

# Incidence and prevalence of multiple sclerosis during eras of evolving diagnostic criteria—a nationwide population-based registry study over five decades

*Multiple Sclerosis Journal—  
Experimental, Translational  
and Clinical*

January–March 2025, 1–9

DOI: 10.1177/  
20552173251326173© The Author(s), 2025.  
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permissions](https://sagepub.com/journals-permissions)Anna Maunula , Sini M Laakso , Matias Viitala , Merja Soilu-Hänninen ,  
Marja-Liisa Sumelahti\*  and Sari Atula\* 

## Abstract

**Background:** Impact of changing diagnostic criteria for the population-based incidence of multiple sclerosis (MS) has not been investigated.

**Objective:** To assess the effect of changing diagnostic criteria on national MS incidence and prevalence in Finland from 1974 to 2021.

**Methods:** We identified patients with MS (pwMS) through the National MS registry and the national Care Register for Healthcare and divided them into four groups based on the year of MS diagnosis: 1) Schumacher criteria (1974–1982), 2) Poser criteria (1983–2000), 3) Earlier McDonald criteria (2001–2016), and 4) Current McDonald criteria (2017–2021). Age-adjusted incidence and prevalence were calculated.

**Results:** Age-adjusted incidence per 10<sup>5</sup> person years increased from 3.7 (95% CI 3.5–3.8) during the Schumacher criteria period to 9.2 (95% CI 9.0–9.4) during the earlier McDonald criteria. During the Current McDonald criteria incidence stabilized to 8.6 (95% CI 8.3–9.0). Prevalence increased from 24.3 (95% CI 22.8–25.8) to 241.5 (95% CI 237.3–245.6) per 10<sup>5</sup> person years.

**Conclusion:** Both incidence and prevalence of MS increased significantly. Incidence showed a sharp increase when entering the twenty-first century, after which it stabilized. Increasing incidence was likely related to incorporation of MRI in the diagnostic criteria. Current diagnostic criteria did not further increase the incidence.

**Keywords:** Multiple sclerosis, MS, incidence, prevalence, epidemiology, diagnostic criteria

Date received: 23 October 2024; accepted 20 February 2025

## Introduction

Multiple sclerosis (MS) is an immune-mediated disease of the central nervous system and one of the leading causes of neurological disability in young adults.<sup>1</sup> The prevalence of MS has increased globally from 1960 to date<sup>2–4</sup> with rising prevalence recorded in all regions of the world.<sup>4</sup> Data from the twentieth century, from several geographical areas, show increased incidence of MS,<sup>3,5–8</sup> whereas incidence in the late twentieth and early twenty-first century seems to become stable<sup>9–12</sup> Highest age-standardized

prevalence rates have been reported for North America, Western Europe and Australasia.<sup>2</sup> A recently published systematic review, covering the published peer-reviewed literature on the change in worldwide MS incidence over time, challenged the concept of a global increase in the incidence of MS over the past three decades;<sup>13</sup> research protocols using consistent criteria for patient identification and with high population coverage showed stable trends, whereas increases were seen in studies limited in these aspects.

\* Equal contribution

Correspondence to:  
Anna Maunula, Faculty of  
Medicine, Translational  
Immunology Research  
Program, University of  
Helsinki, Haartmaninkatu 8,  
00014 Helsinki, Finland;  
HUS Neurocenter,  
Department of Neurology,  
Hyvinkää Hospital,  
Hyvinkää, Finland.  
[anna.maunula@helsinki.fi](mailto:anna.maunula@helsinki.fi)



**Anna Maunula,**  
Translational Immunology  
Research Program,  
University of Helsinki,  
Helsinki, Finland  
HUS Neurocenter,  
Department of Neurology,  
Hyvinkää Hospital,  
Hyvinkää, Finland

**Sini M Laakso,**  
Translational Immunology  
Research Program,  
University of Helsinki,  
Helsinki, Finland  
HUS Neurocenter, Helsinki  
University Hospital,  
Helsinki, Finland

**Matias Viitala,**  
StellarQ Ltd, Turku, Finland

**Merja Soilu-Hänninen,**  
Clinical Neurosciences,  
University of Turku, Finland  
Neurocenter, Turku  
University Hospital, Turku,  
Finland

**Marja-Liisa Sumelahti,**  
Faculty of Medicine and  
Health Technology, Tampere  
University, Tampere, Finland

**Sari Atula,**  
HUS Neurocenter, Helsinki  
University Hospital,  
Helsinki, Finland  
Department of Clinical  
Neurosciences, University of  
Helsinki, Helsinki, Finland

Nationwide prevalence of MS in Finland has not been studied since the 1960's.<sup>14</sup> The focus of studies has been on regional occurrence, particularly in high-risk western parts of Finland.<sup>5,7,8,15–22</sup> Recent occurrence updates in the twenty-first century support the observation that Finland is a high-risk area of MS.<sup>7,15,22</sup> They also support the observation of an East-West gradient, made originally in 1966, that Western Finland has a higher prevalence of MS compared to Eastern Finland.<sup>14,22</sup> This may suggest specific genetic susceptibility for MS, although environmental factors can also be at play.<sup>23–25</sup>

The Schumacher criteria in 1965<sup>26</sup> and the Poser criteria in 1983<sup>27</sup> relied mainly on patient-reported symptoms and neurological findings, supported by increased immunological activity in cerebrospinal fluid (CSF) and possible alterations in neurophysiological and/or urological testing. MRI criteria were first included in the McDonald criteria in 2001.<sup>28</sup> Since then, the criteria have been updated several times.<sup>29,30</sup> The most recent update in 2017<sup>31</sup> enabled diagnosis after the first demyelinating event, if MRI criteria for dissemination in space are fulfilled and criteria for dissemination in time (DIT) are fulfilled or oligoclonal bands are detected in the CSF. This was a significant change to earlier criteria where two relapses or further MRI evidence for DIT were required.

