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Increased vision impairment reports linked to semaglutide: analysis of FDA adverse event data

Marine Massy[1,2,3], Stefanie Marti[1], Helly Hammer[1] and Robert Hoepner[1*]

Abstract

Background Semaglutide, a GLP-1 receptor agonist widely prescribed for type 2 diabetes and obesity, has recently raised concerns about its ocular safety. This study aimed to investigate the association between semaglutide use and vision impairment using data from the FDA Adverse Event Reporting System (FAERS).

Methods We conducted an analysis of FAERS data, comparing reports of vision impairment associated with semaglutide to those associated with other antidiabetic and weight loss medications. The main outcome measure was the reporting odds ratio (rOR) for vision impairment linked to semaglutide use compared to other medications.

Results Semaglutide showed significantly higher reporting of vision impairment compared to other GLP-1 receptor agonists (rOR 1.95, 95% CI 1.75–2.17, $p < 0.0001$), DPP-4 inhibitors (rOR 2.46, 95% CI 2.12–2.86, $p < 0.0001$), SGLT2 inhibitors (rOR 3.89, 95% CI 3.35–4.51, $p < 0.0001$), and metformin (rOR 2.23, 95% CI 1.90–2.62, $p < 0.0001$). Similar findings were observed when compared to phentermine (rOR 1.57, 95% CI 1.07–2.31, $p = 0.026$) and orlistat (rOR 3.77, 95% CI 2.96–4.81, $p < 0.0001$). Topiramate was the sole exception, showing higher vision impairment reporting than semaglutide (rOR 0.30, 95% CI 0.20–0.45, $p < 0.0001$).

Conclusions These findings suggest a potentially elevated risk of vision impairment with semaglutide use compared to other diabetes and weight loss medications, warranting further investigation and vigilant post-marketing surveillance. Future studies should assess the clinical impact of this potential increased risk on an absolute scale to better inform treatment decisions.

Keywords Semaglutide, Vision impairment, Diabetes, Obesity

Background

The recent study by Hathaway et al. published in JAMA Ophthalmology raises important questions about the ocular safety of semaglutide, a widely prescribed glucagon-like peptide 1 receptor agonist (GLP-1 RA) for the treatment of type 2 diabetes (T2D) and obesity [1]. In their retrospective matched cohort study, the authors report a significant association between semaglutide use and an increased risk of nonarteritic anterior ischemic optic neuropathy (NAION), a potentially vision-threatening condition.

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The study, which analyzed data from 16,827 patients evaluated by neuro-ophthalmologists at a single academic institution over a six-year period, found that patients prescribed semaglutide had a substantially higher risk of developing NAION compared to those prescribed non-GLP-1 RA medications. Specifically, in patients with type 2 diabetes, the hazard ratio for NAION was 4.28 (95% CI 1.62–11.29), while in overweight or obese patients, the hazard ratio was even higher at 7.64 (95% CI 2.21–26.36).

Given the rapidly increasing use of semaglutide and other GLP-1 RAs, these findings warrant careful consideration. However, it is crucial to contextualize these results within the broader landscape of pharmacovigilance. To this end, we conducted an analysis of the U.S. Food and Drug Administration (FDA) Adverse Event Reporting System (FAERS) database, a post-marketing, open access pharmacovigilance database, focusing on the association between semaglutide and vision impairment. This brief report aims to contribute to a more comprehensive understanding of the potential ocular risks associated with semaglutide use.

Methods

We analyzed reports submitted to FAERS [2] with T2D or obesity treatments as single suspect product active ingredient and T2D or obesity as reason for use (refer to Additional file 1: Table S1 for number of reports), and compared cases that mention vision impairment as reaction to cases that do not report vision impairment (see Additional file 1: Methods for details and Additional file 1: Tables S1–S3). A supplementary analysis was also conducted to investigate retinopathy cases only (defined as all cases with at least one of the following terms mentioned in the reactions list: "Diabetic Retinopathy", "Retinopathy", "Retinopathy Haemorrhagic", "Retinopathy Hypertensive", "Retinopathy Proliferative") (see Additional file 1: Table S4 for number of reports). Table 1 presents the comprehensive list of search terms used to classify adverse event reports into two distinct indication groups: obesity and type 2 diabetes mellitus. These standardized terms were systematically applied to categorize the reported reason for use in the pharmacovigilance database.

