Introduction
Multiple sclerosis (MS) usually presents at a highly productive stage of life when people are planning families and building careers and as such MS can have a significant impact on affected individuals, their families and society. The growing arsenal of disease-modifying therapies offers opportunities to reduce disability and extend survival of people with MS; however, a cure is still lacking and the etiology of the disease remains incompletely understood. Thus, there is a continued, compelling need for high-quality epidemiologic data worldwide to improve our understanding of disease risk, support health policy aimed at meeting the diverse needs of people with MS and support advocacy efforts.

Compiled by the Multiple Sclerosis International Federation (MSIF), the Atlas of MS (www.atlasofms.org) is an open-source global compendium of data regarding the epidemiology of MS, and the availability of resources for people with MS reported at country, regional and global levels. The first edition was produced in 2008 in collaboration with the World Health Organization (WHO) and it was updated in 2013.3 Herein, we discuss the approach to epidemiologic data collection from the third edition of the Atlas, including methodological improvements, key findings and future directions.

Development of the Atlas of MS, third edition
Between September 2019 and March 2020, MSIF collected epidemiologic data from 115 countries representing 87% of the world’s population. Consistent with previous editions of the Atlas, country coordinators reported the incidence and prevalence of MS in...
adults and children, separately for males and females; diagnostic criteria employed in their country; and key clinical characteristics such as age and MS type at diagnosis. Coordinators also reported their data sources which potentially included publications and presentations, registries, government/health system statistics, administrative data sets, electronic medical records and opinions of experts (typically neurologists, researchers, or MS societies).

In this edition, several methodological changes were made to improve data quality. First, key terms in the survey were explicitly defined. Second, all data sources reported were scored using a confidence tool based on the proportion of the country’s population included, year and method of data collection, MS diagnostic criteria used and peer-review or other validation efforts (see Figure 1). Countries were given a confidence rating for prevalence, incidence, age of MS onset and type of MS at onset based on the confidence scores of their reported data sources. Third, a literature review was conducted to identify prevalence estimates for missing countries and query outliers. Finally, missing data were imputed for the global prevalence calculation by using available prevalence data to calculate pooled prevalence rates for 15 geographic sub-regions based on the Global Health Data Exchange. Sub-region rates were applied to countries with missing data using their 2019 populations.

**Data quality**

Survey responses covered 85%-99% of the population in each WHO region (Europe, Americas, South East Asia, Eastern Mediterranean, Western Pacific) except Africa with only 56% of the population represented. Availability and quality of MS epidemiologic data, and prevalence in particular, seemed to have improved in many regions as evidenced by 84% (87/104) of countries reporting prevalence citing a data source compared with 71% (65/92) in 2013. Peer-reviewed publications were cited by 57% (59/104) of countries compared with 51% (47/92) in 2013 and 27% (28/104) cited MS registries or electronic health records compared with 20% (18/92) in 2013. Two-thirds (67%) of the reported data were collected in the period 2017–2019. Over one-third (38/102) of countries now have a national MS registry and a further 14% (14/102) have a registry covering part of the country’s population. Fifty-four percent (62/115) of countries completing the epidemiology survey rated moderate or high on the confidence tool for prevalence data (Figure 1). Only 10% (1/10) of low-income countries met this threshold compared with 70% (32/46) of high-income countries (using World Bank income categories).

Countries with no prevalence data available tended to be found in regions where countries reported a lower MS prevalence (Figure 1). This means earlier estimates of the global number of prevalent cases using a global median prevalence (old method) to impute missing country data were likely overestimates. Using the old method, we would estimate 3.0 million people live with MS worldwide in 2020, a 30% increase over the same estimate in 2013. Using the improved method, the prevalence is 2.8 million people in 2020. As reported in earlier editions of Atlas of MS, availability and quality of incidence data are poorer than for prevalence; only 75 countries (65% of survey responders) reported incidence.

**Findings**

Highlights from the epidemiology survey are as follows:

- The estimated number of people with MS worldwide has increased to 2.8 million in 2020. When applying the same methodology as in 2013, the estimate is 30% higher than in 2013. The 2020 global prevalence is 35.9 [95% CI: 35.87, 35.95] per 100,000 people.
- MS prevalence has increased in every world region since 2013 (Table 1). Only 14% (11/81) of countries with data at both time points reported stable or declining prevalence.
- The pooled incidence rate across 75 reporting countries was 2.1 [95% CI: 2.09, 2.12] per 100,000 persons/year. We estimate that someone in the world is diagnosed with MS every 5 minutes.
- Recognition of paediatric-onset MS has increased substantially with ≥30,000 cases of MS diagnosed in individuals under 18 years of age reported by 47 countries. In 2013, 7,000 cases were reported by 34 countries.
- Globally, females are twice as likely to have MS as males and this is consistent with both prior editions of the Atlas. However, the ratio of women to men is as high as 4:1 in some countries and in others this ratio has doubled since 2013.