Applying 2017 McDonald criteria has been shown to increase the number of patients receiving diagnosis at the time of first demyelinating event.<sup>32–36</sup> Studies show higher sensitivity (68–100%) but also lower specificity (14–53%) for McDonald 2017 criteria when compared to 2010 McDonald criteria in predicting the second clinical event.<sup>34,37–40</sup> However, with the likelihood of a second event influenced by early initiation of a DMT, and the findings of a similar area under the curve suggesting capture of the same patient population in follow-up, accuracy of 2017 McDonald criteria has been perceived as similar<sup>34,38</sup> or higher<sup>35,37</sup> in comparison to 2010 criteria. Sustained accuracy has also been suggested when comparing 2010 McDonald criteria to 2005 criteria.<sup>36</sup>

Population-based studies on the effect of evolving criteria on the incidence of MS and the accompanying changes in prevalence have, to our knowledge, not been conducted. We aimed to examine the changes in the incidence and prevalence of MS in Finland from 1974 to 2021, using the eras set by altering diagnostic criteria to evaluate their effect on the national incidence rate and to discover changes in prevalence.

## Methods

### Study cohort

This study was permitted by Finnish Social and Health Data Permit Authority (Findata), which authorizes secondary use of social and health care data in Finland and can combine information from different national registries.

We identified patients with MS (pwMS) diagnosed between 1974 and 2021. Patients were primarily found from the National MS registry.<sup>41</sup> If a patient was not found in the MS registry data was collected from the National Care Register. All healthcare providers, both publicly and privately funded, are obliged by law to report information to the Care Register, including diagnosis according to ICD codes for all doctor's visits. Patients with at least two separate visits with at least 1 year apart with diagnosis code G35 from 1996 onwards and/or G340 in 1974–1995 were included in the study. Patients that had later received a diagnosis for a neuromyelitis optica spectrum disorder (ICD-10 G36.0, ICD-9 341.0) were excluded from the study.

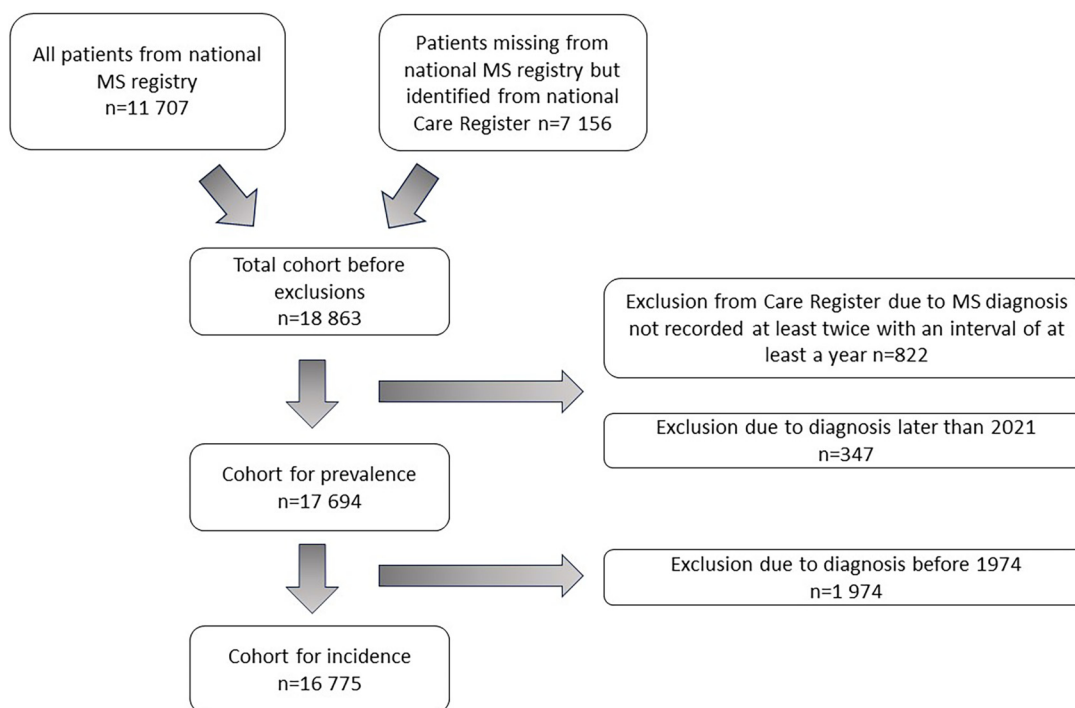
Approximately 80% of the cohort diagnosed in the twenty-first century was identified from the MS-register, whereas the portion was significantly lower, approximately 43%, in the twentieth century. The registry was launched in 2014 is estimated to cover 85–90% of current Finnish pwMS and is described by Laakso et al.<sup>41</sup> The patients not included in the MS-register were identified through a national Care Register for Healthcare (Figure 1).

Main source of MS diagnosis date was the date recorded in the MS registry. Diagnosis date for patients identified through Care Register was derived as first visit using ICD-10/ICD-9 codes G35/340. Information on the MS subtype (relapsing-remitting, progressive) was not included as it was not available for Care Register patients. We identified date of birth, gender, and place of residence at age of 15 years for all pwMS.

