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ORIGINAL ARTICLE OPEN ACCESS

# Breast Cancer Screening in Women With Multiple Sclerosis: A Mixed-Methods Study

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**Keywords:** breast cancer screening | cohort studies | medico-administrative database | mixed-methods | multiple sclerosis

## ABSTRACT

**Background:** There is little information on breast cancer screening (BCS) practices in women with multiple sclerosis (WwMS).

**Objective:** To assess and compare BCS rates in WwMS and in the general population and identify barriers and facilitators.

**Methods:** In a 2012–2020 cohort study, we identified 47,166 WwMS without a history of cancer and matched them (up to 1:4) to 184,124 controls from the French national medico-administrative database. Mammography rates were compared according to age, city-level socio-economic status, period, and DMT use. We used logistic and negative binomial models to identify factors associated with BCS adherence in WwMS. We also carried out semistructured interviews with 20 WwMS and analyzed them using the empirically inductive method.

**Results:** Compared with controls, fewer WwMS underwent BCS at least once (69.9% vs. 76.7%,  $p < 0.001$ ) and had a lower biennial mammography rate (0.55 vs. 0.63;  $p < 0.001$ ). Rate differences increased with age. Once stratified on DMT, age-standardized rates only differed in the non-treated group (0.51 vs. 0.64;  $p < 0.001$ ). Factors associated with lower mammography rates in WwMS were city-level socio-economic status (mostdeprived vs. least deprived; IRR 0.88 95% CI [0.86–0.91]), long MS duration (16–25 years: 0.91 [0.89–0.94]; ref:  $\leq 5$ ) and hospitalization (MS-related: 0.85 [0.82–0.88]; non-MS-related: 0.92 [0.89–0.94]). However, DMT use was associated with higher mammography rates (high efficacy: 1.17 [1.14–1.21]; moderate efficacy: 1.18 [1.16–1.20]). Barriers were physical disability and feeling of excessive medicalization. Facilitators were disability-accessible care and perception of BCS as a routine procedure.

**Conclusion:** BCS among WwMS is suboptimal, especially among those not treated by DMT, and needs to be improved.

## 1 | Introduction

There is no consensus on breast cancer (BC) risk in multiple sclerosis (MS) as literature has been diverging depending of the period, country, or methodology. Some studies found an excess risk in women with MS (WwMS) [1] [2–4], a decreased risk [5, 6] or no difference [7–11]. These variations could be due to case ascertainment bias, specifically different BC

screening (BCS) practices. Indeed, BCS plays a crucial role in early cancer detection and therefore, in better treatment outcomes and survival [12]. Currently, the French Society of Multiple Sclerosis recommends that WwMS follow the general population screening guidelines: all 50- to 74-year-old women should undergo BCS by mammography every 2 years [13, 14]. In the French general population, adherence to BCS is 10 points below the European “acceptable level” of

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70% [15, 16]. Moreover, individuals with physical or mental disability report lower preventive care use, including BCS [17–19].

There is limited information on BCS in WwMS. A Canadian study found that WwMS underwent less mammography exams (~5%) [20], another matched cross-sectional study showed that regardless of the disability level, WwMS were less likely to receive a BC diagnosis through screening (vs. symptomatic) than the population-based controls [21]. This difference was more pronounced in WwMS with physical disabilities. Additionally, studies based on Norwegian data reported no difference in BC incidence in WwMS [8], but a twofold higher BC mortality rate, compared with the general population. The authors hypothesized a diagnosis neglect due to the misattribution of early cancer symptoms to MS [22]. Our group showed a slightly lower BC risk in WwMS than in healthy controls in France. However, once adjusted on BCS, this difference was no longer significant [6]. Lastly, an USA qualitative study reported that MS-specific barriers to BCS were mostly related to physical disability (e.g., transportation, examination positioning, medical professional attitudes) and feelings of excessive medicalization (e.g., “having enough to handle”) [23].

These studies and the high risk of physical disability in MS suggest a lower adherence to BCS, and subsequent increased time to diagnosis and treatment, but this has yet to be formally assessed and quantified. Moreover, the driving factors are still to be determined. The present study, through a mixed-methods approach, aimed to compare mammography rates in WwMS and matched controls from the general population and identify BCS barriers and facilitators.

