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Cannabis-based product use in multiple sclerosis: a Swiss nationwide, registry-based observational study

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Summary

BACKGROUND: Cannabis-based products are commonly used to manage multiple sclerosis (MS) symptoms such as spasticity and pain. However, the prevalence of cannabis-based product use, types of products used and factors associated with use remain unexplored in the Swiss MS population.

OBJECTIVE: To estimate the prevalence of cannabis-based product use, identify factors associated with use and characterise use patterns among people with MS enrolled in the Swiss Multiple Sclerosis Registry (SMSR). Additionally, we explored trends in cannabis-based product types, prescription status and insurance reimbursement over time.

METHODS: This exploratory observational study analysed self-reported data collected between 2016 and 2024. Prevalence estimates and associated factors were assessed using descriptive statistics and multivariable logistic regression on participants' baseline responses. Follow-up data from cannabis-based product users were analysed descriptively to evaluate temporal trends.

RESULTS: Of the 2193 participants, 330 (14.4%) reported current cannabis-based product use at baseline. Use varied by year of baseline questionnaire completion, ranging from 12.2% in 2016 to 25.6% in 2022. Cannabis-based product use was positively associated with reporting five or more symptoms (odds ratio [OR]: 2.41, 95% confidence interval [CI]: 1.19–5.24), presence of dysphagia (OR: 2.02, 95% CI: 1.27–3.17), spasms (OR: 1.59, 95% CI: 1.13–2.23), pain (OR: 1.48, 95% CI: 1.07–2.05) and greater gait disability (OR: 2.05, 95% CI: 1.39–3.01 for moderate; OR: 2.76, 95% CI: 1.56–4.85 for severe vs mild). Male sex (OR: 1.44, 95% CI: 1.06–1.96) was associated with higher odds of cannabis-based product use, while older age (OR: 0.98 per year, 95% CI: 0.96–0.99) and use of disease-modifying therapies (OR: 0.68, 95% CI: 0.49–0.95) were associated with lower odds. Follow-up data from 469 cannabis-based product users, providing 876 responses, showed cannabidiol was the most frequently used product between 2018 and 2022 but declined from 40% of reported use in 2019–2020 to 25% in 2023. In contrast, nabiximols use increased from 20% in 2018 to 30% in 2023, becoming the most commonly used product. The proportion of prescribed cannabis-based products rose from approximately 30% to 40%, while insurance reimbursement increased from 76% to 93% over the follow-up period.

CONCLUSIONS: Cannabis-based product use among people with MS exceeded rates seen in the general population in Switzerland. Higher symptom burden and greater disability may be key drivers of use. Increasing prescription and reimbursement rates over time suggest a shift towards more regulated, medically supervised use, likely influenced by evolving policy.

Introduction

Despite advances in disease-modifying therapy for multiple sclerosis (MS), many people with MS continue to struggle with symptom management. Cannabis-based products, including synthetic tetrahydrocannabinol (THC), oromucosal sprays like nabiximols (Sativex®) and oral cannabis extracts with varying THC-to-cannabidiol ratios, have emerged as complementary treatments for symptom relief [1]. Some of these products have demonstrated efficacy in alleviating spasticity and neuropathic pain [2, 3], with potential benefits for urinary incontinence and sleep disturbances [4-6], while also exhibiting distinct safety profiles compared to conventional symptomatic treatments in MS [7]. However, use patterns of cannabis-based products, including prevalence, product types and determinants of use, may vary widely depending on regulatory and healthcare settings [8]. In Switzerland, these aspects remain uncharacterised. A clearer understanding is crucial to maximising potential therapeutic benefits, minimising risks and managing healthcare costs effectively, ultimately improving patient care.

In recent years, Switzerland's regulatory framework for medical cannabis has evolved, facilitating access to cannabis-based products under medical supervision. In 2013, nabiximols became the first, and remains the only, cannabis-based product approved for the treatment of spasticity in MS in Switzerland [9]. In 2022, the Federal Office of Public Health removed the requirement for prior exemption approval for prescribing cannabis-based products, allowing physicians to prescribe nabiximols and compounded cannabis formulations directly [10]. Despite these changes, access remains limited due to strict prescribing criteria for nabiximols, THC content restrictions for compounded products and financial barriers, as mandatory insurance covers prescribed cannabis-based products only in exceptional cases [11]. Consequently, people with MS may turn to the informal market for cannabis-based products, increasing the risks of unsupervised use, incorrect dosing, adverse effects and exposure to unsafe products [2, 5].

Beyond regulatory and financial aspects, patient characteristics also influence cannabis-based product use by people with MS, though how these factors may impact use in Switzerland remains unclear. International studies suggest that younger people with MS, men, those with lower income, greater disability, severe spasticity or chronic pain, and those unmarried are more likely to use cannabis-based products [6, 12, 13]. Furthermore, dissatisfaction with conventional treatments or preference for holistic approaches may drive people with MS to use complementary therapies, including cannabis-based products [14, 15]. Understanding these factors within Switzerland's specific healthcare and regulatory context is essential for ensuring appropriate access and use of cannabis-based products.

To address gaps in the literature, we analysed patterns of cannabis-based product use among people with MS enrolled in the Swiss Multiple Sclerosis Registry. We estimated the prevalence of use, identified associated factors and described user characteristics. Additionally, we examined cannabis-based product forms, prescription status and cost coverage over time to assess the potential impact of recent regulatory changes.

Methods

Data source and study population

Self-reported data from the Swiss Multiple Sclerosis Registry were used for this study. The Swiss Multiple Sclerosis Registry is an ongoing, rolling-enrolment study that recruits people with MS who are at least 18 years old and either live in or receive treatment in Switzerland. Participation is voluntary and requires a signed informed consent form as well as confirmation of an MS diagnosis or clinically isolated syndrome. Participants complete baseline and follow-up surveys, which are available online and in paper format in three languages: German, French and Italian. Further details are available elsewhere [16, 17].

This study used Swiss Multiple Sclerosis Registry baseline and follow-up questionnaires, analysed separately as two independent analyses with distinct objectives and outcomes.

Baseline data and outcomes

The baseline questionnaire, administered at enrolment, collected extensive sociodemographic, health and MS-related information, including cannabis-based product use. Baseline data collected from the start of the Swiss Multiple Sclerosis Registry in 2016 to October 2024 (the data collection cut-off for this study) were used to estimate the prevalence of cannabis-based product use (the

primary outcome). Secondary outcomes in the baseline data analysis included identifying factors associated with cannabis-based product use and estimating the predicted probability of cannabis-based product use across different age groups. To be included in this analysis, participants had to have a confirmed MS diagnosis and available data on cannabis-based product use. Participants with clinically isolated syndrome and those with missing data on cannabis-based product use were excluded. All eligible participants constituted the baseline analysis sample, henceforth referred to as the total sample, while those with complete data on all variables tested for association with cannabis-based product use formed the complete case sample.

Follow-up data and outcomes

Data from five follow-up questionnaires, administered at 6- to 12-month intervals between 2018 and 2023, constituted the follow-up dataset and were analysed to explore how cannabis-based products were used. The 2021 questionnaire was excluded from analysis because the Swiss Multiple Sclerosis Registry survey was modified that year to address the COVID-19 pandemic and omitted questions about the use of cannabis-based products. The primary outcomes at follow-up were the most frequently used forms of cannabis-based products, prescription status and reimbursement methods. The secondary outcome was changes in cannabis-based product use patterns across the five follow-up waves. For inclusion in the follow-up data analysis, participants needed to report their MS subtype and actively use cannabis-based products. At each follow-up assessment, we excluded participants who were non-users, had incomplete data on cannabis-based product use or reported clinically isolated syndrome.

All questions from the Swiss Multiple Sclerosis Registry surveys that were used are provided in the appendix.

Outcomes of interest

The outcomes of interest included self-reported use of cannabis-based products (including the initiator of use), the forms of used products, prescription status and payment sources for prescribed products. Participants who indicated non-use were prompted to skip the related questions.

Use of cannabis-based products and initiative

Use of cannabis-based products was assessed in both the baseline and follow-up questionnaires using a multiple-choice question with the following response options: “No”, “Yes, on my own initiative” and “Yes, in consultation with a doctor”. At baseline, this referred to current use, whereas in follow-ups it pertained to use within the last six months. In cases where participants did not answer the question about cannabis-based product use, but responded to a subsequent question on the form of the cannabis-based product used, a separate category – “Yes, initiation unknown” – was introduced. For the purposes of defining cannabis-based product users and non-users at both baseline and follow-up, a simplified binary variable (Yes/No) was created by merging “Yes, on my own initiative”, “Yes, in consultation with a doctor” and “Yes, initiation unknown” into a single “Yes” category.