### Study intervals set by the evolving diagnostic criteria

Patients were allocated into four study subgroups based on the year of MS diagnosis:

1. Schumacher criteria (1974–1982)<sup>26</sup>
2. Poser criteria (1983–2000)<sup>27</sup>
3. Earlier McDonald criteria (2001–2016)<sup>28–30</sup>
4. Current McDonald criteria (2017–2021)<sup>31</sup>



**Figure 1.** Flow chart of the process of forming the cohort.

The first time frame (1974–1982; Schumacher criteria) was limited to these years because data from Care Register is available from 1969 forwards and a 5-year run-in period was needed for incidence calculations.

#### Statistical analysis

Data analysis and visualization were performed on pseudonymized data using RStudio (Version 2023.09.1). Partial dates were imputed as the middle of the month or year. Numerical variables were expressed as means with standard deviations or medians with interquartile ranges. Categorical variables were expressed as frequencies and proportions based on non-missing data.

Age-adjusted incidence and prevalence ratios were calculated based on yearly reported Finnish population statistics (Statistics Finland) and European Standard Populations (revision 1976 for diagnoses between 1974 and 2000 and revision 2013 for diagnoses between 2001 and 2021)<sup>42</sup> using 5-year age periods. Standard population distributions were used as weights for each age-specific rate. Incidence analysis was done using diagnosis year subgroups summing population counts and newly diagnosed patients within each year interval. Prevalence analysis was done separately for each year. Analyses were separated for both sex categories. Analyzed ratios were reported with 95% confidence intervals based on Poisson approximation.

## Results

### Changes in incidence and prevalence

Both crude and age-adjusted incidence showed a sharp increase when entering the era of the earlier McDonald criteria (2001–2016) (Table 1). Age-adjusted incidence during the earlier McDonald criteria was  $9.2/10^5$  person years (95% CI 8.3, 9.0) and during the current 2017 McDonald criteria  $8.6/10^5$  person years (95% CI 8.9, 9.4), showing a slight decline (Figure 2(a)).

When examining the effect of sex, an increased incidence during earlier McDonald criteria (2001–2016) was seen in both males and females, being more pronounced in females with age-adjusted incidence rate up to  $13.1/10^5$  person years.

Age-specific distribution of incidence by age groups at diagnosis was similar throughout the study period (Figure 2(b)). A peak at 30–34 years was seen during earlier McDonald criteria (2001–2016), whereas it was slightly higher, at 35–39 years, during 2017 McDonald criteria. When dividing by sex, peak age at diagnosis in the twenty-first century was at a younger age for females (Supplementary Figure 1).

When looking at age-adjusted prevalence, it showed a tenfold increase from  $24.3$  per  $10^5$  person years in

**Table 1.** Patient demographics with incidence and prevalence according to eras of diagnostic criteria.

	<b>Schumacher criteria (1974–1982) (n = 1558)</b>	<b>Poser criteria (1983–2000) (n = 5183)</b>	<b>Earlier McDonald criteria (2001–2016) (n = 7758)</b>	<b>Current McDonald criteria (2017–2021) (n = 2276)</b>
<b>Sex (Females); n (%)</b>	955 (61.3%)	3500 (67.5%)	5487 (70.7%)	1581 (69.5%)
<b>Age at MS diagnosis (years); Mean (SD)</b>	39.5 (12.9)	39.8 (12.1)	39.7 (13.1)	40.6 (13.4)
Females	39.4 (13.0)	39.7 (12.0)	39.4 (13.0)	39.7 (13.0)
Males	39.7 (12.9)	40.0 (12.2)	40.7 (13.2)	42.6 (13.9)
<b>Age at MS diagnosis (years); Median (Q1-Q3)</b>	37.5 (30.0–48.0)	39.0 (31.0–48.0)	38.0 (30.0–48.0)	39.0 (31.0–48.0)
Females	37.0 (30.0–48.0)	39.0 (31.0–48.0)	38.0 (29.0–48.0)	38.0 (30.0–47.0)
Males	38.0 (30.0–49.0)	39.0 (31.0–48.0)	39.0 (30.0–50.0)	41.0 (32.0–52.0)
<b>Age-adjusted incidence rate per 10<sup>5</sup> person years (95% CI)</b>	3.7 (3.5–3.8)	5.6 (5.4–5.7)	9.2 (9.0–9.4)	8.6 (8.3–9.0)
Females (95% CI)	4.4 (4.1–4.7)	7.6 (7.3–7.8)	13.1 (12.8–13.5)	12.2 (11.6–12.8)
Males (95% CI)	2.9 (2.7–3.1)	3.6 (3.4–3.8)	5.3 (5.1–5.6)	5.2 (4.8–5.6)
<b>Incidence female/male ratio (95% CI)</b>	1.5 (1.4–1.7)	2.1 (2.0–2.2)	2.5 (2.3–2.6)	2.4 (2.2–2.6)
<b>Age-adjusted prevalence rate per 10<sup>5</sup> person years (95% CI)<sup>a</sup></b>	24.3 (22.8–25.8)	111.3 (108.5–114.2)	218.4 (214.4–222.4)	241.5 (237.3–245.6)
Females (95% CI) <sup>a</sup>	27.9 (25.7–30.1)	151.2 (146.5–155.8)	309.7 (303.0–316.3)	344.2 (337.3–351.3)
Males (95% CI) <sup>a</sup>	20.7 (18.7–22.7)	71.6 (68.4–74.8)	127.0 (122.7–131.3)	138.8 (134.4–143.3)

