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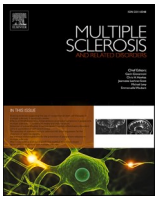

Experiences of persons with multiple sclerosis with the Covid-19 vaccination: A cross-sectional study of the Swiss Multiple Sclerosis Registry

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ABSTRACT

Background: Despite strong recommendations for coronavirus disease 2019 (Covid-19) vaccination by multiple sclerosis (MS) organizations, some persons with MS (pwMS) remain vaccine hesitant. The Swiss MS Registry conducted a survey to explore Covid-19 vaccine hesitancy, self-reported side effects and changes in MS symptoms following vaccination in adult pwMS.

Methods: Self-reported data were analyzed cross-sectionally. Multivariable logistic regression was used to explore participant characteristics associated with Covid-19 vaccine hesitancy.

Results: Of 849 respondents, 73 (8.6%) were unvaccinated. Hesitation to vaccinate was most often a personal preference ($N = 42$, 57.53%). Factors negatively associated with vaccine hesitancy included older age (OR = 0.97 per year, 95% CI [0.94, 0.99]) and regularly seeing healthcare professionals (OR = 0.25, 95% CI [0.07, 0.85]). A history of confirmed Covid-19 infection (OR = 3.38, 95% CI [1.69, 6.77]) and being underweight (OR = 4.50, 95% CI [1.52, 13.36]) were positively associated with vaccine hesitancy. Of 768 participants who provided information, 320 (41.2%) and 351 (45.2%) reported vaccination side effects after the first and second vaccinations, respectively. Changes in MS symptoms were reported by 49 (6.3%) participants after the first and 67 (9.0%) participants after the second vaccination, and were most often described as increased or new-onset fatigue ($N = 17/49$ (34.7%) after the first and $N = 21/67$ (31.3%) after the second dose).

Conclusions: Covid-19 vaccine hesitancy was low among surveyed pwMS. The risk of vaccine hesitancy was higher among younger pwMS, those with a history of Covid-19 infection, and those without regular contact with healthcare professionals.

1. Introduction

Vaccination against severe acute respiratory syndrome virus 2 (Sars-CoV-2) and coronavirus disease 2019 (Covid-19) continues to be recommended by authorities worldwide. Booster vaccination are encouraged for individuals with underlying medical conditions, including chronic diseases and use of immunosuppressive or immunomodulatory therapies, which is often the case in persons with multiple sclerosis (MS) (Mbaeyi et al., 2021).

Although early publications have described cases of relapses in persons with multiple sclerosis (pwMS) after Covid-19 vaccination (Nistri et al., 2021; Maniscalco et al., 2021) and a possible reduction in vaccine efficacy in persons receiving certain disease modifying therapies (DMTs) (Witman Tsur et al., 2021), Covid-19 vaccines have been shown

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to be safe and effective in pwMS (Cabreira et al., 2021; Dreyer-Alster et al., 2022; Achiron et al., 2021). Willingness to be vaccinated with the Covid-19 vaccine was very high in pwMS, ranging from 80% to 90% (Huang et al., 2021; Ehde et al., 2021; Serrazina et al., 2021). The strong recommendations by MS organizations (Swiss MS Society, 2021) and state agencies for Covid-19 vaccination have likely contributed to the lower vaccine hesitancy in pwMS compared to the general population (Ehde et al., 2021; Arena and Kister, 2022). The initial vaccine hesitancy in pwMS was reduced as more information became available (Huang et al., 2021; Ehde et al., 2021), underscoring the importance of adequate information and knowledge dissemination. Older age and higher education level were among the factors associated with both higher willingness to receive Covid-19 vaccination and higher uptake, while no MS-related factors were associated with vaccine hesitancy (Ehde et al., 2021; Marrie et al., 2022). Safety concerns and lack of information were among the main reasons for vaccine hesitancy in both general population and pwMS (Boziki et al., 2021; Xiang et al., 2021; Robinson et al., 2021), while pwMS also had concerns related to MS itself, such as fear of reduced efficacy of DMTs (Nabavi et al., 2022).

We conducted a retrospective, cross-sectional, nationwide study of Covid-19 vaccination uptake and hesitancy, along with self-reported side effects and changes in MS symptoms after vaccination, using the data from the Swiss MS Registry (SMSR). We descriptively compared vaccinated and unvaccinated SMSR participants, as well as those who reported vaccination side effects or changes in MS symptoms with those who did not. Finally, we explored factors associated with Covid-19 vaccine hesitancy.

2. Methods

2.1. Data source

The present study used data from the SMSR, an ongoing observational study of adult pwMS living or receiving treatment in Switzerland. The SMSR collects self-reported information from participants using online and paper questionnaires. Participation in the SMSR is voluntary and only possible with a signed informed consent form and confirmation of MS diagnosis. The SMSR was approved by the Ethics Committee of the Canton of Zurich (PB-2016–00894; BASEC–NR 2019–01027). Further details are provided elsewhere (Puhan et al., 2018; Steinemann et al., 2018).

For this study, we used data from the brief survey released in late November 2021 that focused on Covid-19 vaccination. We analyzed data on vaccination status, reasons for vaccine hesitancy, use of medical advice prior to vaccination, self-reported vaccination side effects and changes in MS symptoms following the vaccination, and other MS-, Covid-19- and vaccination-related information collected up to May 1st, 2022. We also used data from previous SMSR questionnaires, such as self-reported presence of comorbidities, education level, and work status.

All active SMSR participants received the invitation to participate in the survey. Participants who did not respond to the invitation or did not report their vaccination status were classified as nonrespondents and were not analyzed. All respondents were included in the full sample analysis, while participants for whom data on all variables of interest were available were included in the complete cases analysis.

2.2. Outcome variables

The present study had three primary outcomes of interest: vaccine hesitancy, self-reported vaccination side effects and self-reported changes in MS symptoms following vaccination.

In defining vaccine hesitancy, we were guided by the Strategic Advisory Group of Experts Working Group on Vaccine Hesitancy, which defined vaccine hesitancy as a delay in acceptance or refusal of vaccination despite availability of vaccination services (MacDonald, 2015). Since vaccination had been widely available for months before survey dissemination and the percentage of vaccinated individuals in Switzerland has remained virtually unchanged from the end of 2021 until now (Swiss Federal Office of Public Health FOPH, 2023), we considered nonvaccination at the time of data collection equal to vaccine hesitancy, unless medical advice, contraindication, or inability to get a vaccination appointment were reported. Vaccine hesitancy was assessed based on a multiple-choice question addressing prior Covid-19 vaccination with at least one vaccine dose and was analyzed as a dichotomous variable (yes or no). Participants who indicated they were unvaccinated were asked about their reasons for hesitation and instructed to skip other vaccine-related questions. Thus, questions described below were available only to participants who reported vaccination.

