reingold S, et al. A systematic review of the incidence and prevalence of comorbidity in multiple sclerosis: Overview. *Mult Scler Houndmills Basingstoke Engl* 2015;21:263–81. <https://doi.org/10.1177/1352458514564491>.
- [27] Guilleux, Alice, Jonathan Roux, David Travers, et Emmanuelle Leray. « Prevalence of Mental Disorders Is Higher in Patients with Multiple Sclerosis than in the General Population or in Patients with Rheumatoid Arthritis in France ». *Multiple Sclerosis Journal - Experimental, Translational and Clinical* 6, n° 3 (2020): 2055217320941540. <https://doi.org/10.1177/2055217320941540>.
- [28] Giannopoulos V, Palaiodimou L, Kitsos D, Papagiannopoulou G, Stavrogianni K, Chasiotis A, et al. The Prevalence of Diabetes Mellitus Type II (DMII) in the Multiple Sclerosis Population: A Systematic Review and Meta-Analysis. *J Clin Med* 2023;12:4948. <https://doi.org/10.3390/jcm12154948>.
- [29] Marrie RA, Reider N, Cohen J, Stuve O, Trojano M, Sorensen PS, et al. A systematic review of the incidence and prevalence of cancer in multiple sclerosis. *Mult Scler Houndmills Basingstoke Engl* 2015;21:294–304. <https://doi.org/10.1177/1352458514564489>.
- [30] Moisset X, Perié M, Pereira B, Dumont E, Lebrun-Frenay C, Lesage FX, et al. Decreased prevalence of cancer in patients with multiple sclerosis: A case-control study. *PLOS ONE* 2017;12:e0188120. <https://doi.org/10.1371/JOURNAL.PONE.0188120>.

[31] Fiche 16 - La couverture maladie universelle complémentaire (CMU-C). DREES; 2019.

**Figures (all printed in color)**

Figure 1. Venn diagram showing the MS identification criteria, December 31, 2021: n=134,062.