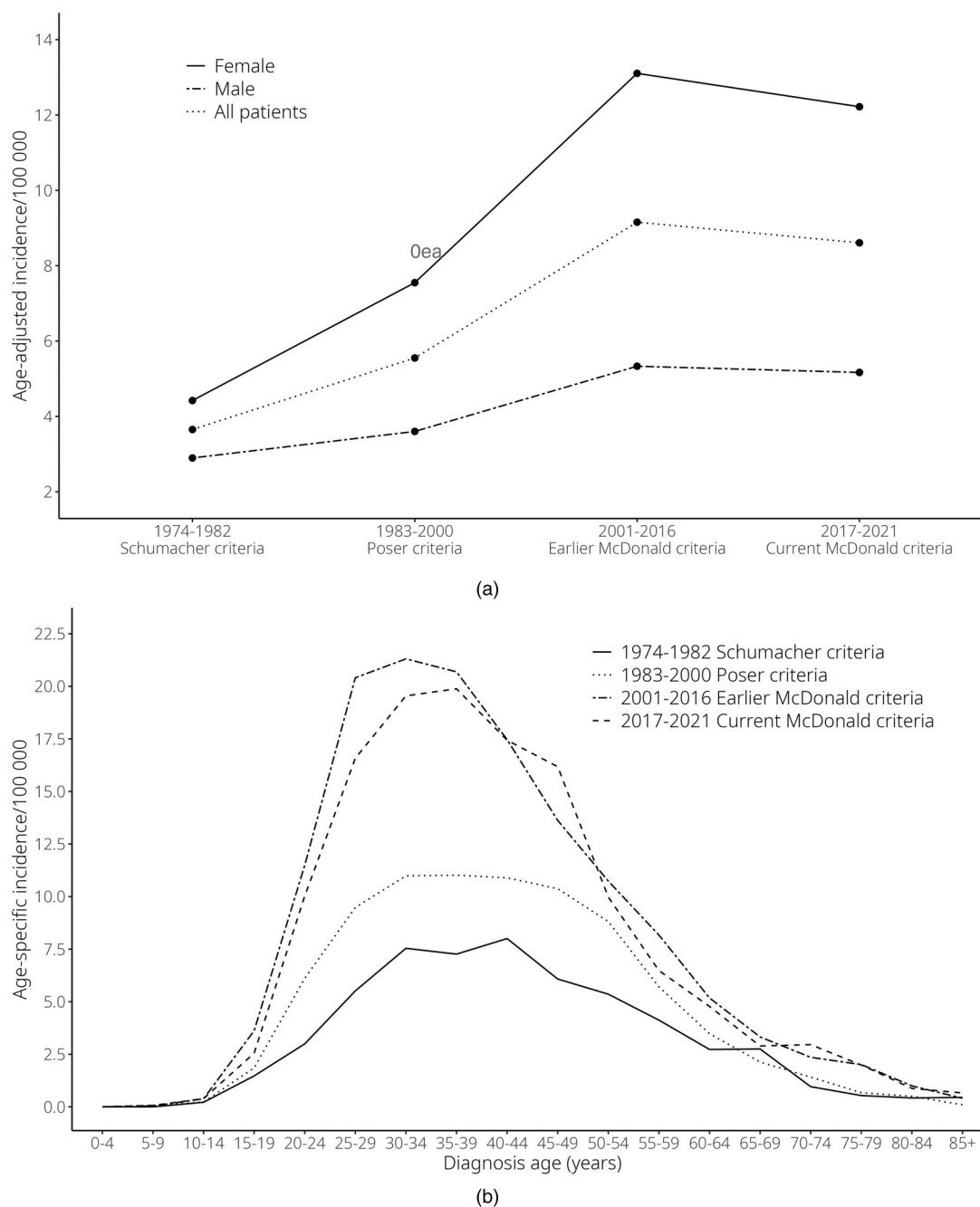
<sup>a</sup>Age-adjusted prevalence rate in this table is from the years 1974, 2000, 2016 and 2021. SD: standard deviation.

1974 to 241.3 per 10<sup>5</sup> person years in 2021 (Figure 3). This was mainly attributed to a steep rise in incidence in the late 1990s, which was more pronounced in females.

#### *Mean age at diagnosis and female-to-male ratio*

For females, mean age at MS diagnosis was stable throughout the study period, around 40 years, whereas a rise was seen in males, from 39.7 during

the Schumacher criteria to 42.6 during the current McDonald criteria (Table 1). Median age was slightly lower compared to mean age especially in the first period studied. Care Register for healthcare had higher mean diagnosis age throughout the study period ranging from 12.2 years higher during the first criteria period to 3.6 years higher in the last study period (Supplementary Table).

