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Digital epidemiology confirms a latitude gradient of MS in France

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ABSTRACT

Background: A gradient of prevalence of MS has been previously reported, and this may be due to different environmental and genetic features of the different populations, but also to methodological issues. In France, for example, three studies analysed the presence of such a gradient with conflicting results. The aim of this study was to assess whether digital epidemiology could confirm the presence of such a gradient.

Methods: through Google Trends, we analysed the relative search volume (RSV) for 'multiple sclerosis' in France, from 2004 to 2017, and assessed if an association with the decimal degree of latitude existed.

Results: Latitude was correlated with crude RSV (r^2 0.39, p 0.04) in the 21 regions considered, with a southwest/northeast gradient. A multiple linear regression model adjusted for sex and age confirmed the existence of such a latitudinal effect, with an increase of 2.43 RSV units for each unit increase in latitude (95% CIs 0.62–4.24, $p < 0.01$, adjusted r^2 0.61).

Conclusions: our study provides additional evidence for the existence of a latitude gradient in MS, and the value of Internet-acquired data as real-time surveillance tools and alerts for healthcare systems.

Multiple sclerosis (MS) prevalence is heterogeneous worldwide, while in Europe and North America, a latitudinal gradient of incidence or prevalence has also been previously reported (Koch-Henriksen and Sorensen, 2010). This gradient has been the subject of debate as it could reflect a combination of different environmental and genetic features of the different populations. However, it could also be due to methodological issues (McGuigan et al., 2004).

In France, for example, three studies analysed multiple sclerosis prevalence nationwide, obtaining conflicting results: while a south-west—northeast gradient of prevalence was found in farmers and independent workers, this was not apparent for employees (Vukusic et al., 2007; Fromont et al., 2010; Ha-Vinh and Nauelau Clements).

The communication revolution unfolding during the past few decades has led to a new course of epidemiology: real-time mobile or social digital data – including epidemiologically relevant behaviours, such a Google searches for diseases or symptoms – could now be used for improving public health or preventing/minimizing disease outbreaks (International Telecommunication Union, 2011; Brownstein et al., 2008). Google Trends, a Google Inc. portal, generates data on geographical and temporal patterns according to specified keywords searched. Therefore, this current 13-year retrospective web-based research investigated whether a latitude gradient of Google Trends search volumes for multiple sclerosis **(*sclérose en plaques*)** exists in France.

In order to do successfully investigate whether this lateral gradient exists, we assessed the search volumes for the term 'multiple sclerosis' from 2004 to 2017 in France on Google Trends. Google Trends automatically normalizes data for the overall number of searches, and presents them as relative search volumes (RSV, on a scale from 0 to 100), in order to compare variations of different search terms across regions and periods. Considering that a peak for the search term 'multiple sclerosis' was found in 2004, that year was removed from the analysis and replaced with the average number derived from the entire time series. We calculated the crude RSV at a regional level (excluding islands and overseas departments). Age and sex representation of the population at a regional level were retrieved from the *Institute National d'études démographiques* (www.ined.fr/), and their means, over the period of time considered, were used for the final analysis. Pearson correlation was used to examine the relationship of crude RSV and decimal degrees of north latitude. Latitudes were those of capital cities of the regions (*préfectures de régions*). A multiple linear regression model was used to examine the relationship of crude RSV with latitude, and to correct for important covariates such as age and sex.

The demographics and crude RSV at a regional level are reported in Table 1.

Latitude (in absolute terms to take into account the southern hemisphere) was correlated with crude RSV (r^2 0.39, p 0.04) in the 21 regions (Supplementary data), and a visual southwest/northeast gradient clearly appeared when the RSVs were mapped (Fig. 1).

Confirming the visual approach, the multiple linear regression model showed the existence of such a latitudinal effect. RSV was correlated with latitude in the regions of France independently of the age and sex representation of the cohort, with an increase of 2.43 RSV units for each unit increase in latitude (95% CIs 0.62–4.24, $p < 0.01$, adjusted r^2 0.61).