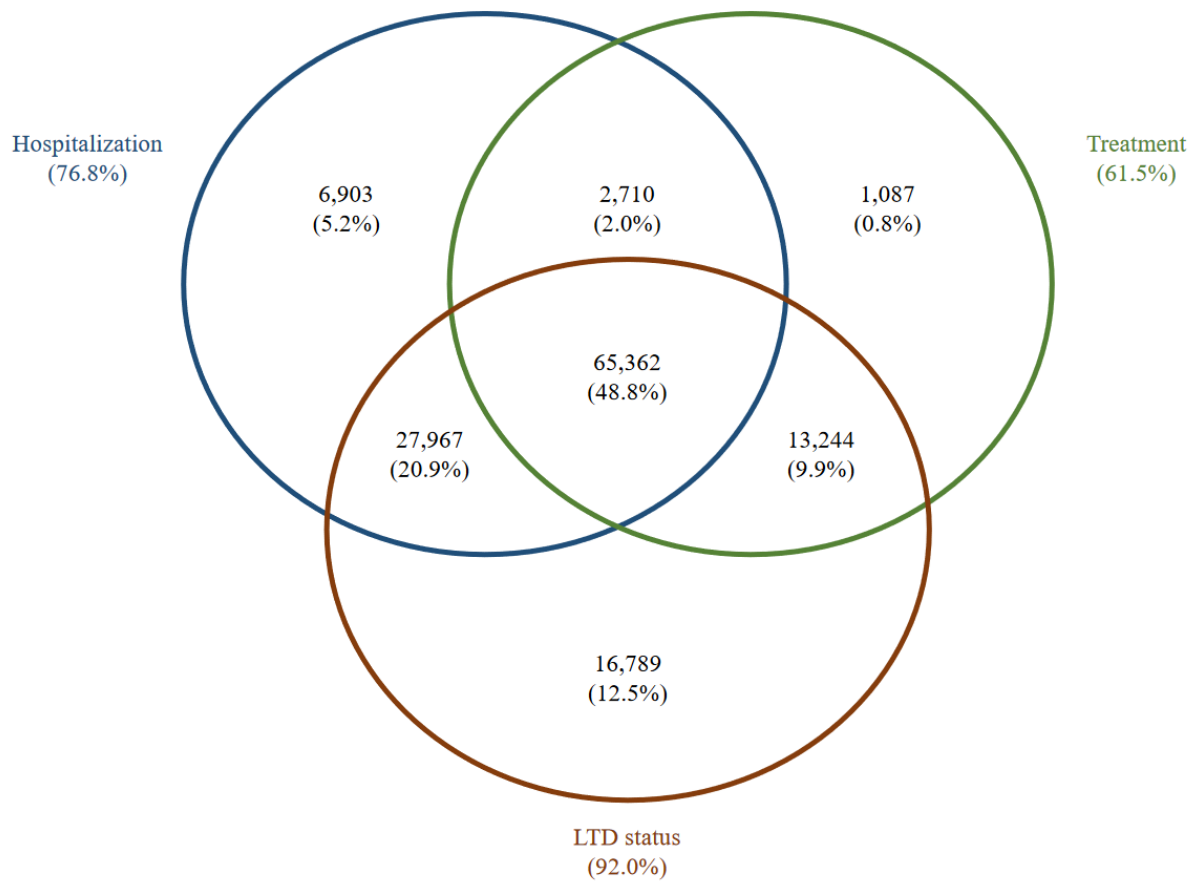


Figure 2. Age and sex pyramid of the French population with MS on December 31, 2021 (n=134,062).

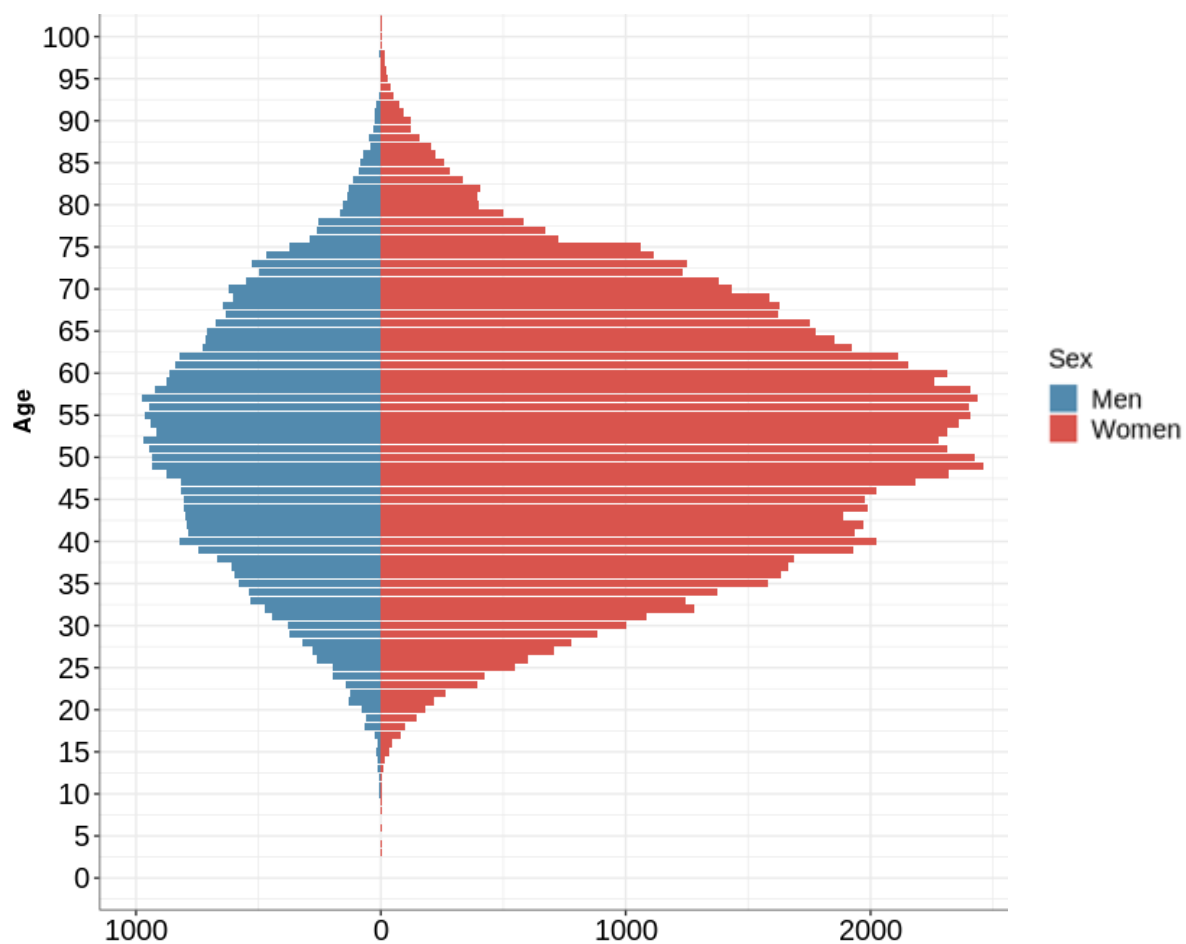
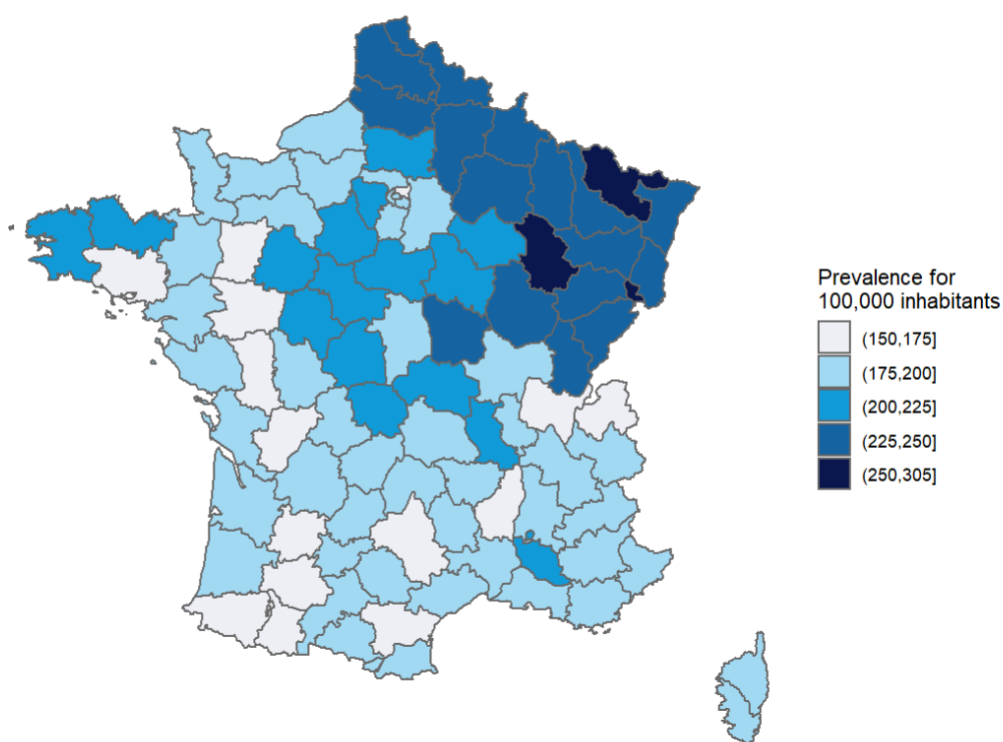