## 2 | Methods

In the mixed-methods approach, a research question is addressed with a quantitative and a qualitative approach. In the present study, both components were collected and analyzed separately, and findings were integrated during the interpretation stage, following a parallel analysis method [24].

## 2.1 | Quantitative Component

### 2.1.1 | Population

This retrospective cohort study used data from the *Système National des Données de Santé* (SNDS), the French national medico-administrative database that covers 99% of the French population [25]. It collects data on any healthcare consumption conducted in France, including hospitalizations (in- and outpatient), ambulatory care, and screening procedures.

This study included all WwMS eligible for BCS in France between 2012 and 2021 and without a history of cancer in the 3 years before inclusion. WwMS were included at the latest date among the following: January 1, 2012, date of MS identification, or 50th birthday, which was defined as the index date. They were followed until the first censoring event: December 31, 2021, their 75th birthday, first cancer treatment (not restricted to breast cancer), or death. WwMS with less than 2 years of available follow-up were excluded. Up to four controls, matched exactly on birth year, health insurance status, residence, and index date were included (Figure 1). WwMS were selected from the French medico-administrative MS cohort. MS was identified through an algorithm using MS long-term disease status (LTD), hospitalizations, and MS-specific drug prescriptions and previously used in MS studies [6, 26–30].

### 2.1.2 | Outcomes & Additional Data

The main outcome was the biennial mammography rate, defined as the mammography incidence per person per 2 years (i.e., two-person-years) over follow-up. If the population followed the national guidelines of one mammography every 2 years, the observed biennial mammography rate would be 1. Additionally, two secondary binary outcomes were computed: (i) having undergone at least one mammography during the follow-up period and (ii) having done at least one mammography every 3 years. The interval period was made longer than the national BCS guidelines (2 years) to account for potential organizational and appointment availability challenges while still identifying individuals with consistent BCS behavior.

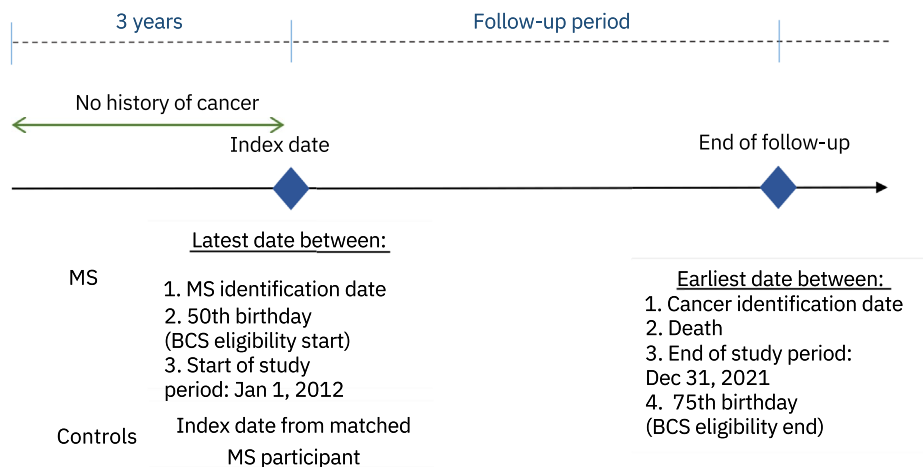


FIGURE 1 | Quantitative study design.

All mammography exams related to organized (CCAM code: QEQK004) and individual (QEQK001, QEQK005) BCS were collected. The following information also was retrieved: FDep, an ecological social deprivation index at the city level (based on the household median income, percentage of high school graduates, percentage of industrial and manual workers and unemployment rate; quasi-log-linear relationship with mortality) [31]; individuals with “Couverture Médicale Universelle” (CMU; universal health insurance) that provides access to healthcare services to those who may not have adequate coverage and is an indicator of social deprivation; and healthcare consumption, such as hospitalizations (MS-related or not) and disease-modifying therapy (DMT) reimbursements to act as proxy variables of the general health state and MS management. As comorbidities have been shown to be associated with screening adherence [32], the mortality-related morbidity index (MRMI) was calculated at baseline. The MRMI is a validated morbidity score, developed specifically for the French database, predictive of all-cause mortality that was and that has been shown to be more discriminant and better calibrated than the age-adjusted Charlson Comorbidity index in these data [33]. MS duration was defined as the time between MS identification in the database and cohort entry.