Self-reported vaccination side effects were queried in two multiple-choice questions, each referring to the specific vaccine dose and were analyzed as dichotomous variables (yes or no, with the multiple-choice answer "Yes, but I am unsure they are related to the vaccine" regarded as yes). Further multiple-choice questions about the vaccination side effects concerned the type of the side effects, onset of symptoms, diagnosis, and persistence, and were used for descriptive analysis. Information on symptom duration was not systematically collected. We calculated and reported the median time elapsed between vaccination and questionnaire completion for participants who were not yet recovered at the time of questionnaire completion. No questions specifically addressed the third vaccine dose.

Self-reported changes in MS symptoms after vaccination referred to the reoccurrence, amplification, or new MS symptoms and were assessed per vaccine dose as dichotomous variables (yes or no). Participants could describe the symptoms in an open text field. Information on symptom duration or resolution was not systematically collected.

Questions used in this study are available in the **Supplementary material**.

2.3. Variables of interest

The following sociodemographic characteristics were included in the descriptive analysis and considered for the logistic regression models: age, sex (female or male), Swiss citizenship (yes or no), highest education level (university degree or other), employment (employed, not working, retired or receiving disability pension), and marital status (married and in registered partnership or not). Health-related factors, such as a history of positive polymerase chain reaction (PCR) or rapid antigen test for Covid-19 infection (yes or no), Body Mass Index (BMI, categorized in underweight, normal weight, preobesity and obesity), smoking (previously, now or never), self-reported presence of cancer, type 2 diabetes (T2D), hypertension, cardiac diseases, depression (yes or no) or at least one of those (yes or no) were also considered. The following MS-related variables were analyzed: duration of MS since the onset of symptoms in years, self-reported MS type (relapsing remitting MS (RRMS), primary progressive MS (PPMS), secondary progressive MS (SPMS), clinically isolated syndrome (CIS) and transition between RRMS and SPMS), use of DMTs in the year prior to the survey (no DMTs, anti-CD20 B cell depleting DMTs or any other DMT) and self-reported disability status scale (SRDSS) categorized as mild, moderate, and severe gait disability (Kaufmann et al., 2020). We cross-checked the MS type with the information provided in the previous SMSR questionnaires for consistency. We reviewed the open text box following the multiple-choice question on MS type for participants who reported transition stage. If the information provided indicated a transition between RRMS and SPMS, the participants were classified accordingly (e.g., "RRMS to SPMS, not yet confirmed" or "Last relapse in 2016. Before and now again, secondary progressive is assumed"). Finally, we looked at the use of the healthcare system, i.e., regularly seeing a primary care physician or neurologist (no regular visits, visits to the primary care physician only, to the neurologist only and visits to both primary care

physician and neurologist) and whether they used complementary medicine covered by the health insurers in Switzerland (acupuncture, osteopathy, traditional Chinese medicine, homeopathy, and natural healing, yes or no).

2.4. Statistical analysis

To be considered for the analysis participants had to answer the question on vaccination status, as well as to have available data on age, sex and MS type. Descriptive analyses included calculation of frequencies for the outcomes of interest. Frequencies and medians of sociodemographic, MS- and health-related characteristics were calculated and compared between vaccinated and unvaccinated participants, respectively those with and without self-reported changes in MS symptoms or vaccination side effects. Univariable and multivariable logistic regression was used to explore the associations of variables of interest and vaccine hesitancy. Age, sex, and MS type were included in the multivariable model as confounders. Other variables were added sequentially and maintained in the model if the Akaike Information Criterion (AIC) decreased by 2 or more units, following the rule of thumb (Burnham and Anderson, 2004). Variable selection was performed on the subset of complete cases. We then used multiple imputation to create and analyze 20 multiply imputed datasets, and the regression estimates from the imputed, full sample analysis were shown for comparison. All analyses were performed using R (version 4.2.0) and R Studio (version 2022.02.3 + 492) software and the following packages: tidyverse, performance, mice, table 1 (R Core Team, 2013).

3. Results

2263 registered SMSR participants received the invitation to the survey. Of those invited, 1414 pwMS did not respond (Fig. 1). **Supplementary material** includes a descriptive comparison between respondents and nonrespondents based on the SMSR baseline data.

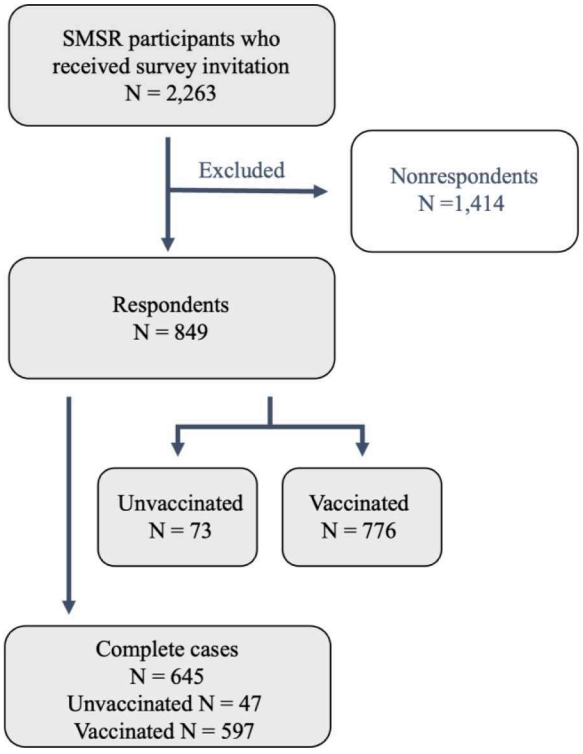

Fig. 1. Study design flowchart. The selection of variables for the multivariable model of the association between the variables of interest and nonvaccination was based on the subset of **complete cases**. Multiple imputation for the said model was performed using the full sample of all **respondents**. Vaccination counseling, self-reported vaccination side effects and changes in MS after vaccination were examined in the sample of **vaccinated** participants.

3.1. Vaccination status and vaccine hesitancy

Data from 849 SMSR participants were included in the analysis. Four (0.4%) participants who answered "I prefer not to answer that question" to the multiple-choice question on vaccination status were classified as unvaccinated. Thus, 73 (8.6%) of the respondents were unvaccinated. Table 1 shows the descriptive comparison between vaccinated and unvaccinated respondents.

Of 73 unvaccinated respondents, 25 (34.2%) named one, eight (11.0%) named two and 35 (47.9%) named three or more reasons to remain unvaccinated, while five (6.8%) did not answer the question. Personal preference was the most often cited reason to remain unvaccinated ($N = 42$, 57.53%) (Fig. 2). Examples of other reasons to remain unvaccinated provided in the open text field included ongoing or recent ocrelizumab treatment, pregnancy, and suspected presence of antibodies from previous Covid-19 infection. Although there were individuals who reported not being able to get a vaccination appointment or currently being treated with ocrelizumab, these participants had also provided other reasons for not vaccinating that clearly indicated vaccine hesitancy, such as personal preference. Therefore, all unvaccinated participants included in the analysis were classified as vaccine hesitant.