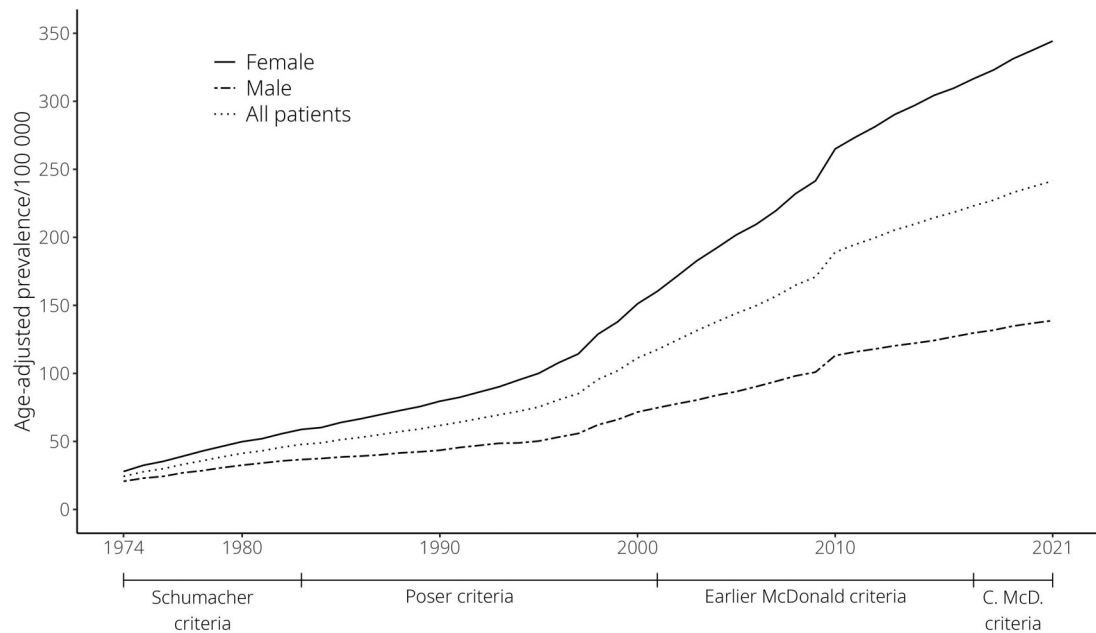


**Figure 2.** Incidence of MS during the diagnostic eras. Values are point estimates for each diagnostic era separately. (a) Age-adjusted incidence per 10<sup>5</sup> person years by eras of diagnostic criteria. (b) Age-specific incidence per 10<sup>5</sup> person years by age group at diagnosis shown for different eras of diagnostic criteria.

Female-to-male ratio (F/M-ratio) showed an increase during the entire study period from 1.5 to 2.4 (Table 1). The change was most prominent when entering from Schumacher to Poser criteria (1.5 to 2.1). Care register had a lower percentage of females compared to the national MS register (64% vs 71%).

### Discussion

Our nationwide analysis showed that both the incidence and prevalence of MS increased during the study period from 1974 to 2021 in Finland. After a sharp increase in incidence when entering the twenty-first century, rates showed a stabilizing trend, similar to what has been seen in other studies<sup>9-12</sup>



**Figure 3.** Trend of age-adjusted prevalence per  $10^5$  person years from 1974 to 2021. C.McD. Criteria = Current McDonald Criteria.

Incidence rate in the twenty-first century in this study was similar to other studies.<sup>8,11,43</sup> The stabilizing, even slightly decreasing trend of incidence comparing earlier and current McDonald criteria indicates that the current diagnostic criteria are accurate and reflect the true incidence of MS. The increasing incidence of MS entering the twenty-first century is most likely due to changes in diagnostic criteria. Also, the use of MRI in diagnostic set up has increased in Finland, similar to what has been previously concluded.<sup>5,7</sup> The introduction of immunomodulating medications in the mid 1990's might also have affected the number of new diagnoses, since the availability of treatments could encourage neurologists to more avidly seek and set an MS diagnosis. Stabilizing incidence during the last decade could be attributed to decreasing smoking<sup>44</sup> and improving vitamin D nutrition at the population levels.<sup>45</sup>

Increased prevalence witnessed in our study is likely due to a rise in both incidence and survival. The nationwide prevalence of MS in Finland in 1966 was reported to be  $18.6/10^5$ .<sup>14</sup> However, this result was based on pension applications, thus missing mild cases of MS. The study estimated the true prevalence being around  $40/10^5$ , which is in line with later research from 1975 where prevalence for the city of Helsinki, considered a medium-risk area, was  $44.2/10^5$ .<sup>14</sup> Our study shows somewhat lower prevalence,  $24.3/10^5$  in 1974–1982. This is most likely due to the more complete population coverage in this

study. However, the Finnish regional prevalence studies during the twenty-first century are, more in line with our study, with reported age-adjusted prevalence ranging from  $168/10^5$  in Eastern Finland up to  $280/10^5$  in Western Finland.<sup>15,22</sup> We found a prevalence of  $218$ – $241/10^5$  in the twenty-first century for both of the McDonald criteria separately, which is similar to previous reports from the other high-risk areas in the world.<sup>9,10,11</sup>

Mean age at the diagnosis was around 40 years in our study, similar to reports in the twenty-first century from other geographical areas,<sup>9,46</sup> although also markedly lower numbers of around 32 to 37 years have been reported.<sup>6,8,11</sup> Mean age remained stable throughout the study period. This, combined with increasing incidence, suggests similar pathophysiology captured with the altering diagnostic criteria and a true increase in the MS incidence. The difference between mean age in MS-register compared to the Care register could partly be explained by the demographics of the regions not using MS-register. Care register data had a larger proportion of males, who are more prone to develop primary progressive MS (PPMS).<sup>47,48</sup> PPMS patients have a higher median age at diagnosis, which could explain the difference.<sup>47,49</sup> MS-register is a hand-curated database filled by a clinician, whereas Care Register is register-based data and there is some uncertainty considering the method used for identification of pwMS and

could thus have a time lag on the date of diagnosis which could further explain the difference.