Figure 3. Age- and sex-standardized prevalence by department in metropolitan France in 2021.

## Tables





**Table 1:** Characteristics of the population with MS in France on December 31, 2021 (n=134,062).

<b>Demographics</b>	<b>n (%)</b>
Sex at birth	
Men	37,805 (28.2)
Women	96,257 (71.8)
Age in years, median (IQR)	53 (42-63)
≤18	494 (0.4)
19 - 30	8,688 (6.5)
31-40	21,519 (16.1)
41-50	29,531 (22.0)
51-60	32,816 (24.5)
61-70	24,832 (18.5)
71≤	16,182 (12.1)
Insurance scheme	
General scheme	117,189 (87.4)
SLM	7,291 (5.4)
MSA	4,528 (3.4)
Other scheme	2,897 (2.2)
Missing	2,157 (1.6)
CMU	
Yes	10,556 (7.9)
No	120,763 (90.1)
Missing	2,743 (2.0)
FDep index, quintile	
1 (least deprived)	26,249 (19.6)
2	25,934 (19.3)
3	26,370 (19.7)
4	25,860 (19.3)
5 (most deprived)	25,051 (18.7)
Missing	4,598 (3.4)
<b>Comorbidities (n=129,449)</b>	
Psychiatric disorder or psychotropic drug treatment	42,402 (32.7)
Antidepressants use	30 178 (23.3)
Anxiolytics use	18 084 (14.0)
Paraplegia	11,785 (9.1)
Cardio-neurovascular diseases	10,236 (7.9)
Cancer	7,600 (5.9)
Diabetes	7,624 (5.9)