The latitudinal gradient in RSV for MS we observed through Google Trends is in line with previous studies, showing that the prevalence of the disease increases in a southwest-northeast direction among farmers and those who are self-employed (Vukusic et al., 2007; Ha-Vinh and Nauelau Clements). This gradient was not apparent in a different French population consisting of employees, and possible methodological issues such a selection bias in these observational studies, have been suggested to explain the discrepancy. The results we obtained through Google Trends highlight the presence of such a latitudinal gradient of the disease and support the hypothesis that this gradient may have been masked in a young sector of the population who are more prone to relocating for professional reasons and who are less likely to perform outdoor jobs.

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Table 1
Region-specific demographics between 2004 and 2017 and Google Trends Relative Search Volumes for Multiple Sclerosis.

Region	Capital city	Age representation (%)					Female representation (%)	Latitude (decimals)	Longitude (decimals)	RSV
		0–19	20–39	40–59	60–74	> 75				
Languedoc-Roussillon	Montpellier	0.23	0.23	0.27	0.17	0.11	0.52	43.610	3.877	77
Provence-Alpes-Cote d'Azure	Marseille	0.23	0.23	0.27	0.17	0.11	0.52	43.296	5.381	78
Aquitaine	Bordeaux	0.22	0.22	0.27	0.17	0.11	0.52	44.840	−0.580	78
Pays-de-Loire	Nantes	0.25	0.23	0.26	0.15	0.10	0.51	47.217	−1.553	81
Rhone-Alpes	Lyon	0.25	0.24	0.27	0.15	0.09	0.51	45.748	4.846	80
Midi-Pyrenees	Toulouse	0.23	0.23	0.27	0.17	0.11	0.52	43.604	1.443	79
Ile-de-France	Paris	0.26	0.29	0.27	0.12	0.07	0.52	48.858	2.348	83
Auvergne	Clermont-Ferrand	0.25	0.24	0.27	0.15	0.09	0.51	45.779	3.086	88
Limousin	Limoges	0.22	0.22	0.27	0.17	0.11	0.52	45.833	1.261	89
Poitou-Charentes	Poitiers	0.22	0.22	0.27	0.17	0.11	0.52	46.580	0.340	87
Centre	Orleans	0.24	0.22	0.27	0.16	0.10	0.51	47.902	1.909	83
Picardy	Amiens	0.26	0.25	0.27	0.14	0.08	0.51	49.894	2.295	83
Brittany	Rennes	0.24	0.22	0.27	0.16	0.10	0.51	48.111	−1.674	89
Upper-Normandie	Rouen	0.25	0.23	0.27	0.16	0.10	0.52	49.443	1.099	80
Lower-Normandy	Caen	0.25	0.23	0.27	0.16	0.10	0.52	49.182	−0.370	88
Alsace	Strasbourg	0.24	0.24	0.28	0.15	0.09	0.51	48.583	7.745	94
Burgundy	Dijon	0.23	0.22	0.27	0.17	0.11	0.51	47.322	5.041	91
Nord-pas-de-Calais	Lille	0.26	0.25	0.27	0.14	0.08	0.51	50.629	3.057	85
Lorraine	Metz	0.24	0.24	0.28	0.15	0.09	0.51	49.119	6.172	94
Franche-Comte	Besancon	0.23	0.22	0.27	0.17	0.11	0.51	47.237	6.024	100
Champagne-Ardenne	Chailons-en-Champagne	0.24	0.24	0.28	0.15	0.09	0.51	48.953	4.367	92