To complement Hathaway et al.'s findings [1], we analyzed reports from the FAERS database, focusing on the association between semaglutide use and vision impairment. We calculated reporting odds ratios (rOR) for vision impairment associated with semaglutide compared to other medications used for diabetes management and weight loss, filtering for type 2 diabetes and obesity indications. For patients with both obesity and type 2 diabetes indications recorded, we included them in both the obesity and type 2 diabetes subgroup analyses to capture the full scope of potential risk. The rOR analysis compares the rate of vision-related reports in a specific drug with the rate of vision-related reports in comparator medications. Furthermore, we dissected the "other GLP-1 receptor agonists" group and computed the reporting odds ratio for semaglutide vs. each of these substances for reports with at least one reaction term related to visual impairment as listed in Table S3 of Additional file 1 (except Optic Neuritis) versus reports without. All available FAERS data up to June 30, 2024 were included in our analysis, regardless of the time since drug approval.

Table 1 Indication filter list. Search terms for classifying reports into type 2 diabetes or obesity cases

Indication group	Reason for use search term
Obesity	Body Mass Index Increased
Obesity	Obesity
Obesity	Overweight
Obesity	Weight Control
Obesity	Weight Increased
Obesity	Weight Loss Diet
Type 2 diabetes	Diabetes Mellitus
Type 2 diabetes	Diabetes Mellitus Inadequate Control
Type 2 diabetes	Diabetes Mellitus Management
Type 2 diabetes	Diabetes With Hyperosmolarity
Type 2 diabetes	Glucose Tolerance Impaired
Type 2 diabetes	Insulin Resistance
Type 2 diabetes	Insulin Resistant Diabetes
Type 2 diabetes	Insulin-Requiring Type 2 Diabetes Mellitus
Type 2 diabetes	Ketosis-Prone Diabetes Mellitus
Type 2 diabetes	Type 2 Diabetes Mellitus

Results

A total of 302,706 reports, of which 197,045 (65.1%) are from the US, 65,006 (21.5%) from an unspecified country, and 40,655 (13.4%) from 122 other countries, met our criteria (Additional file 1: Figure S1). 17,853 reports mention "obesity" as indication, 283,238 mention T2D as indication, and 1,615 mention both (Additional file 1: Table S1).

Our analysis revealed a consistent pattern of increased vision impairment reporting with semaglutide use compared to most other medications (Fig. 1). Among the 11,558 reports for semaglutide, we identified 417 cases specifically related to visual impairment or ischemic optic neuropathy (ION). Semaglutide showed significantly higher reporting compared to other GLP-1 RA (rOR 1.95, 95% CI 1.75–2.17, $p < 0.0001$), suggesting a potentially higher risk specific to semaglutide within its drug class.