Increasing incidence and prevalence among women resulted in an increase in the F/M-ratio. This is in line with previous research showing an increase in the F/M-ratio with increased incidence.<sup>3,6,7,50</sup> Also stable,<sup>12</sup> or even decreasing ratios have been reported<sup>10</sup> but in the latter case the F/M-ratio was high, over two during the whole study period, similar to our results. The cause of increasing F/M-ratio is unclear but environmental factors, such as fewer childbirths, increased occurrence of obesity and increased cigarette consumption have been suspected to have a role in this change.<sup>6</sup>

Updates of diagnostic criteria for MS have undoubtedly been shown to enable earlier diagnosis.<sup>32,34,36,37,51,52</sup> Although the timing of diagnosis was not the topic of this study, a stabilizing trend in the incidence of MS during the twenty-first century seen here may indicate that the current McDonald 2017 criteria just allow for an earlier diagnosis in the patients who would have eventually been diagnosed with earlier McDonald criteria as well, thus not resulting in an increasing, but rather stable incidence. Similar results have previously been seen with the 2005 criteria compared with the 2010 criteria by Runia et al., when the follow-up time was extended to 5 years.<sup>36</sup>

The strength of our study is a population-based dataset, covering the whole nation and with registry data from 1969 onwards. Our limitation is the retrospective study design based on registry data. Care registries have previously shown to have moderate to good (79–93%) ability to identify pwMS.<sup>53,54</sup> The Finnish Care register for Healthcare has previously been shown to have from satisfactory to very good accuracy and completeness, with 95% of discharges recorded and a positive predictive value between 75 and 95% depending on diagnosis.<sup>55</sup> Unfortunately, MS validity for the Care Register has to our knowledge not been studied. Results could also be affected by a possible delay in implementation of diagnostic criteria. In the future, it would be of interest to study the most common onset symptom in relation to evolving diagnostic criteria. Also, an analysis of the changing incidence and prevalence rates regarding the east-west gradient on a national level in Finland, with genetic linkage studies, could bring about further understanding on the drivers of increased incidence of MS and especially in females.

In conclusion, our study confirms previous results of Finland being a high incidence and prevalence area

for MS. We show a stable incidence during the previous and current McDonald diagnostic criteria and a stable age at diagnosis, both suggesting no major decline in diagnostic accuracy. F-M-ratio shows a drastic increase also in Finland, which is to be investigated further.

### Acknowledgements

The authors acknowledge the continuous work of improving the MS register by StellarQ Ltd and MS register steering committee.

### Declaration of conflicts of interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Anna Maunula: Congress expenses AbbVie, Biogen; Marja-Liisa Sumelahti: Industry consultant fees, travel reimbursement and congress fees: Abbvie, TEVA, Lundbeck, Pfizer, Novartis, Lilly, Merck. Matias Viitala: Nothing to disclose. Merja Soilu-Hänninen lecture fees Merck, Teva, Sanofi; congress expenses Merck, Novartis; advisory fee Argenx, Biogen, Merck, Novartis, Roche, Sanofi; investigator for the clinical study Clarion (Merck), Magnify MS (Merck) and Hercules and Gemini (Sanofi). Sini Laakso: lecture fees Argenx, Biogen, Janssen, Lundbeck, Merck, Novartis, Roche, Sanofi; congress expenses Merck, Novartis, UCB Pharma; advisory fee Alexion, Argenx, Novartis, Roche, Sanofi, UCB Pharma; investigator for the clinical study Clarion (Merck) and subinvestigator for the clinical study Fenhance (Roche). Sari Atula: lecture fees Novartis, Merck, UCB Pharma, Amgen, Lundbeck; congress expenses Merck; Principal Investigator for the Clinical Study Fenhance (Roche); advisory fee Biogen, sanofi, UCB Pharma.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Anna Maunula: Finska Läkaresällskapet, Research Funding of the State of Finland governed through HUS Neurocenter. Matias Viitala: Funding of the State of Finland governed through Helsinki University Hospital. Merja Soilu-Hänninen Funding of the State of Finland governed through Neurocenter, Turku University Hospital.

### Ethical considerations







The study was approved by Findata (research permit no THL-708-14.02.00-2022-Mssyopa). Approval from an ethics committee was not required. The pseudonymized data from Findata was transferred to HUS Academic - a secure and audited virtual operating environment that fulfills the Findata requirements for data security. The data processing practices followed the EU Data Protection Directive rules. This manuscript adheres to the applicable

Strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement.

### Availability of data and materials

Only anonymized aggregated data can be shared and published. Pseudonymized data cannot be shared due to Finnish permit conditions for secondary data.

### ORCID iDs

Anna Maunula  <https://orcid.org/0000-0003-1499-0554>  
 Sini M Laakso  <https://orcid.org/0000-0002-0104-2849>  
 Matias Viitala  <https://orcid.org/0000-0003-2854-2410>  
 Merja Soilu-Hänninen  <https://orcid.org/0000-0001-6930-0229>  
 Marja-Liisa Sumelahti  <https://orcid.org/0000-0001-6581-0483>  
 Sari Atula  <https://orcid.org/0000-0003-1293-9325>

### Supplemental material

Supplemental material for this article is available online.