Forms of cannabis-based products

The forms of cannabis-based products used were assessed during follow-up using a multiple-choice question that listed various products (e.g. nabiximols, cannabis oil and cannabidiol-only products). This variable was treated as categorical, and the follow-up data were used to describe temporal trends in the forms of cannabis-based products used.

Prescription status of cannabis-based products

Follow-up questionnaires assessed whether the cannabis-based product used was prescribed by a doctor. Response options were “Yes” or “No” and this variable was treated as categorical and reported at each follow-up.

Cost coverage for prescribed cannabis-based products

Cost coverage for cannabis products prescribed by a doctor was assessed in the follow-up questionnaires using a multiple-choice question. The available options included “Self-payment”, “Health insurance” and “Other”, along with an open-text field for comments. In early follow-up questionnaires, responses were collected only as open-text entries. These responses were subsequently

analysed and reclassified into the predefined categories and a new category, "Both self-payment and health insurance", was created. This variable was treated as categorical and follow-up data were used to describe temporal trends in payment sources over time.

Variables of interests

Sociodemographic, health- and MS-related characteristics, along with the year of questionnaire completion, were used to describe the sample and explore potential associations with the use of cannabis-based products.

Sociodemographic variables were recorded at baseline and included sex (binary: Female / Male), highest education level (categorical: Did not complete mandatory schooling / Mandatory schooling / High school / Apprenticeship, higher professional education / University or applied university degree) and age in years (continuous), which was calculated separately at baseline and at each follow-up as the difference between the year of birth and the year of questionnaire completion.

Health- and MS-related characteristics were collected at baseline and each follow-up. MS duration in years (continuous) was calculated separately at baseline and each follow-up as the difference between the self-reported year of diagnosis and the year of questionnaire completion. MS subtype was determined using a multiple-choice question (categorical: Relapsing-remitting MS / Primary progressive MS / Secondary progressive MS). Furthermore, the presence of MS symptoms was assessed through a multiple-choice question listing various symptoms – such as visual disturbances, fatigue and spasms – with each symptom treated as a separate binary variable (Yes/No). Additionally, a summary symptom variable was created as a three-level categorical variable based on the number of reported symptoms (categorical: No symptoms / 1–5 symptoms / ≥5 symptoms). Gait disability was assessed using the Self-Reported Disability Status Scale [18], a validated proxy for the Expanded Disability Status Scale, based on three multiple-choice questions on mobility (categorical: Mild/Moderate/Severe gait disability). Use of disease-modifying therapies was assessed through a multiple-choice question listing both generic and commercial drug names and was treated as a binary variable (Yes/No). The presence of a chronic comorbidity was assessed using a multiple-choice question listing conditions like diabetes, hypertension, cancer, rheumatoid diseases, musculoskeletal disorders, depression and skin diseases (binary: Yes/No).

The year of questionnaire completion was recorded as a timestamp for online participants and as the year the questionnaires were returned to the Swiss Multiple Sclerosis Registry for participants using the paper format. This information was used to assess trends in cannabis-based product use over time.

Statistical analysis

To assess the prevalence of cannabis-based product use, we reported the frequency and percentage of Swiss Multiple Sclerosis Registry participants who reported cannabis-based product use at baseline. To characterise cannabis-based product users, we conducted a descriptive analysis of the baseline variables, reporting counts and percentages for categorical variables and summarising continuous variables using the mean and standard deviation. Additionally, we reported and descriptively compared prevalence of cannabis-based product users at each follow-up, along with the forms of cannabis-based products used, prescription status and cost coverage, using counts and percentages. We also analysed cannabis-based product forms by decision-makers/supervision over time.

To explore cross-sectional associations between cannabis-based product use and variables of interest, we applied multivariable logistic regression to the baseline data. The initial analysis was performed on a subset of participants with complete baseline data to determine the optimal model. The model was first fitted with all relevant variables, including individual MS symptoms, with cannabis-based product use as the outcome. Collinearity was assessed using generalised variance inflation factors (GVIF) adjusted for degrees of freedom. A GVIF value of 1 indicated no collinearity, while values above 5 suggested that the corresponding variable should be excluded [19]. Given the exploratory nature of this study, automated stepwise elimination based on the Akaike Information Criterion was used to identify a parsimonious model. However, sex, age, MS subtype, MS duration, education level and comorbidity presence were manually retained due to their established relevance for cannabis-based product use in the literature [6, 13], while pain and spasticity were retained as they represent the primary indications for nabiximols use [20].

Following model finalisation, multiple imputation was applied to the total sample to address missing data, under the missing at random assumption. Imputation was performed using predictive mean matching for continuous variables (disease duration), logistic regression for binary variables (individual MS symptoms, disease-modifying therapy use, comorbidity) and polytomous regression for categorical variables (symptom severity, MS subtype, gait disability, education). Ten imputed datasets were generated. Convergence was assessed by inspecting trace plots of the imputation chains, and the distribution of imputed values was compared against observed values to verify plausibility. Regression analyses were rerun on each imputed dataset and pooled. Odds ratios (OR) and 95% confidence intervals (CI) are reported for both complete case and imputed analyses as a mutual sensitivity check.

To estimate the probability of cannabis-based product use across different ages, we used the multivariable logistic model estimates from both the complete case and imputed analysis, as a mutual sensitivity check. A reference dataset was generated in which age ranged continuously from the minimum to maximum observed age in the sample, while all other variables included in the final model were held at their mode (for categorical variables) or mean (for continuous variables). Predicted probabilities and their 95% confidence intervals were derived from each model using conditional prediction, applied to the reference dataset described above.

All analyses were conducted using R (version 4.5.2, GPL-2/GPL-3 licence) [17], with the following packages: *data.table* version 1.17.18, *haven* version 2.5.5, *openxlsx* version 4.2.8.1 for data management, *ggplot2* version 4.0.0 for data visualisation, *mice* version 3.19.0 for multiple imputation and *car* version 3.1-5 for collinearity assessment, *hmisc* version 5.2-5 for logistic regression, and *labelled* version 2.15.0 and *gtsummary* version 2.5.0 for tables. The analytical code is available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the Ethics Committee of Zürich Canton (PB-2016-00894; BASEC-NR 2019-01027).

Results

By the data cut-off, 2246 people with MS had completed the baseline Swiss Multiple Sclerosis Registry questionnaire. Of these, 53 (2.4%) did not respond to the cannabis-based product use question and were excluded, leaving a final study sample of 2193. An additional 385 participants lacked data on at least one of the variables of interest and were excluded from the complete case analysis, resulting in a final complete case sample of 1793 (figure 1). Table 1 summarises participant characteristics at baseline by cannabis-based product use.

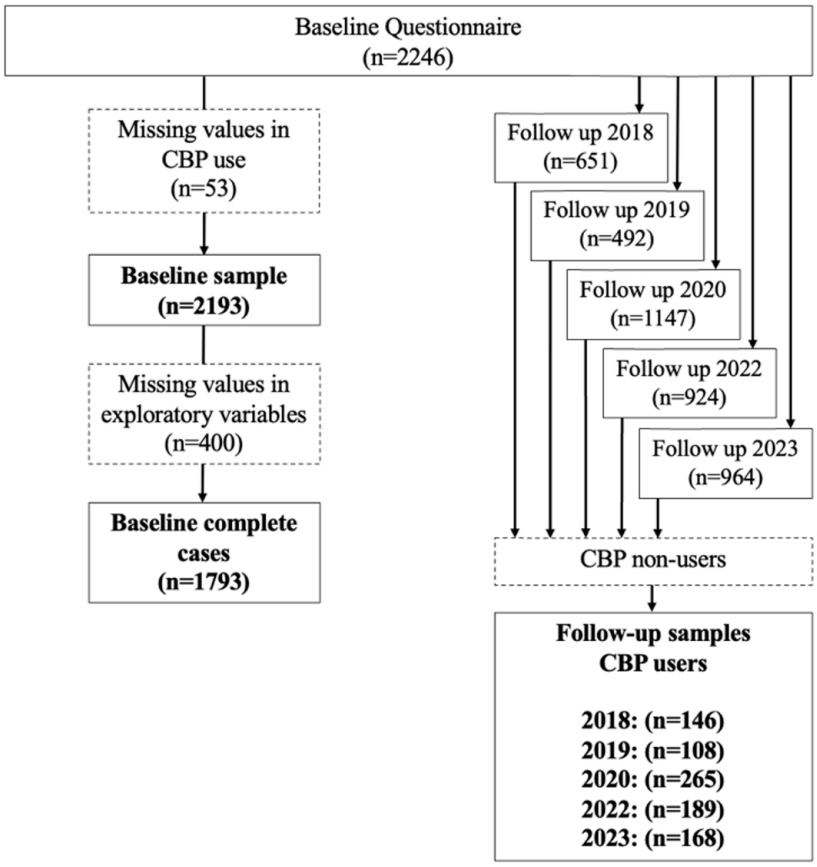


Figure 1: Study flowchart. On the left, derivation of the baseline analysis samples is shown, with exclusions indicated by dashed boxes and final sample sizes in bold. On the right, the follow-up analysis sample is shown, with annual waves displaying total respondents and cannabis-based product users; sample sizes vary across waves due to naturally fluctuating response rates. Follow-up analyses were conducted independently of the baseline analysis sample, as all participants with a completed baseline questionnaire were eligible for follow-up irrespective of missing data at baseline.