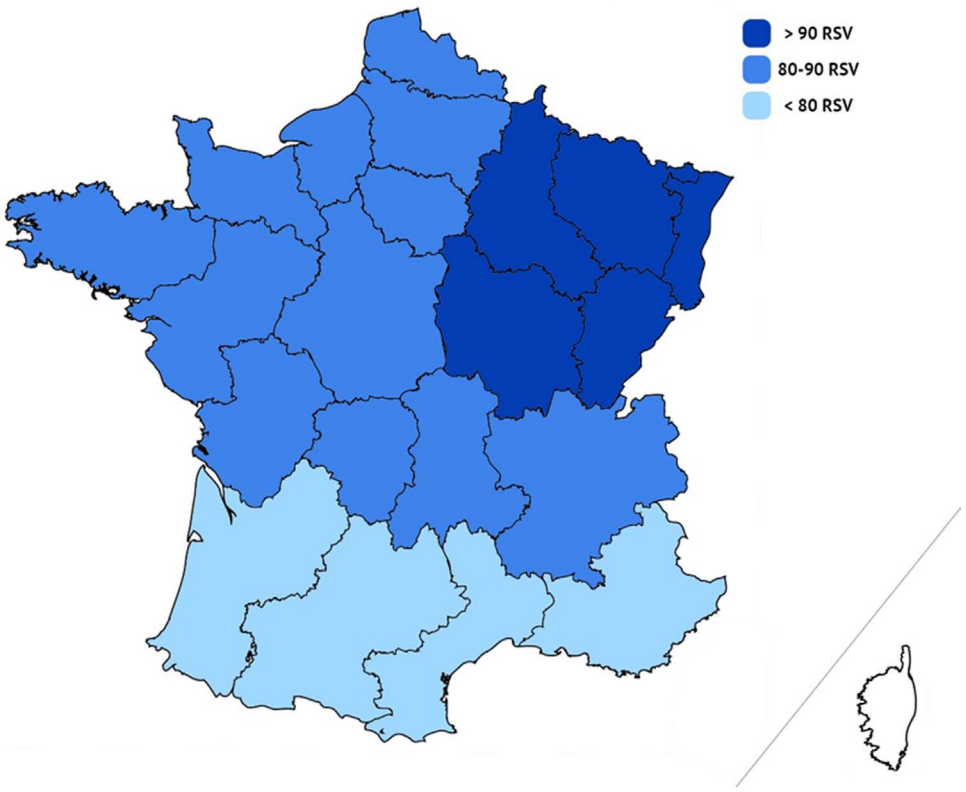

Fig. 1. Google Trends relative search volumes (RSV) for search term 'multiple sclerosis' in France between 2004 and 2017.

Indeed, digital epidemiology, the application of Internet-derived information, has been recently recognized as a valuable tool for epidemiological investigation (Brownstein et al., 2008; Ginsberg et al., 2009). Google Trends, in particular, has been shown to be able to precede traditional control systems in detecting seasonal or annual outbreaks of infectious (ie, flu, scarlet fever, etc) and non-infectious diseases (ie, cancer, arthritis, etc) presenting specific patterns in different parts of the world (Nuti et al., 2014). Relative search volumes on Google Trends may not be accurately representative of the prevalence of MS in France as they may have been produced not by patients with MS, but by those who, nevertheless have an interest in the disease. Furthermore, a non-representative sampling bias might limit this study as it may have occurred owing to different factors, such as disability, income, or preferred search engine. Nevertheless, the current study provides additional evidence for the existence of a latitude gradient in MS and the value of Internet-acquired data as a real-time surveillance tool as an alert for healthcare systems.

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Statement of authorship

Dr G Dalla Costa and Dr A Giordano contributed to the concept, data collection, analysis and drafting of the article. Prof G Comi and Dr V Martinelli supervised the data collection, the analysis of the data, and revised the manuscript.

Disclosures

Dr G Dalla Costa, Dr A Giordano, Dr M Romeo, and Dr F Sangalli report no disclosures. Prof G. Comi has received personal compensation for consulting services and/or speaking activities from Novartis, Teva, Sanofi, Genzyme, Merck, Biogen, Excemed, Serono Symposia International Foundation, Roche, Almirall, Receptos, Celgene, Forward Pharma. Dr V. Martinelli has received honoraria for activities with Biogen, Merck Serono, Bayer Schering, TEVA and Sanofi Aventis as a speaker.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.msard.2018.01.009.

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