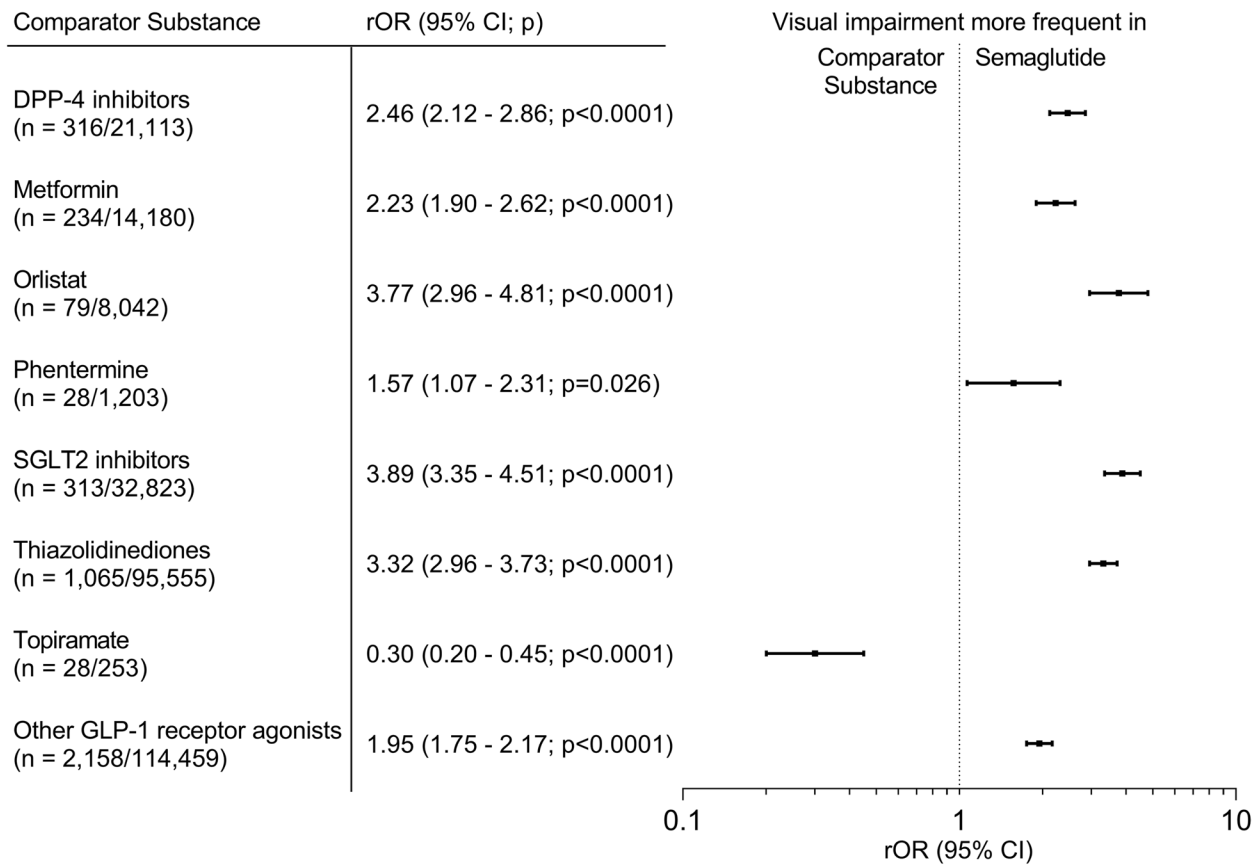

Fig. 1 Semaglutide is associated with visual impairment or optic neuropathy compared to other substances, except topiramate. Analysis of FAERS reports of visual impairment (terms in Additional file 1: Table S3) in filtered reports with T2D or obesity as main indication for semaglutide and Comparator Substance (monotherapy). Numbers of reports for comparator substance are displayed in the graph (report for visual impairment/total number of reports), except for semaglutide ($n = 417/11,558$). rORs were calculated with 95% CI and corresponding p-value (with Yates' correction). Abbreviations: CI: confidence interval, FAERS: Food and Drug Administration (FDA) adverse event reporting system, rOR: reporting odds ratio, T2D: type 2 diabetes

The disparity was more pronounced when comparing semaglutide to other antidiabetic medications: DPP-4 inhibitors (rOR 2.46, 95% CI 2.12–2.86, $p < 0.0001$), SGLT2 inhibitors (rOR 3.89, 95% CI 3.35–4.51, $p < 0.0001$), and metformin (rOR 2.23, 95% CI 1.90–2.62, $p < 0.0001$). Similarly, semaglutide showed higher reporting compared to weight loss medications: phentermine (rOR 1.57, 95% CI 1.07–2.31, $p = 0.026$) and orlistat (rOR 3.77, 95% CI 2.96–4.81, $p < 0.0001$). As an exception, topiramate showed higher vision impairment reporting than semaglutide (rOR 0.30, 95% CI 0.20–0.45, $p < 0.0001$). This aligns with online drug information [3], which lists visual impairment as a "frequent" side effect (affecting 1/10 to 1/100 patients), while no such effects are mentioned for semaglutide.

In a second step, we dissected the other GLP-1 receptor agonists group (number of reports in Table S5, Additional file 1). For all treatments (except lixisenatide, which was excluded due to too low case numbers), we observe significantly higher reporting odds for semaglutide (Fig. 2).

When focusing specifically on retinopathy instead of general visual impairment, we observed similar patterns (Additional file 1: Fig. S2). Notably, semaglutide showed a higher retinopathy risk compared to the other included medications.

A supplementary analysis was conducted using the brand names of the medications (Ozempic, Rybelsus and Wegovy), rather than their generic names or drug classes (Additional file 1: Fig. S3). This subgroup analysis demonstrated results consistent with our primary findings for semaglutide formulations Ozempic and Rybelsus, with statistically significant associations observed. The analysis of Wegovy was limited by insufficient adverse event reports to draw statistical conclusions, precluding meaningful interpretation of risk patterns for this formulation.