Follow-up analyses included 469 participants who used cannabis-based products, contributing 876 responses across five follow-up waves, with sample size per wave ranging from 108 to 265 (figure 1). Of these, 239 participants contributed to only one wave, 118 to two waves and 112 to three or more waves.

Cannabis-based product use and supervision

At baseline, 14.4% of participants (n = 330) reported current use of cannabis-based products. This proportion varied by the year in which the baseline questionnaire was completed, with the lowest rate observed in the first year of the Swiss Multiple Sclerosis Registry (12.2%) and the highest in 2022 (25.6%, tables S1 and S2 in the appendix). Among cannabis-based product users, 63.7% of participants reported initiating use independently, while 36.0% indicated using cannabis-based products in consultation with their physician (data missing for 0.4% participants).

Compared to non-users, participants who used cannabis-based products were more often male, more likely to have progressive MS, exhibited higher levels of gait disability, more often reported experiencing five or more MS-related symptoms concurrently and more frequently had chronic comorbidities (table 1). Participants who used cannabis-based products reported higher frequencies of all individual symptoms, with the most notable differences in pain (reported by 45.8% of users vs 25.1% of non-users) and spasms (50.6% vs 25.8%) (table S3 in the appendix).

Table 1: Characteristics of participants at baseline by cannabis-based product use in total and complete cases samples. Missing values reflect observed data prior to imputation. Multiple imputation was applied exclusively for regression analysis and is not reflected in the descriptive statistics presented in this table.

		Complete cases (n = 1793)		Total sample (n = 2193)	
Variable		**Yes** n = 267	**No** n = 1526	**Yes** n = 330	**No** n = 1863
Sex, n (%)	Female	173 (64.8%)	1133 (74.2%)	218 (66.1%)	1384 (74.3%)
	Male	94 (35.2%)	393 (25.8%)	112 (33.9%)	479 (25.7%)
Language region, n (%)	German	221 (82.8%)	1210 (79.3%)	271 (82.1%)	1456 (78.2%)
	French	38 (14.2%)	257 (16.8%)	49 (14.8%)	332 (17.8%)
	Italian	8 (3.0%)	59 (3.9%)	10 (3.0%)	75 (4.0%)
Age in years, mean (SD)		48 (12)	46 (13)	49 (13)	46 (13)
Years since diagnosis, mean (SD)		11 (10)	10 (9)	12 (10)	10 (10)
	Missing			7 (2.2%)	28 (1.5%)
MS subtype, n (%)	Relapsing-remitting MS	161 (60.3%)	1160 (76.0%)	172 (52.1%)	1245 (66.8%)
	Primary progressive MS	29 (10.9%)	95 (6.2%)	33 (10.0%)	111 (6%)
	Secondary progressive MS	77 (28.8%)	271 (17.8%)	95 (28.8%)	309 (16.6%)
	Missing			30 (9.1%)	198 (10.6%)
Number of symptoms, n (%)	0	11 (4.1%)	235 (15.4%)	11 (3.3%)	280 (15.0%)
	1–5	100 (37.5%)	783 (51.3%)	126 (38.2%)	960 (51.5%)
	>5	156 (58.4%)	508 (33.3%)	190 (57.6%)	618 (33.2%)
	Missing			3 (0.9%)	5 (0.3%)
Disease-modifying therapy use, n (%)	No	80 (30.0%)	318 (20.8%)	106 (32.1%)	407 (21.8%)
	Yes	187 (70.0%)	1208 (79.2%)	220 (66.7%)	1439 (77.2%)
	Missing			4 (1.2%)	17 (0.9%)
Comorbidity, n (%)	No	112 (41.9%)	774 (50.7%)	138 (41.8%)	903 (48.5%)
	Yes	155 (58.1%)	752 (49.3%)	185 (56.0%)	898 (48.2%)
	Missing			7 (2.1%)	62 (3.3%)
Education, n (%)	Did not complete mandatory schooling / Mandatory schooling / High school / Apprenticeship	147 (55.1%)	837 (54.8%)	180 (54.5%)	983 (52.8%)
	Higher professional education	51 (19.1%)	240 (15.7%)	61 (18.5%)	292 (15.7%)
	University or applied university	69 (25.8%)	449 (29.4%)	83 (25.2%)	560 (30.1%)
	Missing			6 (1.8%)	28 (1.5%)
Gait disability, n (%)	Mild	143 (53.6%)	1172 (76.8%)	168 (50.9%)	1382 (74.2%)
	Moderate	88 (33.0%)	280 (18.3%)	104 (31.5%)	341 (18.3%)
	Severe	36 (13.5%)	74 (4.8%)	45 (13.6%)	93 (5.0%)
	Missing			13 (4.0%)	47 (2.5%)

SD: standard deviation; MS: multiple sclerosis

Throughout follow-up, the proportion of survey respondents who had used cannabis-based products within the last 6 months of survey completion remained stable at around 20% (22.4%, 22.0%, 23.1% and 20.4% between 2018 and 2022, respectively [2021 excluded}), with a slight decline in the final follow-up in 2023 (17.4%). Characteristics of the participants who used cannabis-based products were largely consistent across follow-ups, though a slightly higher percentage used disease-modifying therapies in later follow-ups, while relapsing-remitting MS prevalence among users declined (table S4 in the appendix).

Factors associated with the use of cannabis-based products

In addition to the fixed independent variables, the final multivariable logistic regression model also included dysphagia, pain, spasms, epilepsy, tremor, total symptom count and gait disability. Estimates from the imputed analysis closely matched those from the complete case analysis (table 2).

Table 2: Multivariable logistic regression derived odds ratios and 95% confidence intervals in complete cases and imputed analysis.

Characteristic		**Complete cases analysis (n = 1793)**		**Imputed analysis (n = 2193)**	
OR	**95% CI**	**OR**	**95% CI**		
Sex	Female	Ref.	Ref.	Ref.	Ref.
	Male	**1.44**	**1.06–1.96**	**1.39**	**1.06–1.84**
Age (years)		**0.98**	**0.96–0.99**	**0.98**	**0.97–0.99**
Education	Did not complete mandatory schooling / Mandatory schooling / High school / Apprenticeship	Ref.	Ref.	Ref.	Ref.
	Higher professional education	1.23	0.83–1.78	1.13	0.80–1.59
	University or applied university	1.02	0.73–1.42	0.91	0.67–1.23
MS subtype	Relapsing-remitting MS	Ref.	Ref.	Ref.	Ref.
	Primary progressive MS	1.14	0.64–1.97	1.19	0.72–1.96
	Secondary progressive MS	1.14	0.73–1.76	1.25	0.83–1.89
Time since diagnosis (years)		1.00	0.98–1.02	1.00	0.99–1.02
Disease-modifying therapy use	No	Ref.	Ref.	Ref.	Ref.
	Yes	**0.68**	**0.49–0.95**	**0.70**	**0.52–0.95**
Gait disability	Mild	Ref.	Ref.	Ref.	Ref.
	Moderate	**2.05**	**1.39–3.01**	**1.77**	**1.25–2.52**
	Severe	**2.76**	**1.56–4.85**	**2.40**	**1.42–4.05**
Number of symptoms	0	Ref.	Ref.	Ref.	Ref.
	1–5	**2.20**	**1.19–4.48**	**2.57**	**1.35–4.91**
	>5	**2.41**	**1.19–5.24**	**2.71**	**1.33–5.52**
Dysphagia	No	Ref.	Ref.	Ref.	Ref.
	Yes	**2.02**	**1.27–3.17**	**1.67**	**1.10–2.53**
Pain	No	Ref.	Ref.	Ref.	Ref.
	Yes	**1.48**	**1.07–2.05**	**1.63**	**1.22–2.18**
Spasms	No	Ref.	Ref.	Ref.	Ref.
	Yes	**1.59**	**1.13–2.23**	**1.62**	**1.20–2.18**
Depression	No	Ref.	Ref.	Ref.	Ref.
	Yes	1.47	1.00–2.14	1.23	0.87–1.75
Epilepsy	No	Ref.	Ref.	Ref.	Ref.
	Yes	0.28	0.04–1.21	0.84	0.27–2.63
Comorbidity	No	Ref.	Ref.	Ref.	Ref.
	Yes	1.20	0.89–1.61	1.09	0.84–1.43
Year of questionnaire		**1.19**	**1.11–1.29**	**1.12**	**1.06–1.19**

CI: confidence interval; MS: multiple sclerosis; OR: odds ratio.