Comorbidities information missing	4,613 (3.4)
Additional LTD	
0	91,048 (67.9)
1	24,323 (18.1)
2	10,290 (7.7)
3	4,422 (3.3)
4+	3,979 (3.0)
<b>MS-related characteristics</b>	
Disease-modifying treatments	
No DMT	64,786 (48.3)
Any moderate efficacy DMT	43,314 (32.3)
<i>Teriflunomide</i>	13,529 (10.1)
<i>Dimethyl fumarate</i>	12,136 (9.0)
<i>Beta interferon</i>	8,664 (6.5)
<i>Glatiramer acetate</i>	6,650 (5.0)
<i>Mycophenolic mofetil</i>	1,359 (1.0)
<i>Methotrexate</i>	1,459 (1.1)
<i>Azathioprine</i>	1,097 (0.8)
<i>Cladribine</i>	182 (0.1)
<i>Cyclophosphamide</i>	24 (0.02)
Any high efficacy DMT	28,025 (20.9)
<i>Fingolimod</i>	10,776 (8.0)
<i>Ocrelizumab</i>	8,528 (6.6)
<i>Natalizumab</i>	6,258 (4.7)
<i>Rituximab</i>	3,303 (2.5)
All hospitalizations, median (IQR)	0 (0-2)
≥ 1	55,612 (41.5)
MS-related hospitalizations, median (IQR)	0 (0-1)
≥ 1	36,745 (27.4)
<p><i>Abbreviations: DMT, Disease modifying treatments; IQR, interquartile range; FDep, city of residence social deprivation index; LTD, Long-term disease status; MS, Multiple Sclerosis ; SLM, "Sections locales mutualistes"; MSA, "Mutualité sociale agricole"</i></p> <p><i>Notes: All statistics reported as n(%) unless otherwise specified.</i></p> <p><i>MS-related characteristics are reported for the January 1, 2021 to December 31, 2021 period.</i></p> <p><i>Comorbidity percentages were calculated after exclusion of the missing data.</i></p>	

Table 2: Age and sex-stratified MS prevalence rates in France in 2021.

Age in years	Number of MS cases	Number of people living in France	Overall		Women		Men	
			Crude MS prevalence	95% CI	Crude MS prevalence	95% CI	Crude MS prevalence	95% CI
Total France	134,062	67,842,591	197.6	196.5-198.7	274.9	273.2-276.6	115.2	114.0-116.4
<15	106	11,870,954	0.9	0.7-1.1	0.9	0.7-1.1	0.9	0.7-1.1
15-19	591	4,208,524	14.0	12.9-15.1	19.8	17.9-21.7	8.6	7.4-9.8
20-24	2,160	3,922,318	55.1	52.8-57.4	77.2	73.3-81.1	33.9	31.3-36.5
25-29	4,946	3,725,962	132.7	129.0-136.4	187.7	181.5-193.9	77.1	73.1-81.1
30-34	8,358	4,064,176	205.7	201.3-210.1	288.3	281.0-295.6	119.4	114.6-124.2
35-39	11,696	4,200,292	278.5	273.5-283.5	392.9	384.5-401.3	157.1	151.7-162.5
40-44	13,805	4,239,439	325.6	320.2-331.0	452.9	443.9-461.9	192.9	186.9-198.9
45-49	15,213	4,320,709	352.1	346.5-357.7	501.5	492.1-510.9	199.1	193.1-205.1
50-54	16,398	4,454,399	368.1	362.5-373.7	516.9	507.5-526.3	214.7	208.6-220.8
55-59	16,598	4,437,879	374.0	368.3-379.7	522.5	513.1-531.9	217.1	210.9-223.3
60-64	14,327	4,176,777	343.0	337.4-348.6	475.4	466.2-484.6	198.8	192.6-205.0
65-69	11,629	3,904,715	297.8	292.4-303.2	402.8	394.2-411.4	178.5	172.4-184.6
70-74	9,080	3,707,830	244.9	239.9-249.9	321.2	313.3-329.1	155.7	149.8-161.6
75-79	4,900	2,524,031	194.1	188.7-199.5	253.6	245.3-261.9	120.2	113.8-126.6
80-84	2,431	1,802,512	134.9	129.5-140.3	171.8	163.9-179.7	82.8	76.3-89.3
≥85	1,824	2,282,074	79.9	76.2-83.6	93.9	89.1-98.7	50.6	45.5-55.7

Table 3: Crude and standardized MS prevalence rates in France on December 31, 2021.

	Overall	Women	Men
Number of MS cases	134,062	96,257	37,805
2021 population	67,842,591	35,020,367	32,822,224
Crude prevalence rates per 100,000 population	197.6 (196.5-198.7)	274.9 (273.2-276.6)	115.2 (114.0-116.4)
Standardized prevalence rates per 100,000 (2013 World population)	159.2 (158.3-160.1)	224.9 (223.5-226.3)	91.7 (90.8-92.6)
Standardized prevalence rates per 100,000 (2021 World population)	166.3 (165.4-167.2)	234.3 (232.8-235.8)	96.1 (95.1-97.1)
Standardized prevalence rates per 100,000 (1976 European population)	172.1 (171.2-173.0)	244.9 (243.4-246.4)	98.2 (97.2-99.2)
Standardized prevalence rates per 100,000 (2013 European population)	202.2 (201.1-203.3)	279.8 (278.0-281.6)	118.7 (117.5-119.9)
Standardized prevalence rates per 100,000 (2021 European population)	203.5 (202.4-204.6)	281.3 (279.5-283.1)	119.7 (118.5-120.9)

Table 4: Region-specific standardized MS prevalence rates in metropolitan France, 2021.