### 2.1.3 | Statistical Analysis

The main outcome, biennial mammography rate, was compared between WwMS and controls, overall and stratified by age groups, region of residence, and FDep using the Wald test for rate ratios. Age-standardized biennial mammography rates stratified by DMT use of WwMS were calculated and compared to matched controls (direct standardization). Crude and adjusted negative binomial regression models were used to assess factors associated with the overall biennial mammography rate by calculating the incidence rate ratios (IRR) and their 95% confidence intervals (CI).

Both secondary binary outcomes were compared between WwMS and controls with the chi-squared test. Crude and adjusted logistic regression models with the corresponding odds ratios (OR) and 95% CI were computed. All adjusted models included age, FDep quintile, MS duration, region of residence, being a beneficiary of the CMU at inclusion, MS-related and non-MS-related hospitalizations in the year before inclusion, MRMI comorbidity score, paraplegia, and reimbursement of at least two MS-specific DMT during the observation period. The logistic models also included follow-up duration and inclusion year.

Missing data were assessed by comparing characteristics between complete-case and the total population. Data imputation by predictive mean matching was performed using the ‘mice’ R package as a supplementary analysis.

## 2.2 | Qualitative Component

Qualitative data were obtained through semistructured interviews with WwMS eligible to the organized BCS program. Participants were recruited through a call for testimonies on social media platforms and on public health and MS-related

websites. This call did not mention BCS and only referred to MS and preventive services.

An interview guide was drafted and revised after the completion of a scoping note. Among the 55 eligible participants, 20 were selected and interviewed by video conference or telephone between October and November 2023. In a qualitative study, representativeness is not sought and diversity in the respondents' profiles is emphasized, particularly in terms of age, region of residence, MS duration, and physical disability level. Participant selection was carried out to maximize diversity of profiles. Interviews were recorded on *Open Broadcaster Software Studio* after acquisition of the informed consent. After interview anonymization and transcription, the audio recordings were erased. Names were modified in the results. Barriers and facilitators to BCS in WwMS were identified using an empirically inductive thematic method in which patterns or themes are identified and analyzed within qualitative data without imposing preconceived theories or categories [34]. Key topics were identified by the authors (LP and CP), first individually, reviewed, and combined.

### 2.2.1 | Data Access & Availability

Data access approvals for the study were obtained as per the current French legislation (Articles R.1461–11 to R.1461-17 of the French Public Health Code, CNIL-2016-316) and the study was declared to the EHESP SNDS registry, equivalent to an Institutional Review Board approval. According to data protection and French regulations, the authors cannot publicly release SNDS data. A request for data reuse may be made, but it would require the prior approval of the French regulatory authorities.

## 3 | Results

### 3.1 | Quantitative Component

#### 3.1.1 | BCS in WwMS and the General Population

The population characteristics are in Table 1. The study population included 47,166 WwMS who were matched to 184,124 controls (Figure 2). Mean age at baseline among both groups was  $56.2 \pm 6.5$  years, and the mean follow-up was  $7.6 \pm 2.6$  years, with 86.6% ( $n = 200,341$ ) being followed up until the end of the study period (Dec 31, 2021). The mean MS duration was  $10.3 \pm 8.4$  years.

Fewer WwMS had a mammography at least once compared with controls (69.9% vs. 76.6%,  $p < 0.001$ ) and consistently got screened at least once every 3 years (40.6% vs. 48.0%,  $p < 0.001$ ). The biennial mammography rate also was lower in WwMS than in controls (0.55 vs. 0.63,  $p < 0.001$ ).