If the analysis is restricted to countries who reported prevalence data in 2013 and 2020, the increase in global prevalence is higher at 50% (Table 1). All WHO regions reported an increase in prevalence since 2013, consistent with increases reported in several national studies published during this period. The United States validated a case-ascertainment algorithm and reported an almost doubling of prevalent cases to 913,925 in
Figure 1. Map showing geographic variation in MS prevalence and in data confidence scores\(^a\) by country: (a) MS prevalence per 100,000 population by country shown in shades of orange and red as per the key. Countries without prevalence data are shown in grey. (b) Confidence score assigned to each country based on the prevalence data sources provided. Scores of very low, low, moderate or high are shown in shades of orange and red as per the key. Countries without prevalence data or with data but no source information provided are shown in grey.

\(^a\)Country confidence scores were assigned using four variables: (1) size of the population covered by data source, from 0 if unknown to 5 if covering the whole country; (2) year of data collection by source, from 0 if prior to 2009 to 5 if in 2017–2019; (3) type of data source, from 0 if unknown to 5 if peer-reviewed journal publication; (4) additional points were given for meeting certain methodological criteria: using the 2017 McDonald Criteria, performing a validation step or using multiple consistent data sources for the estimate. Confidence ratings were assigned based on the total scores using the following thresholds: $\leq 5$ = very low, 6–10 = low, 11–15 = moderate, $\geq 16$ = high.
2019. An increasing prevalence of MS has also been reported across the Middle East and North African region, in the Russian Federation, Canada, Australia and in several European countries (Denmark, Germany, Poland, the United Kingdom). The Global Burden of Disease (GBD) 2016 Multiple Sclerosis Collaborators similarly reported that the prevalence of MS had risen between 1990 and 2016, estimating that there were 2,221,188 (95% Uncertainty Interval 2,033,866–2,436,858) persons living with MS in 2016. The GBD group relied on information in the literature, and modelling to generate estimates, and the updated United States prevalence figures used in the present Atlas which showed an increase of over 400,000 Americans living with MS were not available at that time.

Across studies, the consensus is that earlier diagnosis, improved ascertainment and longer survival have all contributed to these trends. Experts responding to the Atlas survey supported these views. The top three potential causes for a change in reported prevalence since 2013 from 73 responders were ‘an improvement in MS diagnosis’ (60%), ‘improved MS treatment and support’ (56%) and ‘improved ability to count the numbers of people with MS’ (53%). The Atlas survey observed high variability in the age of diagnosis between countries but comparing the mean (range) across time points does not suggest any trend towards an earlier diagnosis at a global level (2013: 30 (20–44) 2020: 32 (20–50) years).

Regional variation in incidence (per 100,000 persons per year) generally follows the prevalence pattern, with Europe having the highest reported incidence at 6.8, followed by the Americas at 4.8. South East Asia and Africa have the lowest reported incidence rates of 0.4. The number of countries with data in 2013 and 2020 is too low to support comparisons.

### Limitations

A necessary limitation of the Atlas methodology is relying on country representatives to report data but several steps were taken to improve data quality. All sources of data are accepted in the Atlas, including expert opinion in countries where there is no published data or scientific study. Expert opinion accounted for 16% of the reported prevalence estimates and future work should examine the influence of opinion-based estimates on the global prevalence figure. This inclusive approach enables the most comprehensive global data set but makes detailed comparisons across countries and time points difficult due to differing data collection methods. A further challenge to examining trends in the data is the varying participation of countries with each Atlas edition. This has been addressed by restricting analysis to countries reporting data at multiple time points but limits the number of countries included and biases towards higher income countries that have more consistent data collection methods. As with previous editions of the Atlas, gaps in data from Africa and low-income countries persist which introduces some uncertainty with respect to the global prevalence estimate. In addition, data regarding incidence and paediatric-onset MS are limited, although this has improved.

### Future directions

Despite these limitations, the Atlas of MS remains the most comprehensive, open-source data resource for the MS community. The third edition has improved coverage and data quality and thus is likely to provide a more accurate global prevalence estimate. We report here the epidemiology survey results. Data on the clinical management of MS including access to MS therapies will follow. Important gaps in our epidemiologic

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**Table 1.** Prevalence of multiple sclerosis per 100,000 population by world region in 2013 and 2020.

| Number of countries included | 2013 prevalence per 100,000 population [95% CI] | 2020 prevalence per 100,000 population [95% CI] | Increase; absolute (%) |
|-----------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------|
| Global                      | 81 29.26 [29.21, 29.30]                       | 43.95 [43.90, 44.01]                          | 14.69 (50%)           |
| African                     | 6 5.52 [5.41, 5.62]                           | 8.76 [8.64, 8.89]                             | 3.24 (59%)            |
| Americas                    | 15 62.89 [62.72, 63.05]                       | 117.49 [117.27, 117.71]                       | 54.6 (87%)            |
| E. Mediterranean            | 14 23.91 [23.77, 24.04]                       | 33.00 [32.85, 33.15]                          | 9.09 (38%)            |
| European                    | 35 108.25 [108.01, 108.49]                    | 142.81 [142.53, 143.08]                       | 34.56 (32%)           |
| South East Asia             | 4 5.44 [5.41, 5.48]                           | 8.62 [8.58, 8.66]                             | 3.18 (58%)            |
| Western Pacific             | 7 3.64 [3.61, 3.67]                           | 4.79 [4.75, 4.82]                             | 1.15 (32%)            |