On univariable logistic regression analysis, age, MS type, BMI, history of positive Covid-19 PCR or rapid antigen test and contact with healthcare professionals were associated with Covid-19 vaccine hesitancy (Table 2). Multivariable logistic regression analysis of the subset of complete cases revealed that participants who reported testing positive for Covid-19 infection were more than three times more likely to be vaccine hesitant than those who did not have positive PCR or rapid antigen Covid-19 test (OR = 3.38, 95% CI [1.69, 6.77]). Furthermore, participants who regularly visited their primary care physician and neurologist were around four times less likely to be vaccine hesitant compared to the participants who had no regular contact with the healthcare professionals (OR = 0.25, 95% CI [0.07, 0.85]). Underweight participants had more than fourfold higher chances of being vaccine hesitant compared to the participants with normal weight (OR = 4.50, 95% CI [1.52, 13.36]). Finally, likelihood of vaccine hesitancy dropped by 3% with each year of age (OR = 0.97, 95% CI [0.94, 0.99]. Imputed full sample analysis yielded similar findings (Table 2).

Supplementary material shows univariable and multivariable logistic regression models with vaccination uptake coded as an outcome of interest.

3.2. Vaccination uptake and counselling

Out of the respondents who received Covid-19 vaccination, 18 (2.3%) received one dose, 293 (37.8%) received two doses, and 461 (59.4%) received three doses. Data was missing for four (0.5%) participants. The majority of participants received the mRNA-1273 Covid-19 vaccine ($N = 440$, 56.7%), 328 (42.3%) received BNT162b2 mRNA vaccine and three (0.4%) participants received the Ad26.COV2.S vaccine. Data was missing for five (6.4%) participants. The majority of participants who received mRNA-1273 and BNT162b2 vaccines received three doses (56.0% and 65.6%, respectively).

769 vaccinated participants indicated whether they had received medical advice about the possible vaccination side effects. More than one-third ($N = 286$, 36.86%) reported that they had received medical advice. The majority of them indicated in an open text field that they had consulted a healthcare professional before vaccination ($N = 165$, 56.3%), most frequently a neurologist ($N = 131$, 45.8%). A descriptive comparison of participants who received medical advice with those who did not is provided in the **Supplementary material**.

Table 1
Comparison of the vaccinated and unvaccinated respondents to the third Covid-19 related SMSR survey.

	Vaccinated (*N* = 776)	Unvaccinated (*N* = 73)	Total (*N* = 849)
Female sex, N (%)	562 (72.4%)	62 (84.9%)	624 (73.5%)
Age, median [IQR]	52.0 [42.0, 60.0]	48.0 [38.0, 56.0]	52.0 [42.0, 60.0]
Swiss citizenship, N (%)	658 (84.8%)	61 (83.6%)	719 (84.7%)
Missing	44 (5.7%)	5 (6.8%)	49 (5.8%)
Civilian status, N (%)			
Married	414 (53.4%)	31 (42.5%)	445 (52.4%)
Unmarried	303 (39.0%)	35 (47.9%)	338 (39.8%)
Missing	59 (7.6%)	7 (9.6%)	66 (7.8%)
Living situation, N (%)			
Residential home	3 (0.4%)	0	3 (0.4%)
Family	220 (28.4%)	20 (27.4%)	240 (28.3%)
Shared flat	13 (1.7%)	0	13 (1.5%)
Living alone	163 (21.0%)	22 (30.1%)	185 (21.8%)
Parents	8 (1.0%)	2 (2.7%)	10 (1.2%)
Spouse / Partner	319 (41.1%)	22 (30.1%)	341 (40.2%)
Missing	50 (6.4%)	7 (9.6%)	57 (6.7%)
Highest education level, N (%)			
University degree	216 (27.8%)	14 (19.2%)	230 (27.1%)
Other	499 (64.3%)	50 (68.5%)	549 (64.7%)
Missing	61 (7.9%)	9 (12.3%)	70 (8.2%)
Working situation			
Employed	450 (58.0%)	42 (57.5%)	492 (58.0%)
Not working	82 (10.6%)	12 (16.4%)	94 (11.1%)
Retired	88 (11.3%)	5 (6.8%)	93 (11.0%)
Receiving disability insurance	117 (15.1%)	7 (9.6%)	124 (14.6%)
Missing	39 (5.0%)	7 (9.6%)	46 (5.4%)
MS type, N (%)			
CIS	11 (1.4%)	4 (5.5%)	15 (1.8%)
PPMS	88 (11.3%)	6 (8.2%)	94 (11.1%)
RRMS	496 (63.9%)	50 (68.5%)	546 (64.3%)
SPMS	144 (18.6%)	12 (16.4%)	156 (18.4%)
Transition	33 (4.3%)	1 (1.4%)	34 (4.0%)
Missing	4 (0.5%)	0	4 (0.5%)
MS duration, median [IQR]	15.0 [8.9, 23.0]	16.0 [7.5, 22.0]	15.0 [8.0, 23.0]
Missing	40 (5.2%)	6 (8.2%)	46 (5.4%)
Gait disability, N (%)			
None to mild	516 (66.5%)	55 (75.3%)	571 (67.3%)
Moderate	168 (21.6%)	7 (9.6%)	175 (20.6%)
Severe	51 (6.6%)	4 (5.5%)	55 (6.5%)
Missing	41 (5.3%)	7 (9.6%)	48 (5.7%)
Use of DMTs in the last year, N (%)			
Anti-CD20 B cells depleting	149 (19.2%)	9 (12.3%)	158 (18.6%)
Any other DMT	410 (52.8%)	29 (39.7%)	439 (51.7%)
No DMTs	161 (20.7%)	23 (31.5%)	184 (21.7%)
Missing	56 (7.2%)	12 (16.4%)	68 (8.0%)
Use of complementary medicine, N (%)	134 (17.3%)	18 (24.7%)	152 (17.9%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Homeopathy, N (%)	38 (4.9%)	9 (12.3%)	47 (5.5%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Osteopathy, N (%)	31 (4.0%)	4 (5.5%)	35 (4.1%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Traditional Chinese medicine, N (%)	28 (3.6%)	2 (2.7%)	30 (3.5%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Natural healing, N (%)	60 (7.7%)	13 (17.8%)	73 (8.6%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Acupuncture, N (%)	31 (4.0%)	3 (4.1%)	34 (4.0%)
Missing	44 (5.7%)	8 (11.0%)	52 (6.1%)
Smoking, N (%)			
Never	322 (41.5%)	26 (35.6%)	348 (41.0%)
Now	139 (17.9%)	15 (20.5%)	154 (18.1%)
Previously	267 (34.4%)	23 (31.5%)	290 (34.2%)
Missing	48 (6.2%)	9 (12.3%)	57 (6.7%)
BMI, N (%)			
Underweight	34 (4.4%)	6 (8.2%)	40 (4.7%)
Normal weight	359 (46.3%)	39 (53.4%)	398 (46.9%)
Preobesity	201 (25.9%)	10 (13.7%)	211 (24.9%)
Obesity I-III	114 (14.7%)	7 (9.6%)	121 (14.3%)
Missing	68 (8.8%)	11 (15.1%)	79 (9.3%)
Comorbidity present, N (%)	524 (67.5%)	47 (64.4%)	571 (67.3%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Cancer, N (%)	28 (3.6%)	1 (1.4%)	29 (3.4%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Type 2 Diabetes, N (%)	12 (1.5%)	0 (0%)	12 (1.4%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Hypertension, N (%)	110 (14.2%)	3 (4.1%)	113 (13.3%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Cardiac problems, N (%)	28 (3.6%)	1 (1.4%)	29 (3.4%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Depression	93 (12.0%)	7 (9.6%)	100 (11.8%)
Missing	41 (5.3%)	6 (8.2%)	47 (5.5%)
Regular visits to HCP, N (%)			
No regular visits	30 (3.9%)	6 (8.2%)	36 (4.2%)
Primary care physician only	32 (4.1%)	5 (6.8%)	37 (4.4%)
Neurologist only	203 (26.2%)	27 (37.0%)	230 (27.1%)
Primary care physician and neurologist	475 (61.2%)	29 (39.7%)	504 (59.4%)
Missing	36 (4.6%)	6 (8.2%)	42 (4.9%)
History of positive Covid-19 test, N (%)			
Yes	106 (13.7%)	25 (34.2%)	131 (15.4%)
No	666 (85.8%)	48 (65.8%)	714 (84.1%)
Missing	4 (0.5%)	0	4 (0.5%)