The probability of cannabis-based product use is estimated to decline with age, starting around 0.1–0.13 at younger ages and falling below 0.05 by age 70, with minimal differences between MS subtypes, slightly higher in progressive MS and lower in relapsing-remitting MS (figures S1 and S2 in the appendix).

Forms of cannabis-based products

A variety of cannabis-based products were used, with at least 66.7% of all reports indicating use of a THC-containing product, including alongside cannabidiol products (product type was missing for 93 of 876 observations throughout the follow-up). Cannabidiol was the predominant form used in 2018–2022, peaking at around 40% of all cannabis-based products used in 2019–2020 before declining to 25% by 2023. Conversely, nabiximols showed a steady increase from 20% in 2018 to 30% in 2023, becoming the most commonly used cannabis-based product in 2023. Other forms maintained relatively stable usage patterns throughout the study period (figure 2). When analysed by supervision status, nabiximols was the cannabis-based product most frequently used in consultation with a doctor, followed by cannabidiol and tinctures. In contrast, use of cannabis-based products initiated independently by participants primarily involved cannabidiol products, oil and street cannabis (figure S2 in the appendix).

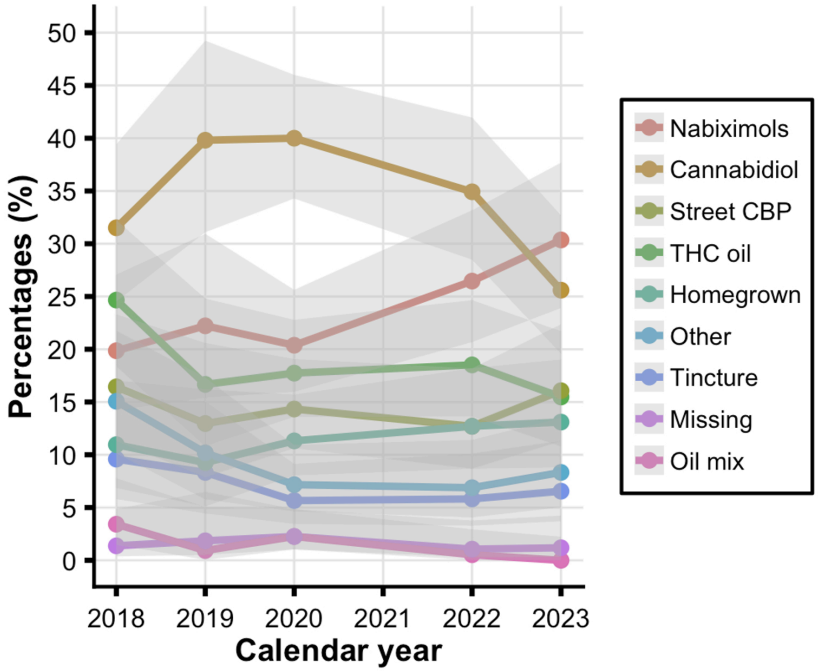


Figure 2: Use of various forms of cannabis-based products from 2018 to 2023.

Prescription status and cost coverage

Across the first three follow-up surveys, approximately 30% of participants reported that their use of cannabis-based products was medically prescribed; this proportion increased to 40% in the final two follow-up surveys (table S5 in the appendix). Among the prescribed products, the majority were covered by health insurance – 76%, 81%, 83% and 81% across the first four follow-ups – with health insurance cost coverage rising to 93% in the final follow-up. At the same time, the proportion of costs paid by participants declined. A smaller number of participants reported other sources of coverage for their prescribed cannabis-based products, such as disability insurance or manufacturer-sponsored test samples (figure 3, table S6 in the appendix).

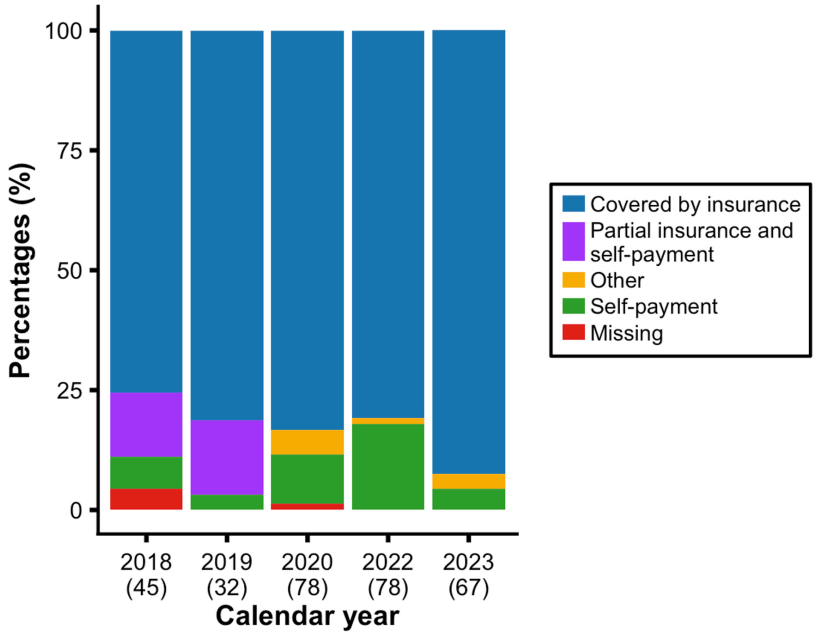


Figure 3: Percentage distribution of cost coverage for prescribed cannabis-based products between 2018 and 2023. The number of participants using cannabis-based products with a prescription per follow-up is given under the calendar year.

Discussion

In this study of 2193 people with MS in Switzerland, we observed that up to one-quarter of participants reported using cannabis-based products between 2016 and 2023. Participants who used cannabis-based products were more often male, had a higher number of comorbidities and more frequently reported having progressive MS forms and experiencing five or more MS-related symptoms concurrently compared to non-users. Greater disease burden, reflected by increased symptom load and gait impairment, as well as male sex, were positively associated with the use of cannabis-based products. While cannabidiols were initially the most commonly used cannabis-based products, nabiximols emerged as the predominant product by 2022. This coincided with a 10% increase in prescribed cannabis-based products and health insurance coverage rising to over 90%.

The prevalence of cannabis-based product use among people with MS in Switzerland appears substantially higher than in the general Swiss population. National data indicate that 30-day cannabis use in the general population was estimated at only 2.7% in 2015 [21], while a separate study using self-reports and wastewater analysis in western Switzerland found 12-month prevalence of cannabis to be 9.4% [22]. Cannabidiol use, legal in Switzerland since 2016, showed a 12-month prevalence of 18.5% among young Swiss men [23]. In contrast, our study found that the prevalence of current cannabis-based product use among people with MS was 14.4%, with use within the previous 6 months reaching up to 23% at follow-ups – higher than in the general population, which mirrors the situation in Italy and the US [24, 25]. This suggests that cannabis-based products may play a distinct and more prominent role among people with MS, likely driven by unmet symptom management needs and enabled by improved access to regulated cannabis-based products.

Our estimates of the prevalence of cannabis-based product use align with those of existing international studies. Recent research from France and Spain found that 23.3% and 20.1%, respectively, of people with MS reported using cannabis and/or formulations such as nabiximols or cannabidiol-rich oils [12]. Data from Canada, the UK and Spain prior to widespread availability of nabiximols indicated higher rates of ever-use of cannabis, exceeding 35–40%, although current use remained lower (between 14% and 18.5%) [13, 26, 27]. The small gap between current and recent use in our cohort suggests that more participants may have tried cannabis-based products in the past but discontinued them, possibly due to adverse effects, loss of efficacy or varying availability and cost [28-30].

Consistent with prior studies, our data revealed that cannabis-based product use was more common among men, younger participants and individuals with greater disability and symptom burden [12, 25, 26], as well as in participants with pain, spasms and dysphagia. This supports the idea that cannabis-based product use is primarily driven by symptom severity [4, 12], particularly in cases where conventional treatments offer limited relief, such as spasticity and pain [26]. Notably, these same symptoms are also those that people with MS perceive cannabis-based products to be most effective in managing [13]. However, the association with dysphagia likely reflects a more advanced disease, rather than a targeted therapeutic effect, as cannabis-based products are not indicated for dysphagia in MS or other conditions, and current evidence on cannabis-based products in gastrointestinal disorders does not extend to swallowing difficulties [31, 32].