### References

- Compston A and Coles A. Multiple sclerosis. *Lancet* 2008; 372: 1502–1517.
- GBD 2016 Multiple Sclerosis Collaborators. Global, regional, and national burden of multiple sclerosis 1990–2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2019; 18: 269–285.
- Koch-Henriksen N and Sørensen PS. The changing demographic pattern of multiple sclerosis epidemiology. *Lancet Neurol* 2010; 9: 520–532.
- Walton C, King R, Rechtman L, et al. Rising prevalence of multiple sclerosis worldwide: insights from the Atlas of MS, third edition. *Mult Scler* 2020; 26: 1816–1821.
- Sarasoja T, Wikström J, Paltamaa J, et al. Occurrence of multiple sclerosis in central Finland: a regional and temporal comparison during 30 years. *Acta Neurol Scand* 2004; 110: 331–336.
- Koch-Henriksen N, Thygesen LC, Stenager E, et al. Incidence of MS has increased markedly over six decades in Denmark particularly with late onset and in women. *Neurology* 2018; 90: e1954–e1963.
- Sumelahti ML, Holmberg MHA, Murtonen A, et al. Increasing incidence in relapsing-remitting MS and high rates among young women in Finland: a thirty-year follow-up. *Mult Scler Int* 2014; 2014: 186950.
- Krökki O, Bloigu R, Reunanen M, et al. Increasing incidence of multiple sclerosis in women in Northern Finland. *Mult Scler* 2011; 17: 133–138.
- Al-Sakran LH, Marrie RA, Blackburn DF, et al. Establishing the incidence and prevalence of multiple sclerosis in Saskatchewan. *Can J Neurol Sci* 2018; 45: 295–303.
- Kingwell E, Zhu F, Marrie RA, et al. High incidence and increasing prevalence of multiple sclerosis in British Columbia, Canada: findings from over two decades (1991–2010). *J Neurol* 2015; 262: 2352–2363.
- Grytten N, Aarseth JH, Lunde HMB, et al. A 60-year follow-up of the incidence and prevalence of multiple sclerosis in Hordaland county, Western Norway. *J Neurol Neurosurg Psychiatry* 2016; 87: 100–105.
- Rotstein DL, Chen H, Wilton AS, et al. Temporal trends in multiple sclerosis prevalence and incidence in a large population. *Neurology* 2018; 90: e1435–e1441.
- Lane J, Ng HS, Poyser C, et al. Multiple sclerosis incidence: a systematic review of change over time by geographical region. *Mult Scler Relat Disord* 2022; 63: 103932.
- Rinne UK, Panelius M, Kivalo E, et al. Distribution of multiple sclerosis in Finland, with special reference to some geological factors. *Acta Neurol Scand* 1966; 42: 385–399.
- Murtonen A and Sumelahti ML. Multiple sclerosis prevalence in 2000 and 2010 in Western Finland. *Acta Neurol Scand* 2020; 141: 311–318.
- Sumelahti ML, Tienari PJ, Wikström J, et al. Increasing prevalence of multiple sclerosis in Finland. *Acta Neurol Scand* 2001; 103: 153–158.
- Wikström J. Studies on the clustering of multiple sclerosis in Finland II: microepidemiology in one high-risk county with special reference to familial cases. *Acta Neurol Scand* 1975; 51: 173–183.
- Tienari PJ, Sumelahti ML, Rantamäki T, et al. Multiple sclerosis in western Finland: evidence for a founder effect. *Clin Neurol Neurosurg* 2004; 106: 175–179.
- Kinnunen E. Multiple sclerosis in Finland: evidence of increasing frequency and uneven geographic distribution. *Neurology* 1984; 34: 457–461.
- Sumelahti M, Tienari P, Hakama M, et al. Multiple sclerosis in Finland: incidence trends and differences in relapsing remitting and primary progressive disease courses. *J Neurol Neurosurg Psychiatry* 2003; 74: 25–28.
- Holmberg M, Murtonen A, Elovaara I, et al. Increased female MS incidence and differences in gender-specific risk in medium- and high-risk regions in Finland from 1981–2010. *Mult Scler Int* 2013; 2013: 182516.
- Pirttialo AL, Soilu-Hänninen M and Sipilä JOT. Multiple sclerosis epidemiology in Finland: regional differences and high incidence. *Acta Neurol Scand* 2019; 139: 353–359.
- Kurki MI, Karjalainen J, Palta P, et al. Finngen provides genetic insights from a well-phenotyped isolated population. *Nature* 2023; 613: 508–518.
- Kerminen S, Havulinna AS, Hellenthal G, et al. Fine-scale genetic structure in Finland. *G3 (Bethesda)* 2017; 7: 3459–3468.
- Salmela E, Lappalainen T, Fransson I, et al. Genome-wide analysis of single nucleotide polymorphisms uncovers population structure in Northern Europe. *PLoS One* 2008; 3: e3519.
- Schumacher GA, Beebe G, Kibler RF, et al. Problems of experimental trials of therapy in multiple sclerosis: report by the panel on the evaluation of experimental