Administrative region of France	Number of MS cases	Number of people living in the region	Overall			Women			Men		
			Standardized prevalence	95% CI	Comparison with 2012	Standardized prevalence	95% CI	Comparison with 2012	Standardized prevalence	95% CI	Comparison with 2012
<b>Total France</b>	131,086	67,842,591	193.1	192.1-194.1	+27.71%	269.1	267.4-270.8	+28.14%	111.9	110.8-113.0	+26.16%
<b>Auvergne-Rhône-Alpes</b>	14,891	8,156,391	183.3	180.4-186.3		255.0	250.2-259.8		107.7	104.5-110.9	
Auvergne	2,752	1,371,196	194.0	186.8-201.2	25.16%	286.3	274.0-298.6	27.30%	98.5	91.1-105.9	22.21%
Rhône-Alpes	12,139	6,785,195	180.9	177.7-184.1	28.85%	248.4	243.1-253.7	28.97%	109.6	106.0-113.2	29.40%
<b>Bourgogne-Franche-Comté</b>	6,452	2,791,006	226.6	221.1-232.1		329.6	320.3-338.9		119.2	113.5-124.9	
Bourgogne	3,541	1,614,708	212.8	205.8-219.8	25.10%	310.2	298.4-322.0	25.49%	110.7	103.65-117.9	25.65%
Franche-Comté	2,911	1,176,298	245.4	236.5-254.3	32.15%	356.3	341.2-371.4	31.67%	130.6	121.3-139.9	36.90%
<b>Bretagne</b>	6,755	3,412,207	195.6	190.9-200.3	33.42%	279.1	271.3-286.9	35.09%	108.7	103.87-113.7	31.44%
<b>Centre Val de Loire</b>	5,515	2,572,636	211.9	206.3-217.5	25.16%	299.7	290.4-309.0	25.40%	119.4	113.54-125.4	25.55%
<b>Corse</b>	675	348,830	182.7	168.9-196.5	45.46%	257.0	234.2-279.8	45.86%	103.2	88.4-118.0	43.73%
<b>Grand Est</b>	13,831	5,561,482	243.9	239.8-248.0		343.6	337.1-350.3		139.5	135.1-143.9	
Alsace	4,745	1,930,273	240.3	233.5-247.1	24.77%	336.5	325.2-347.8	24.86%	139.6	132.2-147.0	26.11%
Champagne-Ardenne	3,127	1,312,778	237.4	229.1-245.7	24.75%	336.7	322.9-350.5	25.82%	132.8	123.9-141.7	22.96%
Lorraine	5,959	2,318,431	250.7	244.3-257.1	25.22%	354.0	343.4-364.6	27.38%	143.0	136.1-149.9	21.70%
<b>Hauts-de-France</b>	13,672	5,985,483	232.4	228.5-236.3		318.6	312.5-325.0		140.6	136.2-145.0	
Nord-Pas-de-Calais	9,231	4,063,753	232.5	227.8-237.2	21.98%	312.5	304.9-320.1	22.55%	146.7	141.3-152.1	20.25%
Picardie	4,441	1,921,730	231.7	224.9-238.5	19.56%	330.9	319.5-342.3	21.34%	127.7	120.5-134.9	16.41%
<b>Ile-de-France</b>	22,561	12,329,432	188.9	187.7-191.4	26.61%	254.8	250.8-258.8	26.08%	117.3	114.5-120.1	26.26%
<b>Normandie</b>	6,424	3,319,743	192.4	188.0-197.1		268.7	261.1-276.5		111.6	106.5-116.7	
Basse-Normandie	2,832	1,468,032	189.5	182.5-196.5	28.04%	264.8	253.3-276.3	28.79%	110.6	103.0-118.2	27.57%
Haute-Normandie	3,592	1,851,711	194.8	188.4-201.2	29.18%	272.0	261.5-282.5	32.42%	112.1	105.1-119.1	20.93%
<b>Nouvelle-Aquitaine</b>	11,291	6,086,584	178.9	175.6-182.2		254.9	249.6-260.4		97.6	94.1-101.1	
Aquitaine	6,473	3,534,811	177.1	172.8-181.4	29.18%	250.1	243.0-257.2	29.32%	98.5	93.9-103.1	27.59%
Limousin	1,479	722,658	195.0	185.1-204.9	34.95%	281.7	265.0-298.4	33.95%	104.3	93.9-114.7	40.00%
Poitou-Charentes	3,339	1,829,115	176.1	170.1-182.1	35.36%	253.9	243.9-263.9	36.07%	93.4	87.2-99.6	33.43%
<b>Occitanie</b>	11,114	6,060,331	180.4	177.0-183.8		253.7	248.4-259.2		102.1	98.5-105.7	
Languedoc-Roussillon	5,424	2,917,252	183.2	178.3-188.1	37.64%	253.9	246.0-261.8	36.07%	105.9	100.5-111.3	39.34%
Midi-Pyrénées	5,690	3,143,079	178.1	173.5-182.7	26.13%	253.9	246.2-261.6	27.46%	98.7	93.8-103.6	24.15%