The rise in prescribed cannabis-based products, primarily nabiximols, which supplanted non-prescription cannabidiols, and the increasing share of costs covered by health insurance point to a broader shift towards regulated, prescription-based access to cannabis-based products following the 2022 regulatory changes. While we cannot directly attribute these trends to the regulatory shift alone, they suggest that clearer policies may have supported greater physician prescribing and patient preference for medically supervised, reimbursable treatments.

However, this shift warrants careful evaluation from both equity and clinical perspectives. If reimbursement relies primarily on supplementary rather than mandatory health insurance, access is likely to follow socioeconomic gradients. This is particularly relevant given that people with MS who do not currently use cannabis-based products express willingness to do so when prescriptions are covered by insurance or otherwise legally accessible [2, 14, 20]. International experience shows that, with few exceptions, many patients worldwide continue to pay out-of-pocket costs [33], limiting access for those with lower socioeconomic status. Ensuring that use reflects appropriate, evidence-based practice is equally essential. Studies indicate that, although more than half of patients initiating nabiximols experience an initial treatment response, only around 40% achieve sustained, clinically meaningful improvement, and approximately half discontinue treatment within six months due to loss of effectiveness or adverse effects [20], primarily drowsiness, dizziness and fatigue [34]. These patterns underscore the importance of systematic monitoring to align prescribing practices with clinical evidence, which may be insufficient [35].

Switzerland's regulatory environment may continue to evolve, with ongoing pilot programmes such as the Züri Can study exploring regulated recreational access to THC-containing cannabis-based products [36]. In neighbouring Germany, the 2017 law permitting physicians to prescribe cannabis for medical purposes, along with subsequent expansions in 2024 that broadened access, was followed by both increased interest in medical cannabis [37] and indications of a rise in adverse effects in the general population [38]. This highlights that potential policy changes expanding access to cannabis-based products require continuous, systematic monitoring of clinical effectiveness and safety, alongside evaluation of broader public health impacts [39]. Real-world data sources, including patient registries such as the Swiss Multiple Sclerosis Registry, can provide valuable evidence on nationwide use of cannabis-based products, therapeutic outcomes and disparities in access.

Strengths and limitations

To our knowledge, this is the first study to quantify and characterise the use of cannabis-based products among people with MS in Switzerland. By drawing on a diverse, nationwide sample, including people with MS treated in private practices, outpatient clinics and academic centres, our findings are likely generalisable to the broader Swiss MS population. The use of both baseline and follow-up data allowed for a more robust estimate of current and recent cannabis-based product use, as well as trends in product types and reimbursement. Nonetheless, several limitations should be considered. First, reliance on self-reported data might have introduced recall and social desirability biases, particularly regarding unsupervised cannabis-based products use. However, prior work suggests that Swiss Multiple Sclerosis Registry participants report disease-modifying therapy use reliably [40], which may extend to other treatments. Second, follow-up sample sizes varied across survey waves, primarily due to a shift in the Swiss Multiple Sclerosis Registry follow-up survey dissemination strategy in 2019 rather than marked changes in underlying participation. This variation may limit comparability across time points. In addition, some participants contributed data at multiple waves, and changes in disease status over time may have influenced cannabis-based product use patterns. Third, data on the safety and efficacy of cannabis-based products were not collected, preventing assessment of their clinical benefits or risks and limiting understanding of

how these factors may have influenced patterns of use. Lastly, the observational design precludes causal inferences, and future longitudinal studies are needed to examine how MS progression and regulatory changes influence treatment uptake and outcomes.

Conclusions

This nationwide study is the first to quantify use of cannabis-based products among people with MS in Switzerland, revealing that up to one-quarter used cannabis-based products between 2016 and 2023 – more than in the general population, likely due to unmet symptom management needs and improved access. Cannabis-based product use was associated with male sex, younger age and greater disease burden, including presence of symptoms such as pain, spasticity and dysphagia. The increase in prescribed nabiximols and broader insurance coverage by 2023 suggests that recent policy changes may have encouraged a shift towards regulated, medically supervised use. These findings highlight the need for further patient-centred regulation and clinical oversight to ensure the safe and effective integration of cannabis-based products into MS care.

Data sharing statement

The datasets generated and analysed during the current study cannot be made publicly available due to the sensitive nature of the patient data and the terms of participant informed consent. Deidentified data and a data dictionary are available from the corresponding author on reasonable request, subject to Swiss Multiple Sclerosis Registry steering committee approval, applicable data protection regulations and a data sharing agreement specifying permitted use, access duration and data destruction conditions.

Notes

Use of AI: The authors declare that no generative artificial intelligence (AI) tools or AI-assisted technologies were used in the drafting, writing or creation of this manuscript.

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Potential competing interests

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Appendix

The SMSR questionnaires

Data for this study were drawn from the SMSR baseline and five follow-up surveys, administered in German, French, and Italian. This Supplementary Material includes only the first page and the specific questions analyzed, translated into English exclusively for this publication. The baseline questionnaire and a follow-up from 2022 are shown, as all five follow-up surveys contained the same questions.

MS Registry
Baseline Survey



Swiss MS Registry

2022

Part A: Personal Information

Below you will find some questions about yourself.

Please indicate your year of birth.

Only numbers are allowed in this field.

A1.

Exp.	*1*	*9*	*6*	*7*	Year	

					Year	

What is your nationality (or nationalities)?

A4.

Multiple answers possible.

O	Swiss	O	Croatian
O	Albanian	O	North Macedonian
O	Bosnian	O	Portugese
O	German	O	Serbian
O	French	O	Spanish
O	Greek	O	Turkish

O Italian

O Kosovar

O Other country

If other country, which one?

Part B: Education / Occupation

Below you will find some questions about your education and professional situation.

B1. **What is your highest level of completed education?**

Please select only one of the following answers.

O Did not complete compulsory school (or up to and including 7th school year)

O Completed compulsory school

O Vocational training (apprenticeship)

O Secondary school diploma, grammar school, vocational baccalaureate, or specialized secondary school

O Advanced vocational education (e.g., technical college)

O University degree (applied university or university)

O Other

If other type of education, which?

Part C: Course of the Disease

The following questions refer to the course of MS (for confirmed as well as suspected diagnoses) and the occurrence of MS in family and relatives.

C1. **Do you have a medically confirmed MS diagnosis?**

Please select only one of the following answers.

O Yes, confirmed diagnosis.

O No, suspected diagnosis.

C4. **When were you diagnosed with MS?**

Please indicate the month (if known) and year.

Only numbers are allowed in this field.

Exp.	0	7	Month	2	0	0	4	Year	

			Month					Year	

C6. **What medical aids do you <u>currently</u> use?**

Please select all applicable answers.

O None

O Walking aid, cane

O Bath boarding aid

O Wheelchair

O Rollator

O Articulated supports

O Arm splint

O Handle grip

O Moisture protection

O Bladder catheter

O Other

If other aids, which ones?

Part E: Physical activity and exercise

Below you will find some questions about physical activity and exercise.

E1. **How far can you <u>currently</u> go on flat terrain?**

Please select only one of the following answers.

O < 5 m

O 5-10 m

O 10-50 m

O 50-100 m

O 100-500 m

O 500-1000 m

O 1-5 km

O > 5 km

Part F: Therapies

Nachfolgend finden Sie einige Fragen zu den Behandlungen der MS-Erkrankung.

F1. **Which of the following immunomodulating medications are you <u>currently</u> receiving?**

Please select all that apply.

O	None	O	Imurek® / Azathioprine
O	Betaferon® / Interferon beta 1b	O	Synacthen® / Corticotropin
O	Extavia® / Interferon beta 1b	O	Sandimmun® / Cyclosporine
O	Avonex® / Interferon beta 1a	O	Endoxan® / Cyclophosphamide
O	Rebif® / Interferon beta 1a	O	MabThera® / Rituxan® / Rituximab
O	Plegridy® / Peginterferon beta 1a	O	Ocrevus® / Ocrelizumab
O	Copaxone® / Glatiramer acetate	O	Mavenclad® / Cladribin
O	Gilenya® / Fingolimod	O	Mayzent® / Siponimod
O	Tysabri® / Natalizumab	O	Arzerra® / Kesimpta® / Ofatumumab
O	Tecfidera® / BG-12 / Dimethyl fumarate	O	Vumerity® / Diroximelfumarat
O	Aubagio® / Teriflunomide	O	Ponvory® / Ponesimod
O	Nerventra® / Laquinimod	O	Other
O	Lemtrada™ / Alemtuzumab	*If other, which?*	
O	Novantron® / Mitoxantron	----------	

F5. **Are you <u>currently</u> using cannabis products because of MS?**

Please select only one of the following answers.

O Yes, in consultation with a doctor

O Yes, on my own initiative

O No

Comments:



If yes → continue with question F6 (next page).

If no → continue with question F9 (page 33).