MS – multiple sclerosis, CIS – clinically isolated syndrome, PPMS – primary progressive multiple sclerosis, SPMS – secondary progressive multiple sclerosis, DMT – disease modifying therapy, BMI – body mass index, HCP – healthcare practitioner.

3.3. Self-reported vaccination side effects

Of the 768 participants who answered the question, 320 (41.7%) reported experiencing side effects after the first vaccine dose. Thereof 91 (28.5%) participants experienced one, 76 (23.8%) experienced two, and 152 (47.7%) experienced three or more side effects. The most commonly reported side effects were symptoms at the injection site (N = 226, 70.6%), feeling tired (N = 168, 52.5%), and headache (N = 128, 40.0%). More participants reported side effects after second Covid-19 vaccine

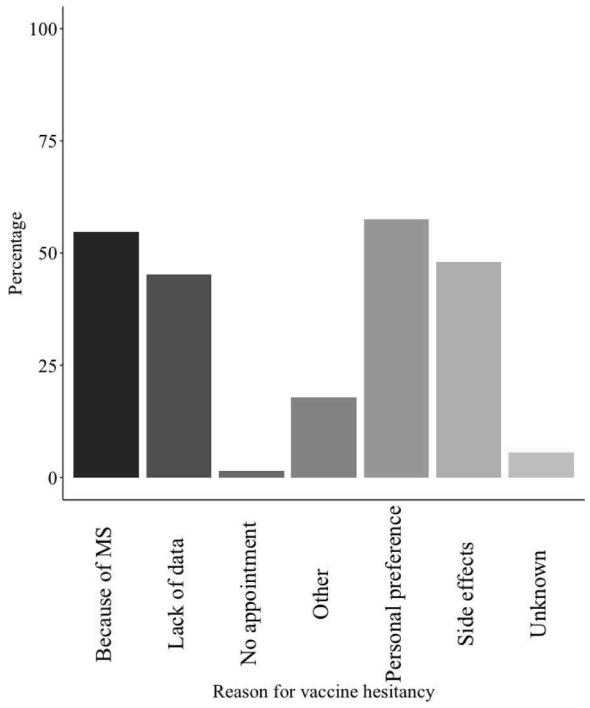

Fig. 2. Frequency of reported reasons for vaccine hesitancy based on the multiple-choice question.

dose ($N = 351/743$, 47.2%). After the second dose of a Covid-19 vaccine, feeling tired was the most commonly reported side effect, with 239 (68.1%) participants reporting it (Fig. 3). The question was not answered by 33 (4.3%) vaccinated participants, three of whom had received a single dosed Ad26.COV2.S vaccine.

Table 3 shows descriptive comparison of the participants who did and did not report side effects after vaccination with the first and second doses of Covid-19 vaccine.

Out of 320 participants who reported side effects of the first vaccine dose, 139 (43.4%) reported symptom onset from three to 11 hours after vaccination. Similarly, 151 out of 351 (43.0%) participants experienced side effects three to 11 hours after the administration of the second vaccine dose. A formal diagnosis of vaccination side effects by a healthcare professional was received by 64 (20.0%) participants after the first dose of vaccine and 55 (15.7%) participants after the second vaccine dose. After a median [interquartile range] of 250.5 [222.2, 312.0] days since the first vaccination, 11 (3.4%) participants reported that they were still experiencing vaccination side effects at the time of data collection. Nine (2.6%) participants reported not being recovered after the second dose, and among them were five who had also reported not being recovered after the first dose.

3.4. Self-reported changes in MS symptoms after Covid-19 vaccination

Of the 727 participants who answered the multiple-choice question about changes in MS symptoms after the first vaccine dose, 49 (6.3%) reported changes. 9.0% (67 out of 710) reported changes after the second dose. Based on input in the free-text field, new-onset or increased fatigue was the most common change in MS symptoms after both the first ($N = 17/49$, 34.7%) and the second dose ($N = 21/67$, 31.3%), followed by amplified gait disturbances ($N = 11$, 22.4% and $N = 11$, 16.4% after the first and second doses, respectively). Other mentions included spasticity, cognitive disturbances and altered sensation. Participants also described resolution of symptoms. Table 4 provides comparison between participants who reported changes in MS symptoms after vaccination and those who did not.

Table 2
Vaccine hesitancy: univariable and multivariable logistic regression derived odds ratios and corresponding 95% confidence intervals.

	Complete case analysis		Imputed full sample analysis
	Univariable OR [95% confidence interval]	Multivariable OR [95% confidence interval]	Multivariable OR [95% confidence interval]
Female sex	1.67 [0.79, 3.52]	1.48 [0.65, 3.37]	1.98 [0.98, 4.04]
Age in years	**0.96 [0.94, 0.99]**	**0.97 [0.94, 0.99]**	0.98 [0.95, 1.00]
Citizenship		–	–
Swiss	1.46 [0.44, 4.86]		
Other than Swiss	Ref.		
Civilian status		–	–
Married	Ref.		
Unmarried	1.47 [0.81, 2.65]		
Highest education level		–	–
University degree	0.74 [0.38, 1.46]		
Other	Ref.		
Working situation		–	–
Employed	Ref.		
Not working	1.52 [0.64, 3.60]		
Retired	0.50 [0.15, 1.68]		
Receiving disability insurance	0.71 [0.29, 1.74]		
MS type			
CIS	**4.44 [1.12, 17.55]**	4.84 [0.92, 25.42]	**4.27 [1.15, 15.84]**
PPMS	0.76 [0.26, 2.23]	1.13 [0.35, 3.64]	0.94 [0.36, 2.41]
RRMS	Ref.	Ref.	Ref.
SPMS	0.77 [0.33, 1.78]	1.10 [0.40, 3.05]	1.17 [0.54, 2.52]
Transition	0.42 [0.06, 3.21]	0.33 [0.04, 2.76]	0.27 [0.03, 2.18]
MS duration		–	–
0–9 years	Ref.		
10–19 years	0.69 [0.34, 1.42]		
20–29 years	1.02 [0.48, 2.18]		
30+ years	0.40 [0.11, 1.38]		
Gait disability		–	–
None to mild	Ref.		
Moderate	0.50 [0.21, 1.22]		
Severe	0.64 [0.15, 2.75]		
Use of DMTs in the last year		–	–
No DMTs	Ref.		
Anti-CD20 B cells depleting	0.43 [0.18, 1.06]		
Any other DMT	0.52 [0.27, 1.01]		
Use of complementary medicine		–	–
No	Ref.		
Yes	1.86 [0.97, 3.59]		
Smoking		–	–
Never	Ref.		
Now	1.15 [0.54, 2.45]		