Accepted manuscript

<b>Pays de la Loire</b>	7,087	3,882,895	183.7	179.4-188.0	31.78%	267.0	259.8-274.2	33.30%	96.7	92.3-101.1	29.62%
<b>Provence-Alpes-Côte d'Azur</b>	9,790	5,139,817	187.3	183.6-191.0	32.65%	257.5	251.5-263.5	32.80%	110.2	106.1-114.3	29.49%
<b>Overseas departments*</b>	1,028	2,195,754	50.1	47.0-53.2		67.3	62.5-72.1		29.6	26.1-33.1	

*Comparison with 2012 from Foulon et al 2017*

*Reference population: French population on January 1, 2022*

## Appendix

Supplemental Table 1: Department-specific standardized MS prevalence rates in metropolitan France, 2021.

Administrative 'department' of France	Number of MS cases	Number of people living in the 'department'	Overall		Women		Men	
			Standardized prevalence	95% CI	Standardized prevalence	95% CI	Standardized prevalence	95% CI
Total Metropolitan France	130,059	65,646,837	197.4	196.3-198.5	275.5	273.7-277.3	114.3	113.1-115.5
Ain	1,102	666,971	164.7	155.0-174.4	232.4	216.2-248.6	94.7	84.2-105.2
Aisne	1,238	524,723	233.8	220.8-246.8	333.6	311.8-355.4	130.1	116.2-144.0
Allier	778	333,500	221.5	205.9-237.1	324.4	298.2-350.6	112.9	96.9-128.9
Alpes-de-Haute- Provence	315	166,198	177.2	157.6-196.8	251.3	218.7-283.9	99.0	78.2-119.8
Alpes-Maritimes	2,086	1,106,233	184.3	176.4-192.2	263.5	250.5-276.5	96.1	87.8-104.4
Ardèche	544	331,214	157.9	144.6-171.2	220.3	198.4-242.2	93.7	79.0-108.4
Ardennes	643	266,690	235.0	216.8-253.2	323.8	293.9-353.7	142.7	122.5-162.9
Ariège	313	154,424	196.3	174.6-218.0	279.3	243.0-315.6	110.1	86.7-133.5
Aube	676	312,183	219.4	202.9-235.9	309.7	282.3-337.1	123.8	106.0-141.6
Aude	684	378,330	174.8	161.7-187.9	249.8	228.0-271.6	93.3	79.6-107.0
Aveyron	507	279,639	172.1	157.1-187.1	240.5	215.5-265.5	103.7	87.2-120.2
Bas-Rhin	2,939	1,161,777	249.4	240.4-258.4	348.5	333.6-363.4	145.3	135.5-155.1
Bouches-du-Rhône	3,893	2,061,919	189.0	183.1-194.9	251.9	242.4-261.4	119.4	112.6-126.2
Calvados	1,380	699,791	197.0	186.6-207.4	273.4	256.4-290.4	115.1	103.7-126.5
Cantal	308	143,803	196.5	174.6-218.4	286.9	249.4-324.4	106.2	83.4-129.0
Charente	618	351,283	166.7	153.6-179.8	241.5	219.3-263.7	87.9	74.4-101.4
Charente-Maritime	1,307	662,822	185.3	175.3-195.3	262.4	245.8-279.0	101.9	91.2-112.6
Cher	596	298,249	191.8	176.4-207.2	290.0	263.4-316.6	89.2	74.3-104.1
Corrèze	480	237,790	189.9	172.9-206.9	272.9	244.4-301.4	104.0	86.1-121.9
Corse	675	348,830	182.7	168.9-196.5	257.0	234.2-279.8	103.2	88.4-118.0
Côte-d'Or	1,292	535,786	241.4	228.2-254.6	350.6	328.5-372.7	125.4	111.8-139.0
Côtes-d'Armor	1,346	606,868	214.5	203.0-226.0	304.2	285.1-323.3	120.9	108.6-133.2
Creuse	262	114,142	203.5	178.9-228.1	321.5	278.0-365.0	83.7	61.0-106.4