After stratification by age, the disparity in mammography rates between WwMS and controls increased with age, from a relative decrease of 6.6% in the biennial mammography rates in WwMS in the  $\leq 55$  years group at inclusion (0.59 [0.59–0.60] vs. 0.63 [0.63–0.64], MS vs. controls, respectively) to a 36.9% decrease in the  $\geq 70$  years group (0.59 [0.58–0.61] vs. 0.37 [0.35–0.40]) (Figure 3). Upon stratification by socioeconomic

**TABLE 1** | Baseline and breast cancer screening characteristics ( $n = 231,290$ ).

|                                          | Study population |                 | Complete case <sup>a</sup> |
|------------------------------------------|------------------|-----------------|----------------------------|
|                                          | MS               | Controls        | MS                         |
|                                          | $n = 47,166$     | $n = 184,124$   | $n = 37,792$               |
| Socio-demographic characteristics        |                  |                 |                            |
| Age, years                               |                  |                 |                            |
| 50–55                                    | 26,033 (55.2)    | 101,530 (55.1)  | 21,590 (57.1)              |
| 56–60                                    | 8739 (18.5)      | 34,286 (18.6)   | 6811 (18.0)                |
| 61–65                                    | 6884 (14.6)      | 26,975 (14.7)   | 5285 (14.0)                |
| 66–70                                    | 4071 (8.6)       | 15,776 (8.6)    | 3009 (8.0)                 |
| 71–74                                    | 1439 (3.1)       | 5557 (3.0)      | 1097 (2.9)                 |
| Mean $\pm$ sd                            | 56.2 $\pm$ 6.5   | 56.2 $\pm$ 6.5  | 55.9 $\pm$ 6.4             |
| Deprivation index—FDep, quintiles        |                  |                 |                            |
| 1st (least deprived)                     | 7839 (16.6)      | 32,631 (17.7)   | 7246 (19.2)                |
| 2nd                                      | 8152 (17.3)      | 34,373 (18.7)   | 7450 (19.7)                |
| 3rd                                      | 8404 (17.8)      | 34,923 (19.0)   | 7682 (20.3)                |
| 4th                                      | 8532 (18.1)      | 35,549 (19.3)   | 7695 (20.4)                |
| 5th (most deprived)                      | 8428 (17.9)      | 36,013 (19.6)   | 7719 (20.4)                |
| Missing                                  | 5811 (12.3)      | 10,635 (5.8)    | 0 (0.0)                    |
| MS duration, years                       |                  |                 |                            |
| 0–5                                      | 16,624 (35.2)    |                 | 13,125 (34.7)              |
| 6–10                                     | 9094 (19.3)      |                 | 7182 (19.0)                |
| 11–15                                    | 8992 (19.1)      |                 | 7173 (19.0)                |
| 16–25                                    | 10,408 (22.1)    |                 | 8613 (22.8)                |
| 26+                                      | 2048 (4.3)       |                 | 1699 (4.5)                 |
| CMU beneficiary                          | 1459 (3.1)       | 10,512 (5.7)    | 1359 (3.6)                 |
| Death                                    | 2808 (6.0)       | 2388 (1.3)      | 2323 (6.1)                 |
| Age at death, mean $\pm$ sd              | 64.3 $\pm$ 6.2   | 64.6 $\pm$ 6.3  | 64.0 $\pm$ 6.3             |
| Mammography use                          |                  |                 |                            |
| $\geq 1$ mammography during follow-up    | 32,979 (69.9)    | 141,217 (76.7)  | 26,657 (70.5)              |
| $\geq 1$ mammography every 3 years       | 19,168 (40.6)    | 88,297 (48.0)   | 15,722 (41.6)              |
| $\geq 1$ mammography every 2 years       | 3018 (6.4)       | 12,957 (7.0)    | 2606 (6.9)                 |
| Biennial mammography rate, mean $\pm$ sd | 0.55 $\pm$ 0.48  | 0.63 $\pm$ 0.48 | 0.56 $\pm$ 0.48            |
| Comorbidities at entry                   |                  |                 |                            |
| MRMI score <sup>b</sup>                  |                  |                 |                            |
| 0 (No comorbidity)                       | 33,171 (70.3)    | 135,997 (73.9)  | 28,633 (75.8)              |
| 1                                        | 7166 (15.2)      | 24,197 (13.1)   | 6367 (16.8)                |
| 2                                        | 2042 (4.3)       | 5469 (3.0)      | 1840 (4.9)                 |
| 3+                                       | 1045 (2.2)       | 2654 (1.4)      | 952 (2.5)                  |
| Missing                                  | 3742 (7.9)       | 15,807 (8.6)    | 0 (0.0)                    |