F6. **In what form are you using cannabis products?**

Please select all that apply.

O Sativex

O Cannabis oil

O Cannabis tincture

O Oily mixture

O Street cannabis

O Home-grown

O Cannabidiol (CBD) only

O Other cannabis products

If other cannabis products, which ones?

F7. **Are these cannabis products medically prescribed?**

Please select only one of the following answers.

O Yes

O No

Comments:

_____

_____



If yes → continue with question F8 (next page).

If no → continue with question F9 (page 33).

F8. **Who is paying for the medically prescribed cannabis products?**

Please enter your answere here.

Part H: Other Conditions

Below you will find some questions about other medical conditions. For a better understanding of MS, it is important to know which other conditions may occur alongside it.

H1. **Apart from MS, are you affected by any other medical conditions? If yes, please indicate which ones.**

Please select all answers that apply.

O	No, none	O	Orthopedic conditions (e.g., joint or back pain)
O	Type I diabetes (insulin-dependent, early onset)	O	Skin diseases (e.g., acne)
O	Type II diabetes (previously referred to as adult-onset diabetes)	O	Psoriasis
O	Cancer	O	Asthma
O	High blood pressure	O	Other
O	Hearth problems		*If other, which ones?*
O	Dpression		
O	Osteoporosis		----------
O	Rheumatic diseases (e.g., arthritis, gout)		----------

Annual
FOLLOW-UP SURVEY



Swiss MS Registry

2022

Part C: Course of the disease

Below you will find some questions about the course of the disease and symptoms

*which may have occurred in **the last six months**.*

C1. **Please state the <u>current</u> type of your MS disease.**

Please select only one of the following answers.

O Clinically isolated syndrome (CIS) / no definitive MS diagnosis

O Relapsing-remitting MS (RRMS)

O Primary progressive MS (PPMS)

O Secondary progressive MS (SPMS)

O Transition between two stages or other forms (please specify below)

Any additional comments on your selection?

C2. **Which of the following symptoms have you had in the last six months?**

Please select all applicable answers.

- O None
- O Visual disturbances
- O Speech disorders
- O Swallowing disorders (dysphagia)
- O Weakness, muscle weakness
- O Symptoms of paralysis
- O Tiredness, fatigue
- O Sensory disturbances, abnormal sensations (e.g. numbness, tingling)
- O Dizziness
- O Pain
- O Gait disturbances
- O Balance disorders
- O Bladder disorders (e.g. bladder weakness)
- O Spasms (muscle cramps)
- O Twitching, tics

Continuation of the symptoms on the next page ...

Continuation of the symptoms

O Trembling (tremor)

O Intestinal disorders (e.g. constipation)

O Epileptic seizure

O Sexual disorders

O Memory disorders

O Depression

O Concentration problems

O Problems with spatial orientation

O Affective instability (mood swings, lack of control over emotions)

O Other

If other symptoms, which ones?

C3. **What medical aids do you <u>currently</u> use?**

Please select all applicable answers.

- O None
- O Walking aid, cane
- O Bath boarding aid
- O Wheelchair
- O Rollator
- O Articulated supports
- O Arm splint
- O Handle grip
- O Moisture protection
- O Bladder catheter
- O Other

  If other aids, which ones?

Part D: Physical activity and exercise

Below you will find some questions about physical activity and exercise.

D1. **How far can you <u>currently</u> go on flat terrain?**

Please select only one of the following answers.

O < 5 m

O 5-10 m

O 10-50 m

O 50-100 m

O 100-500 m

O 500-1000 m

O 1-5 km

O > 5 km

E2. **Which of the following immunomodulating drugs have you received in the last six months? Please also indicate if you have stopped or interrupted an immunomodulating drug in the last six months.**

Please select the applicable answers for the corresponding medication (multiple answers possible).

	In the last six months receive	In the last six months stopped or interrupted
Betaferon® / Interferon beta 1b	O	O
Extavia® / Interferon beta 1b	O	O
Avonex® / Interferon beta 1a	O	O
Rebif® / Interferon beta 1a	O	O
Plegridy® / peginterferon beta 1a	O	O
Copaxone® / glatiramer acetate	O	O
Gilenya® / fingolimod	O	O
Tysabri® / Natalizumab	O	O
Tecfidera® / BG-12 / dimethyl fumarate	O	O
Aubagio® / Teriflunomide	O	O

Continuation of the medication on the next page ...

Continuation of the medication...	In the last six months receive	In the last six months stopped or interrupted
Nerventra® / Laquinimod	O	O
Lemtrada™ / Alemtuzumab	O	O
Novantron® / Mitoxantron	O	O
Imurek® / Azathioprine	O	O
Synacthen® / Corticotropin	O	O
Sandimmun® / cyclosporine	O	O
Endoxan® / cyclophosphamide	O	O
MabThera® / Rituxan® / Rituximab	O	O
Ocrevus® / Ocrelizumab	O	O
Mavenclad® / Cladribine	O	O
Mayzent® / Siponimod	O	O
Arzerra® / Kesimpta® / Ofatumumab	O	O
Vumerity® / diroxime fumarate	O	O
Ponvory® / Ponesimod	O	O
Other medication	O	O

Part H: Complementary medicine and non-pharmacological therapies

*Below you will find some questions on complementary medical treatment and non-pharmacological therapies that you have used in **the last six months**.*

H4. **Have you used cannabis products in <u>the last six months</u> because of MS?**

Please select only one of the following answers.

O Yes, after consultation with a doctor

O Yes, on my own initiative

O No

Comments:



*If yes --> continue with question **H5** (next page).*

*If not --> continue with question **H8** (page 39).*

H5. **In what form did you consume cannabis products?**

Please select all answers that apply.

- O Sativex
- O Cannabis oil
- O Cannabis tincture
- O Oil mixture
- O Street cannabis
- O Home-grown
- O Only Cannabidiol (CBD)
- O Other cannabis products

If other cannabis products, which ones?

H6. **Were these cannabis products prescribed?**

Please select only one of the following answers.

O Yes

O No

Comments:



If yes → continue with question H7 (next page).

If no → continue with question H8 (page 39).

H7. **Who is paying for the prescribed cannabis products?**

Please select only one of the following answers.

O Self

O Health insurance

O Other

If other, who?

Part I: Other diseases

Below you will find some questions about other diseases. For a better understanding of MS, it is important to know which other diseases MS occurs together with.

I1. **Have you been newly diagnosed with any other illnesses <u>in the last 12 months</u>? If yes, please specify which one(s).**

Please select all applicable answers.

O None

O Type I diabetes (insulin-dependent, early onset)

O Type II diabetes (formerly also known as adult-onset diabetes)

O Orthopedic diseases (e.g. joint or back pain)

O Skin diseases (e.g. acne)

O Psoriasis (psoriasis)

O	Cancer	O	Asthma
O	High blood pressure	O	Other
O	Heart problems		*If other illnesses, which ones?*
O	Depression		
O	Osteoporosis		----------
O	Rheumatic diseases		----------

Cannabis-based product use over years

Tables S1 and S2 present the prevalence of cannabis-based product use by the year in which participants completed the baseline questionnaire for the imputed and for the complete cases sample, respectively. The lowest rate was observed in the first year of the SMSR at 12.3 percent, while the highest rates were recorded between 2022 and 2024, approaching 30 percent in the complete cases sample. However, the number of participants in 2023 and 2024 in the complete cases sample were limited.

Table S1. Cannabis-based product use over years assessed at baseline in the imputed sample.

Year	Yes N = 330[1]	No N = 1863[1]	Overall N = 2193[1]
2016	49 (12.3%)	348 (87.7%)	397 (100.0%)
2017	92 (13.8%)	576 (86.2%)	668 (100.0%)
2018	45 (13.4%)	292 (86.6%)	337 (100.0%)
2019	53 (18.2%)	238 (81.8%)	291 (100.0%)
2020	23 (17.2%)	111 (82.8%)	134 (100.0%)
2021	17 (15.9%)	90 (84.1%)	107 (100.0%)
2022	21 (25.6%)	61 (74.4%)	82 (100.0%)
2023	16 (18.6%)	70 (81.4%)	86 (100.0%)
2024	14 (15.4%)	77 (84.6%)	91 (100.0%)

[1]n (%)

Supplementary Table 2. Cannabis-based product use over years assessed at baseline in the complete cases sample.