Accepted manuscript

Deux-Sèvres	609	374,142	158.0	145.5-170.5	234.1	212.7-255.5	79.1	66.4-91.8
Dordogne	812	411,988	180.1	167.7-192.5	253.8	233.3-274.3	102.1	88.7-115.5
Doubs	1,289	548,458	239.5	226.4-252.6	341.1	319.2-363.0	133.7	119.8-147.6
Drôme	942	521,319	178.1	166.7-189.5	246.3	227.7-264.9	105.5	92.9-118.1
Essonne	2,417	1,312,419	193.0	185.3-200.7	269.1	256.4-281.8	112.7	104.3-121.1
Eure	1,136	597,425	188.0	177.1-198.9	271.9	253.6-290.2	99.4	88.0-110.8
Eure-et-Loir	954	429,570	219.5	205.6-233.4	313.0	289.7-336.3	121.9	107.1-136.7
Finistère	2,059	923,400	217.3	207.9-226.7	317.3	301.4-333.2	114.2	104.5-123.9
Gard	1,403	755,497	182.1	172.6-191.6	252.9	237.3-268.5	105.3	94.8-115.8
Gers	342	192,553	163.2	145.9-180.5	239.4	210.1-268.7	83.8	66.1-101.5
Gironde	3,096	1,673,755	184.9	178.4-191.4	260.4	249.7-271.1	102.8	95.8-109.8
Haute-Garonne	2,535	1,452,541	178.6	171.6-185.6	251.4	239.9-262.9	101.6	94.1-109.1
Haute-Loire	429	227,097	179.6	162.6-196.6	270.7	241.2-300.2	87.8	71.1-104.5
Haute-Marne	487	168,881	276.1	251.6-300.6	408.2	366.3-450.1	142.3	117.2-167.4
Hautes-Alpes	294	140,078	198.7	176.0-221.4	274.9	237.5-312.3	120.5	95.2-145.8
Haute-Saône	603	232,619	249.0	229.1-268.9	361.2	327.6-394.8	134.6	113.7-155.5
Haute-Savoie	1,412	853,015	163.9	155.4-172.4	229.9	215.7-244.1	94.9	85.6-104.2
Hautes-Pyrénées	422	230,404	174.0	157.4-190.6	251.1	223.4-278.8	91.5	74.2-108.8
Haute-Vienne	737	370,726	194.2	180.2-208.2	271.9	248.8-295.0	111.3	96.0-126.6
Haut-Rhin	1,806	768,496	227.8	217.3-238.3	319.8	302.4-337.2	132.3	120.9-143.7
Hauts-de-Seine	2,988	1,637,090	184.9	178.3-191.5	240.0	229.6-250.4	122.6	114.7-130.5
Hérault	2,213	1,218,474	182.5	174.9-190.1	248.9	236.6-261.2	109.3	100.8-117.8
Ille-et-Vilaine	1,990	1,108,972	184.2	176.1-192.3	256.1	242.7-269.5	109.4	100.5-118.3
Indre	481	216,241	212.1	193.1-231.1	299.7	268.2-331.2	121.7	101.1-142.3
Indre-et-Loire	1,261	616,107	205.4	194.1-216.7	277.6	259.3-295.9	128.1	115.2-141.0
Isère	2,239	1,288,501	176.1	168.8-183.4	237.5	225.6-249.4	111.7	103.4-120.0
Jura	597	257,304	225.2	207.1-243.3	340.1	309.0-371.2	106.4	88.7-124.1
Landes	796	425,229	175.5	163.3-187.7	249.3	229.1-269.5	97.6	84.5-110.7
Loire	1,548	770,678	203.0	192.9-213.1	284.6	267.9-301.3	116.8	105.8-127.8
Loire-Atlantique	2,743	1,480,188	188.2	181.2-195.2	273.3	261.5-285.1	98.4	91.1-105.7
Loiret	1,512	685,081	223.6	212.3-234.9	316.4	297.7-335.1	125.5	113.4-137.6