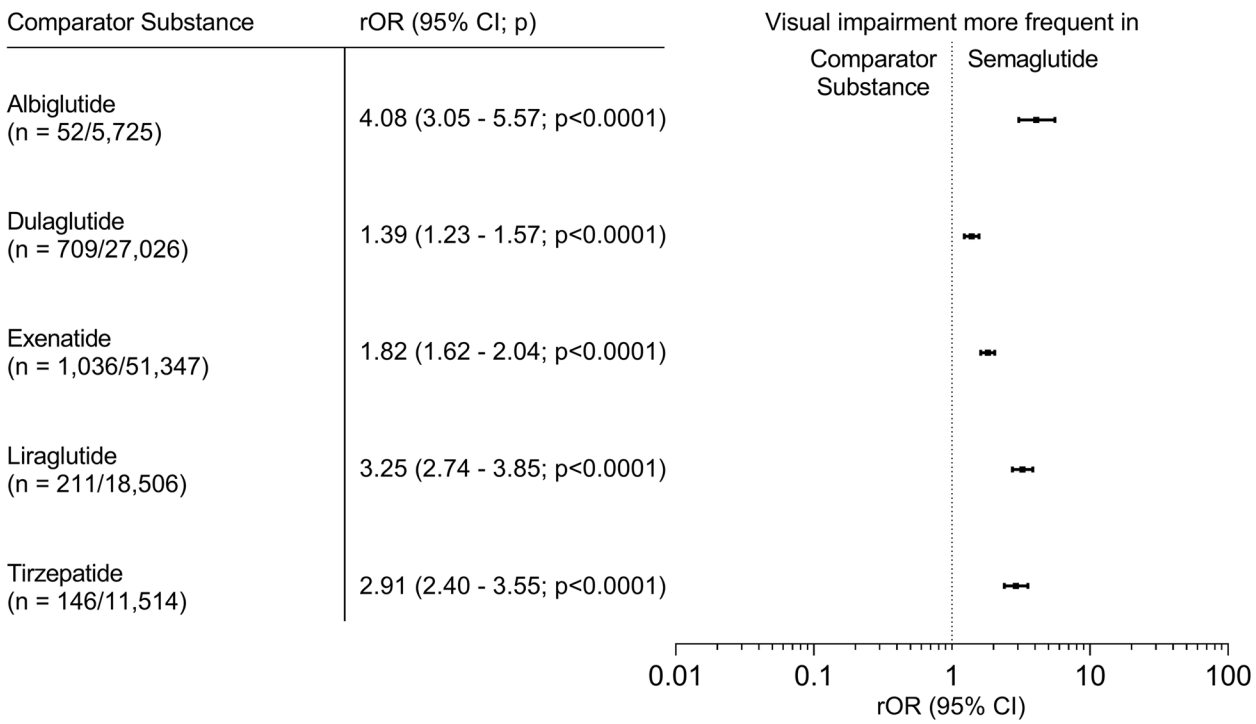

Fig. 2 The observed association between semaglutide and higher risk for visual impairment also holds for individual GLP-1 receptor agonists. Analysis of FAERS reports of visual impairment in filtered reports with obesity or T2D as main indication for semaglutide and Comparator Substance (monotherapy). Numbers of reports are displayed in the graph as: report for visual impairment/total number of reports, except for semaglutide (*n* = 417/11,558). Lixisenatide was excluded due to too low case numbers (see Additional file 1: Table S5 for number of reports). rORs were calculated with 95% CI and corresponding p-value (with Yates' correction). Abbreviations: CI: confidence interval, FAERS: Food and Drug Administration (FDA) adverse event reporting system, rOR: reporting odds ratio, T2D: type 2 diabetes

Discussion

The current analysis with the FAERS database provides several important insights into the potential association of semaglutide use with vision impairment. While the recent JAMA Ophthalmology report by Hathaway et al. [1] on NAION and semaglutide was a motivating factor for our study, our analysis focused on broader vision-related adverse events due to limitations in specific NAION reporting in the FAERS database. The findings presented herein support and further extend the observations by Hathaway et al. [1], strengthening the signal of a possible link between semaglutide and ocular complications. This also holds when semaglutide is compared to individual GLP-1 receptor agonists (Fig. 2). However, further research is necessary to establish causality and elucidate underlying mechanisms.