Year	Yes[1] N = 267	No[1] N = 1526	Overall[1] N = 1793
2016	44 (12.3%)	315 (87.7%)	359 (100.0%)
2017	73 (13.2%)	482 (86.8%)	555 (100.0%)
2018	39 (13.5%)	250 (86.5%)	289 (100.0%)
2019	46 (17.9%)	211 (82.1%)	257 (100.0%)
2020	19 (16.2%)	98 (83.8%)	117 (100.0%)
2021	14 (14.0%)	86 (86.0%)	100 (100.0%)
2022	21 (26.9%)	57 (73.1%)	78 (100.0%)
2023	7 (29.2%)	17 (70.8%)	24 (100.0%)
2024	4 (28.6%)	10 (71.4%)	14 (100.0%)

Table S3. Presence of symptoms at baseline by cannabis-based product use.

Symptoms	Yes N = 330[1]	No N = 1863[1]	Overall N = 2193[1]
None			
No	316 (95.8%)	1,579 (84.8%)	1,895 (86.4%)
Yes	11 (3.3%)	279 (15.0%)	290 (13.2%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Vision disturbances			
No	246 (74.5%)	1,513 (81.2%)	1,759 (80.2%)
Yes	81 (24.5%)	345 (18.5%)	426 (19.4%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Language disturbances			
No	283 (85.8%)	1,747 (93.8%)	2,030 (92.6%)
Yes	44 (13.3%)	111 (6.0%)	155 (7.1%)
Missing	3 (0.9%)	5 (0.2%)	8 (0.4%)
Dysphagia			
No	281 (85.2%)	1,765 (94.7%)	2,046 (93.3%)
Yes	46 (13.9%)	93 (5.0%)	139 (6.3%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Weakness			
No	183 (55.5%)	1,282 (68.8%)	1,465 (66.8%)
Yes	144 (43.6%)	576 (30.9%)	720 (32.8%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Paralysis			
No	257 (77.9%)	1,658 (89.0%)	1,915 (87.3%)
Yes	70 (21.2%)	200 (10.7%)	270 (12.3%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Fatigue			
No	79 (23.9%)	772 (41.4%)	851 (38.8%)
Yes	248 (75.2%)	1,086 (58.3%)	1,334 (60.8%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Paraesthesia			
No	129 (39.1%)	978 (52.5%)	1,107 (50.5%)
Yes	198 (60.0%)	880 (47.2%)	1,078 (49.2%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Dizziness			
No	233 (70.6%)	1,499 (80.5%)	1,732 (79.0%)
Yes	94 (28.5%)	359 (19.3%)	453 (20.7%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Pain			
No	176 (53.3%)	1,390 (74.6%)	1,566 (71.4%)
Yes	151 (45.8%)	468 (25.1%)	619 (28.2%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Gait disturbances			

No	164 (49.7%)	1,238 (66.5%)	1,402 (63.9%)
Yes	163 (49.4%)	620 (33.3%)	783 (35.7%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Balance disturbances			
No	162 (49.1%)	1,158 (62.2%)	1,320 (60.2%)
Yes	165 (50.0%)	700 (37.6%)	865 (39.4%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Bladder dysfunction			
No	175 (53.0%)	1,306 (70.1%)	1,481 (67.5%)
Yes	152 (46.1%)	552 (29.6%)	704 (32.1%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Spasms			
No	160 (48.5%)	1,377 (73.9%)	1,537 (70.1%)
Yes	167 (50.6%)	481 (25.8%)	648 (29.5%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Tics			
No	280 (84.8%)	1,710 (91.8%)	1,990 (90.7%)
Yes	47 (14.2%)	148 (7.9%)	195 (8.9%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Tremor			
No	271 (82.1%)	1,695 (91.0%)	1,966 (89.6%)
Yes	56 (17.0%)	163 (8.7%)	219 (10.0%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Gastrointestinal			
No	218 (66.1%)	1,492 (80.1%)	1,710 (78.0%)
Yes	109 (33.0%)	366 (19.6%)	475 (21.7%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Seizures			
No	322 (97.6%)	1,845 (99.0%)	2,167 (98.8%)
Yes	5 (1.5%)	13 (0.7%)	18 (0.8%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Sexual dysfunction			
No	236 (71.5%)	1,560 (83.7%)	1,796 (81.9%)
Yes	91 (27.6%)	298 (16.0%)	389 (17.7%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Memory issues			
No	207 (62.7%)	1,418 (76.1%)	1,625 (74.1%)
Yes	120 (36.4%)	440 (23.6%)	560 (25.5%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Depression			
No	261 (79.1%)	1,623 (87.1%)	1,884 (85.9%)
Yes	66 (20.0%)	235 (12.6%)	301 (13.7%)
Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)
Other			
No	316 (95.8%)	1,798 (96.5%)	2,114 (96.4%)
Yes	11 (3.3%)	60 (3.2%)	71 (3.2%)

Missing	3 (0.9%)	5 (0.3%)	8 (0.4%)

[1]n (%)

Table S4 presents the sociodemographic and health-related characteristics of participants who reported cannabis-based product use in the follow-up questionnaires. These characteristics remained comparable across the years, with no clear trends observed in any of the variables.

Table S4. cannabis-based product user characteristics over the follow-up period.

Characteristic	FU18 N = 146[1]	FU24 N = 108[1]	FU36 N = 265[1]	FU48 N = 189[1]	FU54 N = 168[1]	Overall N = 876[1]
Sex						
Female	102 (69.9%)	71 (65.7%)	185 (69.8%)	121 (64.0%)	113 (67.3%)	592 (67.6%)
Male	44 (30.1%)	37 (34.3%)	80 (30.2%)	68 (36.0%)	55 (32.7%)	284 (32.4%)
Language						
German	126 (86.3%)	92 (85.2%)	218 (82.3%)	146 (77.2%)	136 (81.0%)	718 (82.0%)
French	16 (11.0%)	13 (12.0%)	37 (14.0%)	38 (20.1%)	28 (16.7%)	132 (15.1%)
Italian	4 (2.7%)	3 (2.8%)	10 (3.8%)	5 (2.6%)	4 (2.4%)	26 (3.0%)
Age	50 (12)	51 (11)	49 (12)	49 (11)	49 (11)	49 (11)
Missing	0	0	13	8	7	28
MS duration	13 (10)	13 (10)	12 (10)	11 (10)	11 (9)	12 (10)
Missing	0	0	16	9	10	35
MS subtype						
RRMS	87 (61.3%)	55 (52.4%)	154 (58.8%)	103 (56.0%)	86 (52.4%)	485 (56.6%)
PPMS	21 (14.8%)	20 (19.0%)	47 (17.9%)	28 (15.2%)	32 (19.5%)	148 (17.3%)
SPMS	34 (23.9%)	30 (28.6%)	61 (23.3%)	53 (28.8%)	46 (28.0%)	224 (26.1%)
Missing	4	3	3	5	4	19
Sum of symptoms						
0	4 (2.8%)	3 (2.8%)	55 (21.0%)	41 (22.2%)	35 (21.1%)	138 (15.9%)
1-5	40 (27.6%)	26 (24.1%)	44 (16.8%)	39 (21.1%)	28 (16.9%)	177 (20.4%)
>5	101 (69.7%)	79 (73.1%)	163 (62.2%)	105 (56.8%)	103 (62.0%)	551 (63.6%)
Missing	1	0	3	4	2	10
DMT						
No	51 (36.2%)	46 (44.2%)	101 (38.4%)	60 (32.1%)	54 (32.7%)	312 (36.3%)
Yes	90 (63.8%)	58 (55.8%)	162 (61.6%)	127 (67.9%)	111 (67.3%)	548 (63.7%)
Missing	5	4	2	2	3	16
Swiss citizenship						
No	23 (15.8%)	18 (16.7%)	43 (16.7%)	29 (15.4%)	28 (16.9%)	141 (16.3%)
Yes	123 (84.2%)	90 (83.3%)	215 (83.3%)	159 (84.6%)	138 (83.1%)	725 (83.7%)
Missing	0	0	7	1	2	10
Gait disability						
Mild	71 (52.2%)	48 (46.2%)	140 (58.8%)	102 (58.3%)	84 (54.5%)	445 (55.1%)
Moderate	50 (36.8%)	36 (34.6%)	73 (30.7%)	53 (30.3%)	55 (35.7%)	267 (33.1%)
Severe	15 (11.0%)	20 (19.2%)	25 (10.5%)	20 (11.4%)	15 (9.7%)	95 (11.8%)
Missing	10	4	27	14	14	69

[1]n (%); Mean (SD)