(*continued on next page*)

Table 2 (*continued*)

	Complete case analysis		Imputed full sample analysis
	Univariable OR [95% confidence interval]	Multivariable OR [95% confidence interval]	Multivariable OR [95% confidence interval]
Previously	0.83 [0.35, 1.97]		
BMI			
Underweight	**2.77 [1.04, 7.34]**	**4.50 [1.52, 13.36]**	2.06 [0.74, 5.73]
Normal weight	Ref.	Ref.	Ref.
Preobesity	0.46 [0.20, 1.07]	0.46 [0.19, 1.12]	**0.41 [0.19, 0.86]**
Obesity I-III	0.83 [0.35, 1.97]	0.95 [0.38, 2.37]	0.6 [0.25, 1.43]
Comorbidity present		–	–
No	Ref.		
Yes	1.88 [0.86, 4.10]		
Cancer		–	–
No	Ref.		
Yes	0.58 [0.08, 4.43]		
Type 2 Diabetes		–	–
No	Ref.		
Yes	0.00 [0.00, Inf]		
Hypertension		**–**	–
No	Ref.		
Yes	0.35 [0.11, 1.14]		
Cardiac problems		–	–
No	Ref.		
Yes	0.51 [0.07, 3.84]		
Depression		–	–
No	Ref.		
Yes	0.76 [0.29, 1.98]		
Regular visits to HCP			
No regular visits	Ref.	Ref.	Ref.
Primary care physician only	0.62 [0.15, 2.59]	1.15 [0.23, 5.88]	1.53 [0.37, 6.23]
Neurologist only	0.50 [0.17, 1.48]	0.54 [0.15, 1.86]	0.80 [0.28, 2.26]
Primary care physician and neurologist	**0.19 [0.06, 0.56]**	**0.25 [0.07, 0.85]**	0.42 [0.15, 1.19]
History of positive Covid-19 test			
No	Ref.	Ref.	Ref.
Yes	**3.60 [1.90, 6.80]**	**3.38 [1.69, 6.77]**	3.34 [1.88, 5.93]

MS – multiple sclerosis, CIS – clinically isolated syndrome, PPMS – primary progressive multiple sclerosis, SPMS – secondary progressive multiple sclerosis, DMT – disease modifying therapy, BMI – body mass index, HCP – healthcare practitioner.

4. Discussion

We cross-sectionally explored Covid-19 vaccination in adult pwMS in Switzerland using self-reported data of 849 SMSR participants. Fewer than 10% of respondents were unvaccinated, primarily due to personal preference. Increasing age and regular visits to both primary care physician and neurologist were negatively associated with vaccine hesitancy, while a history of positive Covid-19 test and being underweight were positively associated. Fewer than half of the vaccinated participants reported vaccination side effects, most commonly injection site symptoms, tiredness, and headache. Less than 10% of surveyed participants reported changes in MS symptoms after vaccination, most often new-onset or increased fatigue.

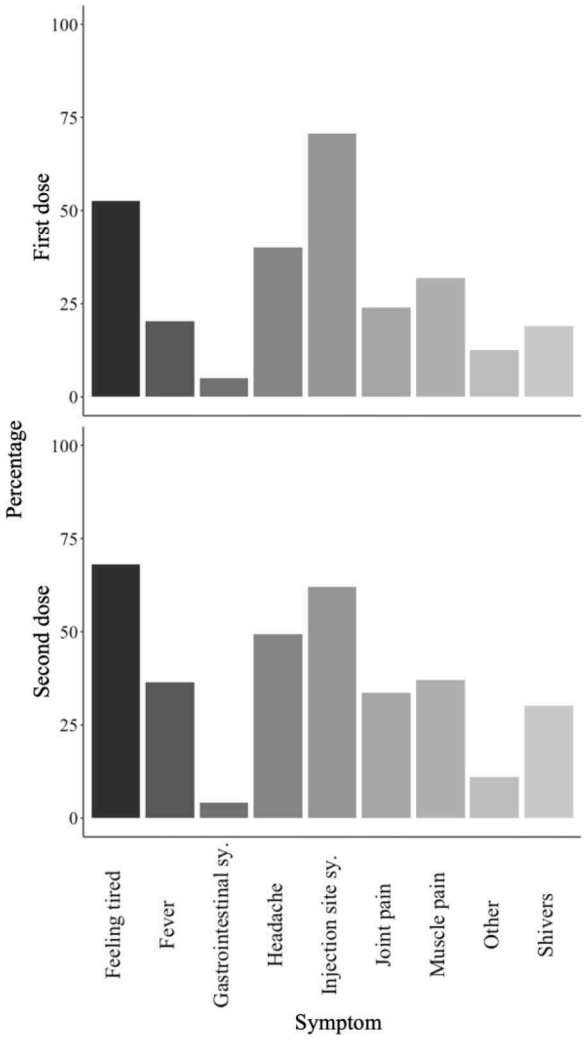

Fig. 3. Frequency of reported perceived side effects after the first and second Covid-19 vaccine.

As of August 2022, almost 70% of the Swiss general population has received at least one dose of a Covid-19 vaccine (Swiss Federal Office of Public Health FOPH, 2022). It was previously found that Swiss persons with chronic diseases were more likely to get vaccinated (Heiniger et al., 2022), while the UK MS Register showed that 94.4% of the surveyed pwMS expressed willingness to receive Covid-19 vaccination (Huang et al., 2021). Other studies in pwMS found high willingness (Boziki et al., 2021), high vaccination rates (Marrie et al., 2022; Allen-Philbey et al., 2022) and increasing readiness to receive a Covid-19 vaccine during 2020 and 2021 (Huang et al., 2021; Ehde et al., 2021). Thus, a markedly low vaccine hesitancy in our study was expected. Vaccine-hesitant participants in our study expressed similar concerns about Covid-19 vaccines to those previously found in pwMS, such as safety or efficacy doubts (Marrie et al., 2022; Ciotti et al., 2022).