Accepted manuscript



Loir-et-Cher	711	327,388	209.3	193.9-224.7	301.3	275.4-327.2	112.9	96.9-128.9
Lot	341	175,196	177.8	158.9-196.7	271.0	238.1-303.9	81.1	63.4-98.8
Lot-et-Garonne	594	329,180	172.4	158.5-186.3	233.3	210.9-255.7	106.9	91.2-122.6
Lozère	155	76,572	188.5	158.8-218.2	288.9	236.6-341.2	89.5	61.0-118.0
Maine-et-Loire	1,387	825,814	172.5	163.4-181.6	248.9	233.7-264.1	92.5	83.0-102.0
Manche	907	493,646	176.6	165.1-188.1	248.7	229.5-267.9	103.0	90.5-115.5
Marne	1,321	565,024	236.6	223.8-249.4	336.1	314.9-357.3	130.4	116.8-144.0
Mayenne	492	305,719	161.4	147.1-175.7	241.3	216.7-265.9	81.1	66.8-95.4
Meurthe-et-Moselle	1,783	730,393	246.0	234.6-257.4	347.2	328.3-366.1	138.8	126.5-151.1
Meuse	454	179,626	244.4	221.9-266.9	361.6	322.9-400.3	126.9	104.1-149.7
Morbihan	1,360	772,967	171.7	162.6-180.8	246.4	231.1-261.7	93.1	83.5-102.7
Moselle	2,875	1,050,548	263.7	254.1-273.3	366.9	351.0-382.8	156.0	145.4-166.6
Nièvre	470	199,379	225.1	204.7-245.5	333.8	299.0-368.6	112.0	91.6-132.4
Nord	5,717	2,607,165	226.8	220.9-232.7	302.0	292.6-311.4	145.4	138.6-152.2
Oise	1,829	831,729	222.2	212.0-232.4	315.4	298.4-332.4	124.4	113.5-135.3
Orne	545	274,595	196.1	179.6-212.6	274.7	247.3-302.1	115.0	97.2-132.8
Paris	4,137	2,117,702	195.9	189.9-201.9	255.4	246.0-264.8	129.3	122.3-136.3
Pas-de-Calais	3,514	1,456,588	241.8	233.8-249.8	330.2	317.2-343.2	148.2	139.2-157.2
Puy-de-Dôme	1,237	666,796	183.5	173.3-193.7	270.7	253.3-288.1	92.6	82.2-103.0
Pyrénées-Atlantiques	1,175	694,659	160.8	151.6-170.0	230.9	215.6-246.2	85.3	75.7-94.9
Pyrénées-Orientales	969	488,379	193.2	181.0-205.4	267.2	247.5-286.9	110.9	97.5-124.3
Rhône	3,531	1,908,625	194.8	188.4-201.2	258.9	248.6-269.2	125.3	117.9-132.7
Saône-et-Loire	1,073	548,526	187.5	176.3-198.7	269.8	251.0-288.6	101.9	90.0-113.8
Sarthe	1,147	567,053	202.2	190.5-213.9	292.7	273.0-312.4	107.9	95.6-120.2
Savoie	821	444,872	179.9	167.6-192.2	256.4	235.8-277.0	100.4	87.3-113.5
Seine-et-Marne	2,693	1,444,389	191.6	184.4-198.8	264.7	252.9-276.5	113.0	105.0-121.0
Seine-Maritime	2,456	1,254,286	198.1	190.3-205.9	272.2	259.4-285.0	118.4	109.7-127.1
Seine-Saint-Denis	2,587	1,673,645	165.6	159.2-172.0	223.0	212.6-233.4	106.1	98.9-113.3
Somme	1,374	565,278	244.0	231.1-256.9	352.2	330.6-373.8	130.0	116.5-143.5
Tarn	735	393,436	180.4	167.4-193.4	255.9	234.3-277.5	100.4	86.3-114.5
Tarn-et-Garonne	495	264,886	185.0	168.1-201.3	266.5	239.1-293.9	99.9	82.8-117.0

Accepted manuscript

Territoire de Belfort	422	137,917	304.0	275.0-333.0	444.1	395.0-493.2	159.5	129.4-189.6
Val-d'Oise	2,230	1,266,471	185.3	177.6-193.0	258.5	245.9-271.1	106.4	98.0-114.8
Val-de-Marne	2,626	1,420,404	191.1	183.8-198.4	255.2	243.5-266.9	121.0	112.6-129.4
Var	2,061	1,102,074	179.9	172.1-187.7	249.3	236.6-262.0	104.6	96.0-113.2
Vaucluse	1,141	563,315	200.4	188.8-212.0	278.3	259.3-297.3	115.6	102.9-128.3
Vendée	1,318	704,121	183.8	173.9-193.7	267.1	250.3-283.9	97.5	87.2-107.8
Vienne	805	440,868	185.1	172.3-197.9	267.7	246.3-289.1	97.4	84.1-110.7
Vosges	848	357,864	227.6	212.3-242.9	330.4	304.5-356.3	121.8	105.9-137.7
Yonne	706	331,017	204.0	189.0-219.0	301.5	275.9-327.1	102.6	87.3-117.9
Yvelines	2,883	1,457,312	203.2	195.8-210.6	279.4	267.3-291.5	121.5	113.2-129.8

---

Accepted manuscript