CI: confidence intervals, E. Mediterranean: Eastern Mediterranean.
*Only countries providing data for 2013 and 2020 editions of the Atlas of MS are included in the analysis. Global and WHO regional totals reported. Reported MS prevalence increased in every WHO region between the 2013 and 2020 versions of the Atlas of MS.
understanding of MS persist and must be filled to enable equitable access to disease-modifying and rehabilitative therapies, resources and support that can improve the lives of people with MS. We call on policymakers, health professionals and MS organisations to:

1. Use Atlas of MS data to stimulate additional research, raise awareness of MS and support evidence-based advocacy efforts. All Atlas data are open-source and available to download from www.atlasofms.org. User-friendly data visualisation tools and country factsheets are available to enhance use of the data for local advocacy.

2. Work with the Multiple Sclerosis International Federation (MSIF) to annually update country statistics in the Atlas of MS. MSIF is introducing mechanisms to enable regular data updates for countries with national surveillance systems or new peer-reviewed publications. We urge stakeholders to report data annually where possible, according to specified data standards.

3. Implement systematic, validated data collection regarding MS, particularly in low- and lower-middle income countries. For countries with national, publicly funded health systems use of administrative (health) data may provide a stable, low-cost mechanism for disease surveillance. To optimise comparability of prevalence estimates across regions, crude estimates as well as estimates which are age- and sex-standardised to the world population should be reported.

4. Prioritise the collection of incidence data to better understand changes in disease risk. Incidence data are important for assessing population-level interventions to reduce disease risk and for directing education and resources towards subgroups at greatest risk.

5. Start reporting on cases of paediatric MS if not already doing so. This will increase awareness that children and youth live with MS and is a first step to ensuring they have access to prompt diagnosis, relevant treatments, specialist healthcare professionals and family support. Data can be enriched by including variables relevant to the paediatric population such as educational attainment.

6. Add the collection of information on race and ethnicity to the surveillance of MS. These data are essential for research to investigate differences in MS risk and outcomes and the disparities in care that exist for people from black and ethnic minority backgrounds. Government data sources and MS registries should add this field to their standard data collection. MS research funders should require funded research to capture ethnicity data where possible.

Acknowledgements
The authors thank the following members of the Atlas of MS third edition working group and our clinical expert advisors for their input to the study design and survey used to collect data for this manuscript: Mona Alkhawajah, Mario Battaglia, Tim Coetzee, Arwenna Davis, Benjamin Davis, Magdalena Fac-Skirtladze, Kazuo Fujihara, Andrew Giles, Riadh Gouider, Aoife Kirwan, Nora Kriauzaitė, Joanna Laurson-Doube, Renuka Malaker, Anna-Lena Roper, Lasse Skovgaard, Marta Szantroch and María José Wuille-Bille. We are grateful to the all the country coordinators listed in Supplementary Table S1 and all those who wish to remain anonymous for contributing data to the Atlas of MS.

Declaration of conflicting interests
The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: CW, RK, AH, CAN, NRi and PB are employees of Multiple Sclerosis International Federation which receives money from a range of corporate sponsors, recently including Biogen, BristolMyersSquibb (formerly Celgene), Genzyme, Med-Day, Merck, Mylan, Novartis, Roche. LR and WK are employees of McKing Consulting Corporation which received contract funding from the National MS Society. EL receives research funding from Fondation ARSEP, Fondation EDMUS and Agence Nationale de Sécurité du Médicament and reports consulting and lecture fees or travel grants from Biogen, Genzyme, MedDay Pharmaceuticals, Merck Serono, Novartis and Roche. RAM receives research funding from the Canadian Institutes of Health Research, the MS Society of Canada, MS Scientific Foundation, the National MS Society, Crohn’s and Colitis Canada, The Arthritis Society and the Consortium of Multiple Sclerosis Centers. NRo receives research funding from the MRC, MS Society, Biogen, Novartis and Genzyme and has received consultancy fees from Abbvie, Novartis, Genzyme and Celgene outside the submitted work. BU received consultancy fees from Genzyme, Merck, Biogen and Novartis, outside the submitted work. NLR, IvdM and MW have nothing to disclose.

Funding
The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Funding for the Atlas of MS, third edition, was provided by the National MS
Society, the MS Society (UK), the Associazione Italiana Sclerosi Multipla, Biogen Idec, Bristol Myers Squibb, Merck Serono, Novartis, Roche, Sanofi Genzyme and Vanneau Trust.

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**Supplemental material**
Supplemental material for this article is available online.

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