Two studies highlighted sufficient information and communication with MS clinicians as a determining factor in the vaccination dilemma (Huang et al., 2021; Panisset et al., 2022). Regular visits to both the neurologist and the primary care physician were associated with a lower risk of vaccine hesitancy in our study, possibly indicating that information received from the primary care physician and the neurologist complement each other and have a critical influence on the decision to vaccinate. Higher education level, socioeconomic status, older age and presence of comorbidities were previously found associated with Covid-19 vaccination uptake in pwMS (Marrie et al., 2022; Ciotti et al., 2022). However, while older age was associated with lower vaccine

Table 3
Comparison of the participants who did and did not experience side effects following vaccination with the first and second dose of a Covid-19 vaccine.

	First Covid-19 vaccine dose		Second Covid-19 vaccine dose	
	No side effects (*N* = 448)	Side effects (*N* = 320)	No side effects (*N* = 392)	Side effects (*N* = 351)
Female sex, N (%)	305 (68.1%)	252 (78.8%)	273 (69.6%)	266 (75.8%)
Age, median [IQR]	53.0 [44.0, 61.0]	51.5 [41.0, 58.0]	54.0 [44.0, 62.0]	51.0 [42.0, 58.0]
Swiss citizenship, N (%)	372 (83.0%)	279 (87.2%)	323 (82.4%)	306 (87.2%)
Missing	26 (5.8%)	18 (5.6%)	24 (6.1%)	17 (4.8%)
Civilian status, N (%)				
Married	251 (56.0%)	158 (49.4%)	204 (52.0%)	189 (53.8%)
Unmarried	164 (36.6%)	137 (42.8%)	151 (38.5%)	143 (40.7%)
Missing	33 (7.4%)	25 (7.8%)	37 (9.4%)	19 (5.4%)
University degree	117 (26.1%)	98 (30.6%)	100 (25.5%)	108 (30.8%)
Missing	39 (8.7%)	22 (6.9%)	38 (9.7%)	19 (5.4%)
Working situation, N (%)				
Employed	260 (58.0%)	186 (58.1%)	215 (54.8%)	215 (61.3%)
Not working	37 (8.3%)	44 (13.8%)	38 (9.7%)	41 (11.7%)
Retired	58 (12.9%)	28 (8.8%)	58 (14.8%)	26 (7.4%)
Receiving disability insurance	70 (15.6%)	46 (14.4%)	59 (15.1%)	55 (15.7%)
Missing	23 (5.1%)	16 (5.0%)	22 (5.6%)	14 (4.0%)
MS type, N (%)				
CIS	6 (1.3%)	5 (1.6%)	6 (1.5%)	4 (1.1%)
PPMS	284 (63.4%)	212 (66.3%)	251 (64.0%)	228 (65.0%)
RRMS	58 (12.9%)	27 (8.4%)	54 (13.8%)	30 (8.5%)
SPMS	82 (18.3%)	61 (19.1%)	65 (16.6%)	72 (20.5%)
Transition	18 (4.0%)	15 (4.7%)	16 (4.1%)	17 (4.8%)
MS duration	15.0 [0, 56.0]	15.0 [0, 53.0]	15.0 [8.0, 24.0]	14.0 [8.0, 22.0]
Missing	23 (5.1%)	17 (5.3%)	23 (5.9%)	15 (4.3%)
Gait disability, N (%)				
None to mild	284 (63.4%)	229 (71.6%)	243 (62.0%)	254 (72.4%)
Moderate	108 (24.1%)	57 (17.8%)	99 (25.3%)	61 (17.4%)
Severe	34 (7.6%)	16 (5.0%)	28 (7.1%)	20 (5.7%)
Missing	22 (4.9%)	18 (5.6%)	22 (5.6%)	16 (4.6%)
Use of DMTs in the last year, N (%)				
No DMTs	89 (19.9%)	68 (21.3%)	76 (19.4%)	71 (20.2%)
Anti-CD20 B cells depleting	98 (21.9%)	72 (22.5%)	71 (18.1%)	96 (27.4%)
Any other DMT	231 (51.6%)	155 (48.4%)	219 (55.9%)	155 (44.2%)
Missing	30 (6.7%)	25 (7.8%)	26 (6.6%)	29 (8.3%)
Use of complementary medicine, N (%)	59 (13.2%)	73 (22.8%)	54 (13.8%)	70 (19.9%)
Missing	25 (5.6%)	19 (5.9%)	27 (6.9%)	14 (4.0%)
Smoking, N (%)				
Never	180 (40.2%)	141 (44.1%)	154 (39.3%)	156 (44.4%)
Now	82 (18.3%)	56 (17.5%)	71 (18.1%)	61 (17.4%)
Previously	156 (34.8%)	106 (33.1%)	138 (35.2%)	118 (33.6%)
Missing	30 (6.7%)	17 (5.3%)	29 (7.4%)	16 (4.6%)
BMI, N (%)				
Underweight	16 (3.6%)	17 (5.3%)	16 (4.1%)	18 (5.1%)
Normal weight	193 (43.1%)	162 (50.6%)	168 (42.9%)	176 (50.1%)
Preobesity	129 (28.8%)	69 (21.6%)	104 (26.5%)	85 (24.2%)
Obesity I-III	67 (15.0%)	47 (14.7%)	62 (15.8%)	50 (14.2%)
Missing	43 (9.6%)	25 (7.8%)	42 (10.7%)	22 (6.3%)
Comorbidity present, N (%)	301 (67.2%)	219 (68.4%)	263 (67.1%)	242 (68.9%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Cancer, N (%)	16 (3.6%)	11 (3.4%)	17 (4.3%)	10 (2.8%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Type 2 Diabetes, N (%)	9 (2.0%)	3 (0.9%)	9 (2.3%)	3 (0.9%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Hypertension, N (%)	68 (15.2%)	41 (12.8%)	59 (15.1%)	45 (12.8%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Cardiac problems, N (%)	19 (4.2%)	8 (2.5%)	16 (4.1%)	10 (2.8%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Depression, N (%)	44 (9.8%)	48 (15.0%)	40 (10.2%)	50 (14.2%)
Missing	24 (5.4%)	17 (5.3%)	23 (5.9%)	14 (4.0%)
Regular visits to HCP, N (%)				
No regular visits	14 (3.1%)	15 (4.7%)	13 (3.3%)	14 (4.0%)
Neurologist	132 (29.5%)	71 (22.2%)	103 (26.3%)	96 (27.4%)
Primary care physician	18 (4.0%)	13 (4.1%)	21 (5.4%)	9 (2.6%)
Primary care physician and neurologist	263 (58.7%)	206 (64.4%)	235 (59.9%)	219 (62.4%)
Missing	21 (4.7%)	15 (4.7%)	20 (5.1%)	13 (3.7%)
History of positive Covid-19 test, N (%)				
No	387 (86.4%)	273 (85.3%)	339 (86.5%)	310 (88.3%)
Yes	60 (13.4%)	45 (14.1%)	52 (13.3%)	39 (11.1%)
Missing	1 (0.2%)	2 (0.6%)	1 (0.3%)	2 (0.6%)