Notably, our findings regarding visual impairment associated with semaglutide contrast with the adverse event profiles reported in the pivotal phase 3 clinical trials for various semaglutide formulations. The SUSTAIN-6 trial reports a higher risk of diabetic retinopathy complications in patients receiving semaglutide [4], and while this finding was followed up in the review of the SUSTAIN 1–7 trials [5], the higher rate of diabetic retinopathy complications was attributed to a greater proportion of patients who had diabetic retinopathy at baseline. However, an analysis of cases without T2D as indication also reveals a trend for a higher rOR of vision impairment under semaglutide compared to orlistat and other GLP-1 receptor agonists (Additional file 1: Fig. S4, other medications excluded due to insufficient number of cases). Similarly, the PIONEER study for Rybelsus primarily highlighted nausea and diarrhea as the most frequent adverse events, without any reference to visual system complications [6]. Furthermore, the STEP trials for Wegovy also failed to report any significant ocular adverse events [7, 8]. The observed differences in visual adverse event patterns between Ozempic and Wegovy (both semaglutide) highlight the role of healthcare context in pharmacovigilance signals. T2D patients often undergo more structured ophthalmological monitoring, which may lead to different reporting patterns compared to patients prescribed semaglutide for obesity, despite overlapping metabolic profiles in both populations. However, this discrepancy between our post-marketing findings and the phase 3 trial results underscores

the importance of ongoing pharmacovigilance and real-world evidence studies in identifying rare but potentially serious adverse effects that may not be captured in pre-approval clinical trials.

Interestingly, the analysis for Wegovy showed less pronounced effects compared to other GLP-1 RAs. This discrepancy could potentially be attributed to the limited number of adverse event reports available at the time of this study, as it is a relatively newer medication, approved by the FDA in June 2021. This consistency across analyses strengthens our findings while highlighting areas for future research.

In our primary analysis, we focused on general visual impairment terms rather than specific retinopathy terminology, although we cannot exclude the possibility that some reported visual impairment cases might represent inaccurately coded retinopathy cases. To explore this further, we conducted a supplementary analysis to specifically examine retinopathy cases (defined as all cases with at least one of the following terms mentioned in the reactions list: "Diabetic Retinopathy", "Retinopathy", "Retinopathy Haemorrhagic", "Retinopathy Hypertensive", "Retinopathy Proliferative") (Additional file 1: Table S4). This supplementary analysis yielded similar patterns. Specifically, semaglutide demonstrated a higher risk of retinopathy compared to other included medications, although several drugs were excluded from this analysis due to insufficient report numbers (Additional file 1: Fig. S2). These findings suggest consistency in the safety signal across both general visual impairment and specific retinopathy terms.

As diabetes is frequently associated with diabetic retinopathy, this comorbidity represents a potential confounder in our analysis. While we could not directly assess this relationship due to incomplete comorbidity data in the database, we did compute the reporting odds ratio for visual impairment under semaglutide for reports where type 2 diabetes is listed under indications (388 with visual impairment, 9′055 in the comparator group) vs. reports where type 2 diabetes is not listed (29 with visual impairment, 2′086 in the comparator group). The rOR is 3.08 (95%CI 2.10 – 4.68), indeed indicating more frequent reporting of visual impairment in patients with T2D. For the "other GLP-1 receptor agonists" group (GLP-1 receptor agonists without semaglutide, Additional file 1: Table S2), the corresponding rOR is 1.88 (95%CI 1.33 – 2.74), i.e. we observe the same effect, but it is less pronounced, pointing towards an effect of semaglutide itself. Indeed, the rOR for visual impairment in patients with T2D under semaglutide vs. other GLP-1 receptor agonists is 2.20 (95%CI 1.97 – 2.46).

Several limitations to the analysis of FAERS data should be acknowledged. First, an inherent limitation of the database is the voluntary reporting structure, by various sources (including health care professional but also manufacturers and consumers). Second, in most cases, information about patients reported in FAERS data is incomplete, with data on detailed health status missing. This might further induce bias because of prescription preferences between classes due to relevant adverse event risk factors. There is also no information on the dose, mode, or duration of treatment, while data on concomitant treatments may be incomplete in the database. Moreover, bias due to differential population characteristics between treatments might be associated with differential reportability. Other external factors, including media coverage, may also exert their influence on the amount reported. In this regard, we wish to emphasize that our study design does not enable us to make causal inferences; therefore, results should be interpreted as associative and not causal. A key limitation of our ratio-based analysis approach is that medications with substantially different adverse event profiles may yield ratios that do not completely capture their true visual impairment risk. Additionally, our analysis cannot provide absolute risk estimates for vision impairment with semaglutide, which limits clinical interpretation. For context, the SUSTAIN-6 trial reported absolute rates of retinopathy complications of 3.0% with semaglutide versus 1.8% with placebo [4], with greater risk among patients with pre-existing retinopathy and rapid glycemic improvement [9]. Additionally, a meta-analysis of 23 randomized trials found that semaglutide was associated with an increased risk of diabetic retinopathy compared to placebo (risk ratio 1.24, 95% CI 1.03—1.50), with higher risks observed in patients aged 60 years or older and those with a diabetes duration of 10 years or more [10]. These findings highlight the need for future studies to assess the absolute clinical impact of this potential increased risk. While our ratio approach helps control for reporting bias and exposure differences, future studies incorporating absolute prescription volumes or patient-years of exposure data would be valuable to validate these findings. Finally, our analysis included all available FAERS data up to June 30, 2024, regardless of the time since drug approval. We acknowledge this may result in different reporting periods for newer versus established medications.