Predicted probability of using cannabis-based products over age

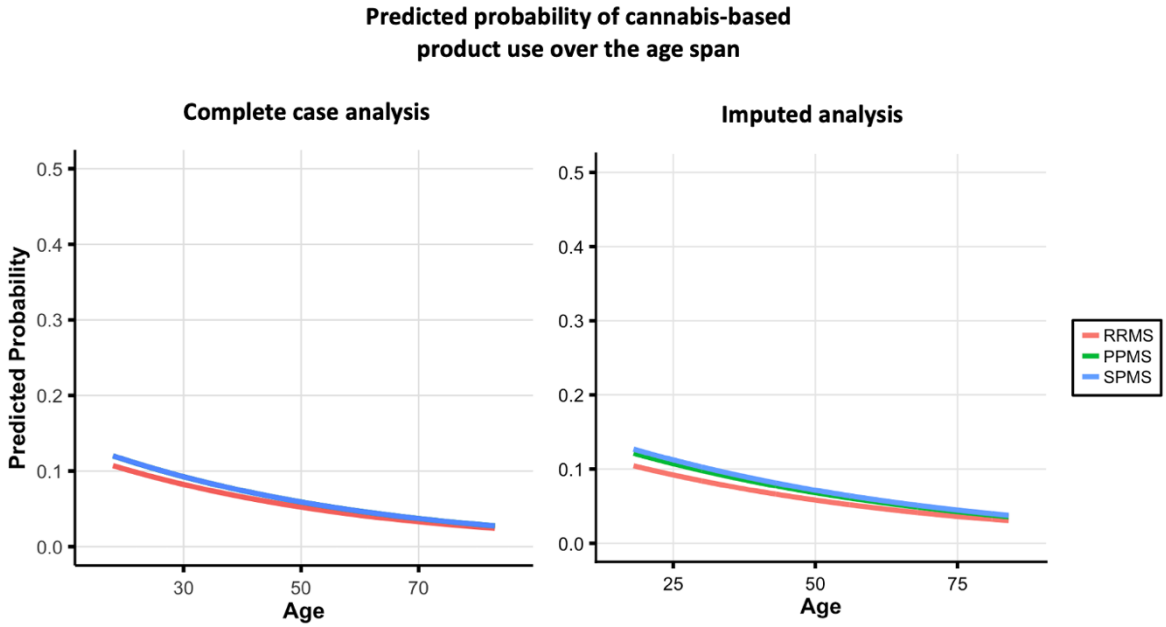


Figure S1 shows the estimated probability of cannabis-based product use across age, stratified by MS subtype: RRMS (red), PPMS (green), and SPMS (blue) based on conditional probabilities derived from complete case (left) and imputed analysis (right). Across all subtypes, the probability of cannabis use decreases with increasing age. Participants with progressive forms of MS (PPMS and SPMS) show slightly higher predicted probabilities of use compared to those with RRMS, particularly at younger ages.

Cannabis-based product forms

Figure S2 illustrates the annual trends in used forms of cannabis-based products, stratified by decision and prescription status from 2018 to 2023. Across all years, cannabidiol products dominated among participants using cannabis-based products without a prescription or by personal choice. In contrast, nabiximols was consistently the most used form among those using cannabis-based products with a prescription or based on a doctor's recommendation, with its use increasing over time. Other forms, such as oil, tincture, and homegrown cannabis, remained less commonly reported across all groups.

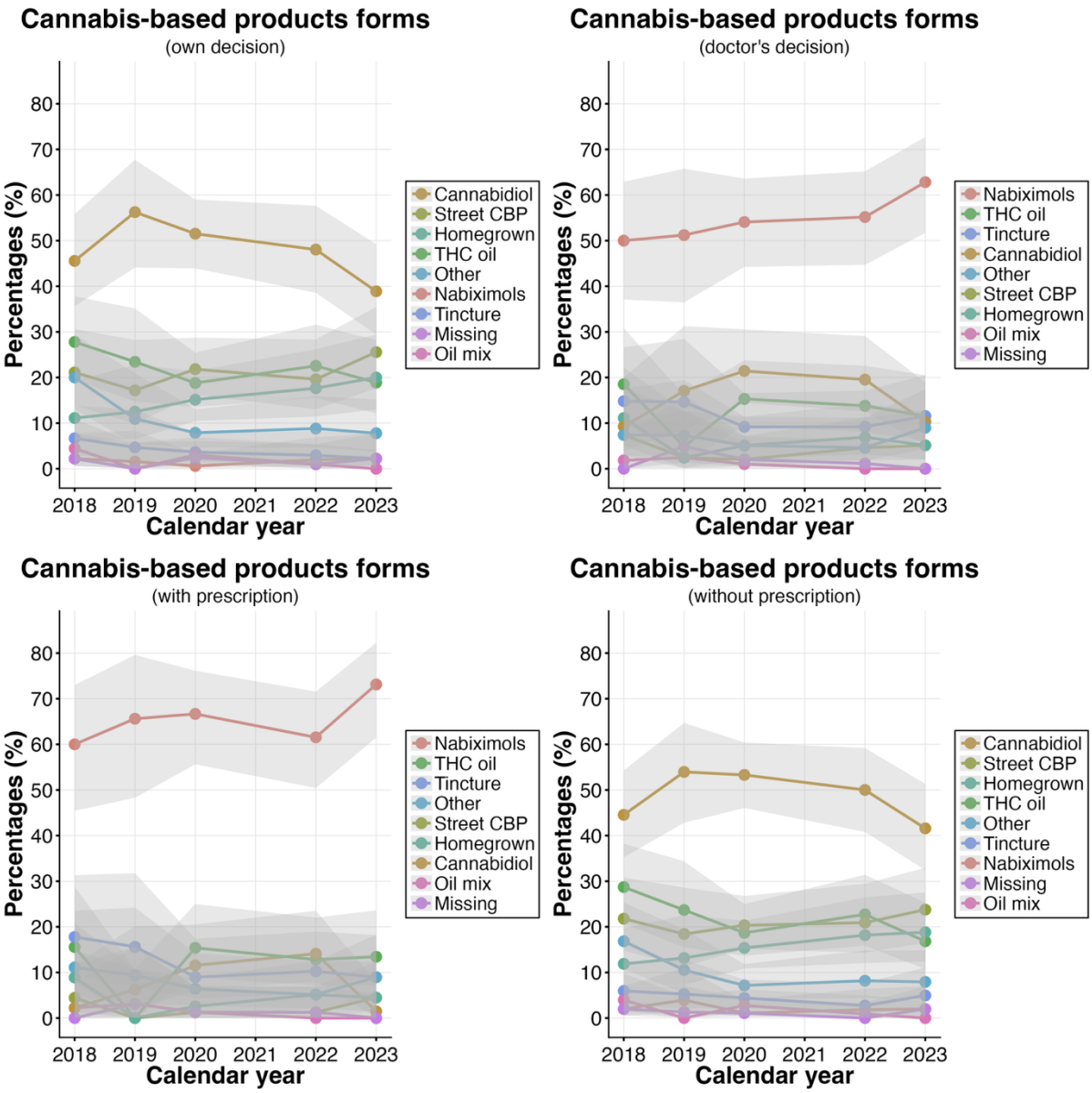


Figure S2. Trends in used cannabis-based product forms by decision and prescription status.

Prescription status and cost coverage

Table S5 presents the prescription status of cannabis-based products used during the follow-up period. Approximately 30 percent of the cannabis-based products were prescribed in the first three years, increasing to 40 percent in 2022 and 2023.

Table S5. Prescription status of the used cannabis-based products throughout follow-up period.

Year	No[1] N = 570	Yes[1] N = 300	Unknown[1] N = 6	Overall[1] N = 876
2018	101.0 (69%)	45.0 (31%)	0.0 (0%)	146.0 (100%)
2019	76.0 (70%)	32.0 (30%)	0.0 (0%)	108.0 (100%)

2020	182.0 (69%)	78.0 (29%)	5.0 (2%)	265.0 (100%)
2022	110.0 (58%)	78.0 (41%)	1.0 (1%)	189.0 (100%)
2023	101.0 (60%)	67.0 (40%)	0.0 (0%)	168.0 (100%)

[1]n (%)

Among the prescribed cannabis-based products, the cost of approximately three quarters was covered by participants' health insurance in 2018, while 7 percent was paid out of pocket. Out-of-pocket coverage peaked at 18 percent in 2022 before decreasing to 4 percent in 2023 (**Table S6**).

Table S6. Cost coverage of the prescribed cannabis-based products throughout the follow-up period.

Cost coverage by	**2018** N = 45[1]	**2019** N = 32[1]	**2020** N = 78[1]	**2022** N = 78[1]	**2023** N = 67
Health insurance	34.0 (76%)	26.0 (81%)	65.0 (83%)	63.0 (81%)	62.0 (93%)
Self	3.0 (7%)	1.0 (3%)	8.0 (10%)	14.0 (18%)	3.0 (4%)
Both	6.0 (13%)	5.0 (16%)	0.0 (0%)	0.0 (0%)	0.0 (0%)
Other	0.0 (0%)	0.0 (0%)	4.0 (5%)	1.0 (1%)	2.0 (3%)
Missing	2.0 (4%)	0.0 (0%)	1.0 (1%)	0.0 (0%)	0.0 (0%)