- trials of therapy in multiple sclerosis. *Ann N Y Acad Sci* 1965; 122: 552–568.
27. Poser CM, Paty DW, Scheinberg L, et al. New diagnostic criteria for multiple sclerosis: guidelines for research protocols. *Ann Neurol* 1983; 13: 227–231.
  28. McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the international panel on the diagnosis of multiple sclerosis. *Ann Neurol* 2001; 50: 121–127.
  29. Polman CH, Reingold SC, Edan G, et al. Diagnostic criteria for multiple sclerosis: 2005 revisions to the ‘McDonald criteria’. *Ann Neurol* 2005; 58: 840–846.
  30. Polman CH, Reingold SC, Banwell B, et al. Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria. *Ann Neurol* 2011; 69: 292–302.
  31. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. *Lancet Neurol* 2018; 17: 162–173.
  32. Ferrand M, Epstein J, Soudant M, et al. Real-life evaluation of the 2017 McDonald criteria for relapsing-remitting multiple sclerosis after a clinically isolated syndrome confirms a gain in time-to-diagnosis. *J Neurol* 2024; 271: 125–133.
  33. Lee DH, Peschke M, Utz KS, et al. Diagnostic value of the 2017 McDonald criteria in patients with a first demyelinating event suggestive of relapsing-remitting multiple sclerosis. *Eur J Neurol* 2019; 26: 540–545.
  34. Filippi M, Preziosa P, Meani A, et al. Performance of the 2017 and 2010 revised McDonald criteria in predicting MS diagnosis after a clinically isolated syndrome: a MAGNIMS study. *Neurology* 2022; 98: e1–e14.
  35. Hyun JW, Kim W, Huh SY, et al. Application of the 2017 McDonald diagnostic criteria for multiple sclerosis in Korean patients with clinically isolated syndrome. *Mult Scler* 2019; 25: 1488–1495.
  36. Runia TF, Jafari N and Hintzen RQ. Application of the 2010 revised criteria for the diagnosis of multiple sclerosis to patients with clinically isolated syndromes. *Eur J Neurol* 2013; 20: 1510–1516.
  37. Zheng Y, Shen CH, Wang S, et al. Application of the 2017 McDonald criteria in a Chinese population with clinically isolated syndrome. *Ther Adv Neurol Disord* 2020; 13: 1756286419898083.
  38. van der Vuurst de Vries RM, Mescheriakova JY, Wong YYM, et al. Application of the 2017 revised McDonald criteria for multiple sclerosis to patients with a typical clinically isolated syndrome. *JAMA Neurol* 2018; 75: 1392–1398.
  39. Gobbin F, Zanoni M, Marangi A, et al. 2017 McDonald criteria for multiple sclerosis: earlier diagnosis with reduced specificity? *Mult Scler Relat Disord* 2019; 29: 23–25.
  40. Habek M, Pavičić T, Ruška B, et al. Establishing the diagnosis of multiple sclerosis in Croatian patients with clinically isolated syndrome: 2010 versus 2017 McDonald criteria. *Mult Scler Relat Disord* 2018; 25: 99–103.
  41. Laakso SM, Viitala M, Kuusisto H, et al. Multiple sclerosis in Finland 2018-data from the national register. *Acta Neurol Scand* 2019; 140: 303–311.
  42. European Commission. *Eurostat. Revision of the European Standard Population: report of Eurostat’s task force: 2013 edition*. LU: Publications Office, <https://data.europa.eu/doi/10.2785/11470> (2013, accessed 18 March 2024).
  43. Affinito G, Palladino R, Carotenuto A, et al. Epidemiology of multiple sclerosis in the Campania Region (Italy): Derivation and validation of an algorithm to calculate the 2015–2020 incidence. *Mult Scler Relat Disord*; 71. Epub ahead of print 1 March 2023. Doi:10.1016/j.msard.2023.104585.
  44. Etusivu - Sotkanet.fi, Tilasto- ja indikaattoripankki, <https://sotkanet.fi/sotkanet/fi/index> (accessed 8 October 2024).
  45. Raulio S, Erlund I, Männistö S, et al. Successful nutrition policy: improvement of vitamin D intake and status in Finnish adults over the last decade. *Eur J Public Health* 2017; 27: 268–273.
  46. Conrad N, Misra S, Verbakel JY, et al. Incidence, prevalence, and co-occurrence of autoimmune disorders over time and by age, sex, and socioeconomic status: a population-based cohort study of 22 million individuals in the UK. *Lancet* 2023; 401: 1878–1890.
  47. Li Y, Saul A, Taylor B, et al. Examining the environmental risk factors of progressive-onset and relapsing-onset multiple sclerosis: recruitment challenges, potential bias, and statistical strategies. *J Neurol* 2024; 271: 472–485.
  48. Kalincik T, Group on behalf of the MsbS, Vivek V, et al. Sex as a determinant of relapse incidence and progressive course of multiple sclerosis. *Brain* 2013; 136: 3609–3617.
  49. Tao C, Simpson S, van der Mei I, et al. Higher latitude is significantly associated with an earlier age of disease onset in multiple sclerosis. *J Neurol Neurosurg Psychiatry* 2016; 87: 1343–1349.
  50. Alonso A and Hernán MA. Temporal trends in the incidence of multiple sclerosis: a systematic review. *Neurology* 2008; 71: 129–135.
  51. McNicholas N, Lockhart A, Yap SM, et al. New versus old: implications of evolving diagnostic criteria for relapsing-remitting multiple sclerosis. *Mult Scler* 2019; 25: 867–870.
  52. Brownlee WJ, Swanton JK, Altmann DR, et al. Earlier and more frequent diagnosis of multiple sclerosis using the McDonald criteria. *J Neurol Neurosurg Psychiatry* 2015; 86: 584–585.
  53. Ducatel P, Debouverie M, Soudant M, et al. Performance of administrative databases for identifying individuals with multiple sclerosis. *Sci Rep* 2023; 13: 18310.
  54. Murley C, Friberg E, Hillert J, et al. Validation of multiple sclerosis diagnoses in the Swedish national patient register. *Eur J Epidemiol* 2019; 34: 1161–1169.
  55. Sund R. Quality of the Finnish hospital discharge register: a systematic review. *Scand J Public Health* 2012; 40: 505–515.