Although subject to these constraints, FAERS offers real-world data on clinically relevant adverse events from drugs. In conjunction with the cohort study by Hathaway et al. [1], our findings support a possible association of semaglutide use with increased risk related to vision problems.

Conclusions

In brief, our findings stress the importance of continued vigilance and further study of the ocular safety profile of semaglutide. Health providers should be aware that this is a possible risk and monitor for vision side effects in patients. Further prospective studies, randomized controlled clinical trials, and mechanistic investigations will be needed to elucidate the semaglutide–vision impairment relationship and its implications for treatment decisions.

Abbreviations

CI	Confidence interval
DPP-4	Dipeptidyl peptidase-4
FAERS	FDA Adverse Event Reporting System
FDA	U.S. Food and Drug Administration
GLP-1 RA	Glucagon-like peptide 1 receptor agonist
ION	Ischemic optic neuropathy
JAMA	Journal of the American Medical Association
NAION	Nonarteritic anterior ischemic optic neuropathy
PIONEER	Peptide Innovation for Early Diabetes Treatment (clinical trial)
rOR	Reporting odds ratio
SGLT2	Sodium-glucose transport protein 2
STEP	Semaglutide Treatment Effect in People with Obesity (clinical trial)
SUSTAIN	Semaglutide Unabated Sustainability in Treatment of Type 2 Diabetes (clinical trial)
T2D	Type 2 diabetes

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12916-025-04031-z.

Additional file 1: Methods, Table S1–S5, Figure S1-S4. Methods. Table S1—Number of reports per treatment group by indication. Table S2—Treatment groups and search terms. Table S3—Reaction filter list. Table S4—Number of reports with at least one retinopathy term listed as reaction. Table S5—Monotherapy reports with and without visual impairment for individual GLP-1 receptor agonists. Figure S1—Number of included reports by country where the event occurred. Figure S2—Cases with at least one retinopathy-associated term mentioned in the reactions list showed an association between semaglutide use and retinopathy risk. Figure S3—Semaglutide active ingredient drugs Ozempic, Rybelsus and Wegovy are associated with visual impairment or optic neuropathy compared to other substances, except topiramate. Figure S4—In cases without T2D as indication, the trend for semaglutide association with visual impairment or optic neuropathy remains for orlistat and other GLP-1 receptor agonists.

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Not applicable.

Use of artificial intelligence

ChatGPT (version 3.5, OpenAI) and Claude (version 3.5 Sonnet, Anthropic) AI language models were used on July 17 2024, for text improvement and refinement.

Authors' contributions

M.M., S.M., and R.H. conceived and designed the study, and acquired, analyzed, and interpreted the data. M.M. and S.M. performed the statistical analysis. M.M. and S.M. wrote the main manuscript text. H.H. contributed to the critical revision of the manuscript for important intellectual content. All authors reviewed the manuscript. S.M. and R.H. supervised the study.

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Data availability

Data are publicly available online via the FDA's adverse event reporting system website.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

Massy M reports no competing interests. Marti S reports no competing interests. Hammer H received research support and travel grants within the last 5 years from Biogen, Merck, Roche & Bristol Myers Squibb, Teva, Johnson&Johnson, Novartis. All not related to that work. Hoepner R received speaker/advisor honorary from Merck, Novartis, Roche, Biogen, Alexion, Sanofi, Janssen, Bristol-Myers Squibb, Teva/Mepha and Almirall. He received research support within the last 5 years from Roche, Merck, Sanofi, Biogen, Chiesi, and Bristol-Myers Squibb. He also received research grants from the Swiss MS Society, the SITEM Insel Support Fund and is a member of the Advisory Board of the Swiss and International MS Society. He also serves as deputy editor in chief for Journal of Central Nervous System disease and is part of the ECTRIMS Young Investigator Committee.

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