MS – multiple sclerosis, CIS – clinically isolated syndrome, PPMS – primary progressive multiple sclerosis, SPMS – secondary progressive multiple sclerosis, DMT – disease modifying therapy, BMI – body mass index, HCP – healthcare practitioner.

hesitancy in our study, neither education nor comorbidities reached statistical significance. In contrast to the pwMS surveyed in the United States (Ciotti et al., 2022), participants in our study who had a history of positive Covid-19 test were more likely to be vaccine hesitant. Although this may reflect the differences in Covid-19 vaccination guidelines, which require a 4-month post-infection waiting period for vaccination in Switzerland (Swiss Federal Office of Public Health, 2023), but shorter or no waiting time elsewhere (Australian Goverment, Department of Health, and Aged Care 2023; Centers for Disease Control and Prevention, 2023), none of our unvaccinated participants with a history of Covid-19 infection cited prior infection as a reason for delaying vaccination. However, some participants indicated that they believed in a "natural immunity" that they had achieved through infection and recovery. In addition, this finding can likely be explained by the use of Covid-19 certificates in Switzerland, which allowed vaccinated and recovered individuals the same access to the public areas or events or the same right to travel, thus not encouraging vaccination through restrictions (Swiss Federal Office of Public Health, 2023). Overall, these findings underscore the importance of adequately communicating the benefits of Covid-19 vaccination after infection. Finally, our finding that underweight pwMS were more hesitant to vaccinate could be coincidental, given the wide confidence intervals and the lack of a strong association in the imputed multivariable analysis.

While the rates of self-reported vaccine side effects in our study were lower than in previous studies that predominately included pwMS vaccinated with the BNT162b2 vaccine, the most common side effects were comparable (Allen-Philbey et al., 2022; Lotan et al., 2021; Briggs

Table 4
Comparison of the participants who did and did not report changes in MS symptoms after the first and second dose of Covid-19 vaccine.

	First Covid-19 vaccine dose		Second Covid-19 vaccine dose	
	No changes in MS symptoms (N = 678)	Changes in MS symptoms (N = 49)	No changes in MS symptoms (N = 634)	Changes in MS symptoms (N = 67)
Female sex, N (%)	489 (72.1%)	41 (83.7%)	460 (72.6%)	49 (73.1%)
Age, median [IQR]	53.0 [43.0, 60.0]	51.0 [39.0, 61.0]	52.0 [43.0, 60.0]	52.0 [42.5, 62.0]
Swiss citizenship, N (%)	578 (85.3%)	44 (89.8%)	545 (86.0%)	58 (86.6%)
Missing	35 (5.2%)	4 (8.2%)	28 (4.4%)	5 (7.5%)
Civilian status, N (%)				
Married or in registered partnership	365 (53.8%)	20 (40.8%)	340 (53.6%)	33 (49.3%)
Unmarried	266 (39.2%)	21 (42.9%)	252 (39.7%)	26 (38.8%)
Missing	47 (6.9%)	8 (16.3%)	42 (6.6%)	8 (11.9%)
University degree, N (%)	190 (28.0%)	10 (20.4%)	182 (28.7%)	14 (20.9%)
Missing	50 (7.4%)	8 (16.3%)	43 (6.8%)	8 (11.9%)
Working situation, N (%)				
Employed	400 (59.0%)	26 (53.1%)	379 (59.8%)	34 (50.7%)
Not working	66 (9.7%)	8 (16.3%)	60 (9.5%)	11 (16.4%)
Retired	78 (11.5%)	1 (2.0%)	75 (11.8%)	3 (4.5%)
Receiving disability insurance	103 (15.2%)	8 (16.3%)	93 (14.7%)	13 (19.4%)
Missing	31 (4.6%)	6 (12.2%)	27 (4.3%)	6 (9.0%)
MS type, N (%)				
CIS	10 (1.48%)	1 (2.08%)	9 (1.4%)	1 (1.5%)
PPMS	75 (11.1%)	5 (10.4%)	68 (10.7%)	9 (13.4%)
RRMS	441 (65.3%)	29 (60.4%)	420 (66.2%)	31 (46.3%)
SPMS	125 (18.4%)	9 (18.4%)	110 (17.4%)	22 (32.8%)
Transition	24 (3.5%)	4 (8.2%)	27 (4.3%)	4 (6.0%)
MS duration	15.0 [8.0, 23.0]	14.5 [8.0, 23.0]	15.0 [0, 56.0]	16.0 [0, 53.0]
Missing	31 (4.6%)	5 (10.2%)	25 (3.9%)	6 (9.0%)
Gait disability, N (%)				
None to mild	459 (67.7%)	26 (53.1%)	440 (69.4%)	30 (44.8%)
Moderate	141 (21.9%)	15 (34.9%)	129 (20.3%)	20 (29.9%)
Severe	45 (6.6%)	2 (4.1%)	38 (6.0%)	9 (13.4%)
Missing	33 (4.9%)	6 (12.2%)	27 (4.3%)	8 (11.9%)
Use of DMTs in the last year, N (%)				
No DMTs	138 (20.4%)	9 (18.4%)	118 (18.6%)	20 (29.9%)
Anti-CD20 B cells depleting	143 (21.1%)	14 (28.6%)	134 (21.1%)	22 (32.8%)
Any other DMT	348 (51.3%)	21 (42.9%)	336 (53.0%)	18 (26.9%)
Missing	49 (7.2%)	5 (10.2%)	46 (7.3%)	7 (10.4%)
Use of complementary medicine, N (%)	112 (16.5%)	12 (24.5%)	100 (15.8%)	20 (29.9%)
Missing	36 (5.3%)	6 (12.2%)	32 (5.0%)	6 (9.0%)
Smoking, N (%)				
Never	287 (42.3%)	17 (34.7%)	271 (42.7%)	26 (38.8%)
Now	119 (17.6%)	11 (22.4%)	118 (18.6%)	10 (14.9%)
Previously	233 (34.4%)	15 (30.6%)	213 (33.6%)	25 (37.3%)
Missing	39 (5.8%)	6 (12.2%)	32 (5.0%)	6 (9.0%)
BMI, N (%)				
Underweight	30 (4.4%)	0	30 (4.7%)	1 (1.5%)
Normal weight	314 (46.3%)	25 (51.0%)	292 (46.1%)	35 (52.2%)
Preobesity	178 (26.3%)	9 (18.4%)	169 (26.7%)	13 (19.4%)
Obesity I-III	100 (14.7%)	6 (12.2%)	93 (14.7%)	9 (13.4%)
Missing	56 (8.3%)	9 (18.4%)	50 (7.9%)	9 (13.4%)
Comorbidity present, N (%)	466 (68.7%)	29 (59.2%)	436 (68.8%)	42 (62.7%)
Missing	34 (5.0%)	5 (10.2%)	9 (1.4%)	0 (0%)
Cancer, N (%)	24 (3.5%)	3 (6.1%)	24 (3.8%)	2 (3.0%)
Missing	34 (5.0%)	5 (10.2%)	27 (4.3%)	7 (10.4%)
Type 2 Diabetes, N (%)	10 (1.5%)	0 (0%)	9 (1.4%)	0 (0%)
Missing	34 (5.0%)	5 (10.2%)	27 (4.3%)	7 (10.4%)
Hypertension, N (%)	98 (14.5%)	6 (12.2%)	90 (14.2%)	6 (9.0%)
Missing	34 (5.0%)	5 (10.2%)	27 (4.3%)	7 (10.4%)
Cardiac problems, N (%)	25 (3.7%)	2 (4.1%)	20 (3.2%)	3 (4.5%)
Missing	34 (5.0%)	5 (10.2%)	27 (4.3%)	7 (10.4%)
Depression, N (%)	71 (10.5%)	10 (20.4%)	67 (10.6%)	14 (20.9%)
Missing	34 (5.0%)	5 (10.2%)	27 (4.3%)	7 (10.4%)
Regular visits to HCP, N (%)				
No regular visits	30 (4.4%)	0 (0%)	25 (3.9%)	0 (0%)
Neurologist	182 (26.8%)	13 (26.5%)	25 (3.9%)	2 (3.0%)
Primary care physician	26 (3.8%)	2 (4.1%)	171 (27.0%)	22 (32.8%)
Primary care physician and neurologist	411 (60.6%)	29 (59.2%)	389 (61.4%)	37 (55.2%)
Missing	29 (4.3%)	5 (10.2%)	24 (3.8%)	6 (9.0%)
History of positive Covid-19 test, N (%)				
No	587 (86.6%)	40 (81.6%)	559 (88.2%)	62 (92.5%)
Yes	87 (12.8%)	9 (18.4%)	73 (11.5%)	5 (7.5%)
Missing	4 (0.6%)	0 (0%)	2 (0.3%)	0 (0%)

MS – multiple sclerosis, CIS – clinically isolated syndrome, PPMS – primary progressive multiple sclerosis, SPMS – secondary progressive multiple sclerosis, DMT – disease modifying therapy, BMI – body mass index, HCP – healthcare practitioner.

et al., 2022). This discrepancy in the frequency of side effects may be due to the fact that the majority of SMSR participants were vaccinated with the 1273-mRNA vaccine. Although no increased risk of relapse has been demonstrated after Covid-19 vaccination (Dreyer-Alster et al., 2022; Achiron et al., 2021), up to 10% of participants in our study reported new or worsening neurological disturbances, which is within the range of previously reported rates of postvaccination MS symptom worsening (Ciotti et al., 2022; Brunn et al., 2022). Whereas sensory disturbances were the most common aggravated MS symptom in a study of 262 mRNA vaccinated pwMS (Lotan et al., 2021), increased fatigue and gait disturbances were more common in our study. Similar disturbances have previously been found to be transient (Dreyer-Alster et al., 2022), and our participants described resolution of symptoms. However, when it comes to fatigue and tiredness, distinguishing MS symptom exacerbation from vaccine side effects may have been challenging, and an overlap between the two may be reflected in our findings.

4.1. Strengths and limitations

To our knowledge, our study is among the first nationwide explorations of Covid-19 vaccination in pwMS to focus on vaccine hesitancy along with vaccination side effects and changes in MS symptoms after vaccination. Strengths of our study include a large sample size for the European context with a low prevalence of missing data, a diverse population with clinically confirmed MS, and a variety of available variables. However, response rate (37.5%) was lower compared to the SMSR semiannual follow-up questionnaires. Because of the over-representation of women and middle-aged individuals among respondents, our results may be less generalizable to younger men. Self-report may have led to information bias, and in the case of self-report on vaccination, possibly social desirability bias. It is likely that vaccinated participants were more likely to have answered the questionnaire and that the rate of vaccine hesitancy was underestimated. Furthermore, our definition of vaccination considered any number of doses rather than a minimum of two. Finally, because of the wording of the questions, we could not systematically analyze the duration and resolution of vaccination side effects and changes in MS symptoms after vaccination.

5. Conclusions

Covid-19 vaccine hesitancy in surveyed pwMS in Switzerland was very low. However, younger pwMS, those with a history of confirmed Covid-19 infection and those without regular contact with healthcare professionals were at higher risk of being vaccine hesitant. Considering that Covid-19 vaccination usually had mild and transient side effects in pwMS and rarely affects MS symptoms, efforts should be made to encourage the undecided to vaccinate, mainly through providing reliable information and promoting contact with healthcare professionals.

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CRediT authorship contribution statement

Mina Stanikić: Conceptualization, Methodology, Formal analysis, Writing – original draft. **Eric Twomey:** Conceptualization, Methodology, Writing – original draft. **Milo A. Puhan:** Conceptualization, Resources, Writing – review & editing. **Christian P. Kamm:** Conceptualization, Resources, Writing – review & editing. **Anke Salmen:** Conceptualization, Resources, Writing – review & editing. **Vladeta Ajdacic-Gross:** Conceptualization, Resources, Writing – review & editing. **Chiara Zecca:** Conceptualization, Resources, Writing – review & editing. **Claudio Gobbi:** Conceptualization, Resources, Writing – review & editing. **Viktor von Wyl:** Conceptualization, Methodology, Supervision, Resources, Writing – review & editing.

Declaration of Competing Interest

Mina Stanikić reports employment by Roche branch in Serbia, Roche d.o.o., from February 2019 to February 2020. Christian P Kamm has received honoraria for lectures as well as research support from Biogen, Novartis, Almirall, Teva, Merck, Sanofi Genzyme, Roche, Janssen, Eli Lilly, Celgene and the Swiss MS Society. Ente Ospedaliero Cantonale (employer) received compensation for Chiara Zecca's speaking activities, consulting fees, or research grants from Almirall, Biogen Idec, Bristol Meyer Squibb, Lundbeck, Merck, Novartis, Sanofi, Teva Pharma, Roche. Chiara Zecca is recipient of a grant for senior researchers provided by AFRI (Area Formazione accademica, Ricerca e Innovazione), EOC. Ente Ospedaliero Cantonale (employer) received compensation for Claudio Gobbi's speaking activities, consulting fees, or research grants from Almirall, Biogen Idec, Bristol Meyer Squibb, Lundbeck, Merck, Novartis, Sanofi, Teva Pharma, Roche. Anke Salmen has received speaker honoraria and/or travel compensation for activities with Bristol Myers Squibb, Novartis, Roche and research support of Baasch Medicus Foundation and the Swiss MS society, not related to this work. Andrew Chan has served on advisory boards for, and received funding for travel or speaker honoraria from Actelion-Janssen, Almirall, Bayer, Biogen, Celgene, Sanofi-Genzyme, Merck, Novartis, Roche and Teva, all for hospital research funds; and research support from Biogen, Genzyme and UCB. Eric Twomey, Milo A. Puhan, Vladeta Ajdacic-Gross and Viktor von Wyl declare no competing interests.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2023.104707.

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