(Continues)

TABLE 1 | (Continued)

|                                                                                | Study population  |                    | Complete case <sup>a</sup> |
|--------------------------------------------------------------------------------|-------------------|--------------------|----------------------------|
|                                                                                | MS                | Controls           | MS                         |
|                                                                                | <i>n</i> = 47,166 | <i>n</i> = 184,124 | <i>n</i> = 37,792          |
| Mean ± sd                                                                      | 0.34 ± 0.73       | 0.26 ± 0.64        | 0.35 ± 0.74                |
| Paraplegia                                                                     | 4687 (9.9)        | 201 (0.1)          | 4026 (10.7)                |
| Healthcare use                                                                 |                   |                    |                            |
| ≥ 1 inpatient hospitalization related to MS during index year <sup>c</sup>     | 3120 (6.6)        |                    | 2594 (6.9)                 |
| ≥ 1 inpatient hospitalization not related to MS during index year <sup>c</sup> | 6830 (14.5)       | 15,349 (8.3)       | 5712 (15.1)                |
| ≥ 2 DMT reimbursements during follow-up                                        | 19,135 (40.6)     |                    | 15,599 (41.3)              |
| Any high efficacy                                                              | 5377 (11.4)       |                    | 4407 (11.7)                |
| Fingolimod                                                                     | 3438 (7.3)        |                    | 2806 (7.4)                 |
| Natalizumab                                                                    | 1474 (3.1)        |                    | 1212 (3.2)                 |
| Ocrelizumab                                                                    | 1363 (2.9)        |                    | 1131 (3.0)                 |
| Any moderate efficacy                                                          | 16,260 (34.5)     |                    | 13,198 (34.9)              |
| Cladribine                                                                     | 10 (<0.1)         |                    | 9 (<0.1)                   |
| Dimethyl fumarate                                                              | 3778 (8.0)        |                    | 3158 (8.4)                 |
| Glatimer acetate                                                               | 4121 (8.7)        |                    | 3334 (8.8)                 |
| Interferon beta                                                                | 8318 (17.6)       |                    | 6549 (17.3)                |
| Teriflunomide                                                                  | 5692 (12.1)       |                    | 4718 (12.5)                |
| Index year <sup>c</sup>                                                        |                   |                    |                            |
| 2012                                                                           | 27,803 (58.9)     | 109,083 (59.2)     | 21,074 (55.8)              |
| 2013                                                                           | 2624 (5.6)        | 10,275 (5.6)       | 2032 (5.4)                 |
| 2014                                                                           | 2748 (5.8)        | 10,749 (5.8)       | 2131 (5.6)                 |
| 2015                                                                           | 2838 (6.0)        | 10,981 (6.0)       | 2488 (6.6)                 |
| 2016                                                                           | 2833 (6.0)        | 10,995 (6.0)       | 2551 (6.8)                 |
| 2017                                                                           | 2773 (5.9)        | 10,722 (5.8)       | 2485 (6.6)                 |
| 2018                                                                           | 2790 (5.9)        | 10,715 (5.8)       | 2534 (6.7)                 |
| 2019                                                                           | 2757 (5.8)        | 10,604 (5.8)       | 2497 (6.6)                 |
| Follow-up duration, years, median [IQR]                                        | 8 [5–10]          | 9 [5–10]           | 8 [5–10]                   |
| Follow-up duration, years, mean ± sd                                           | 7.5 ± 2.6         | 7.7 ± 2.6          | 7.3 ± 2.7                  |

Abbreviations: CMU, "Couverture médicale universelle" (i.e., Universal medical coverage); DMT, disease-modifying therapy; FDep, ecological social deprivation index; IQR, interquartile range; MRMI, Mortality-Related Morbidity Index; MS, multiple sclerosis; sd, standard deviation.

<sup>a</sup>Complete case population used for the fully adjusted analysis.

<sup>b</sup>Unadjusted for age, excluding multiple sclerosis and paraplegia.

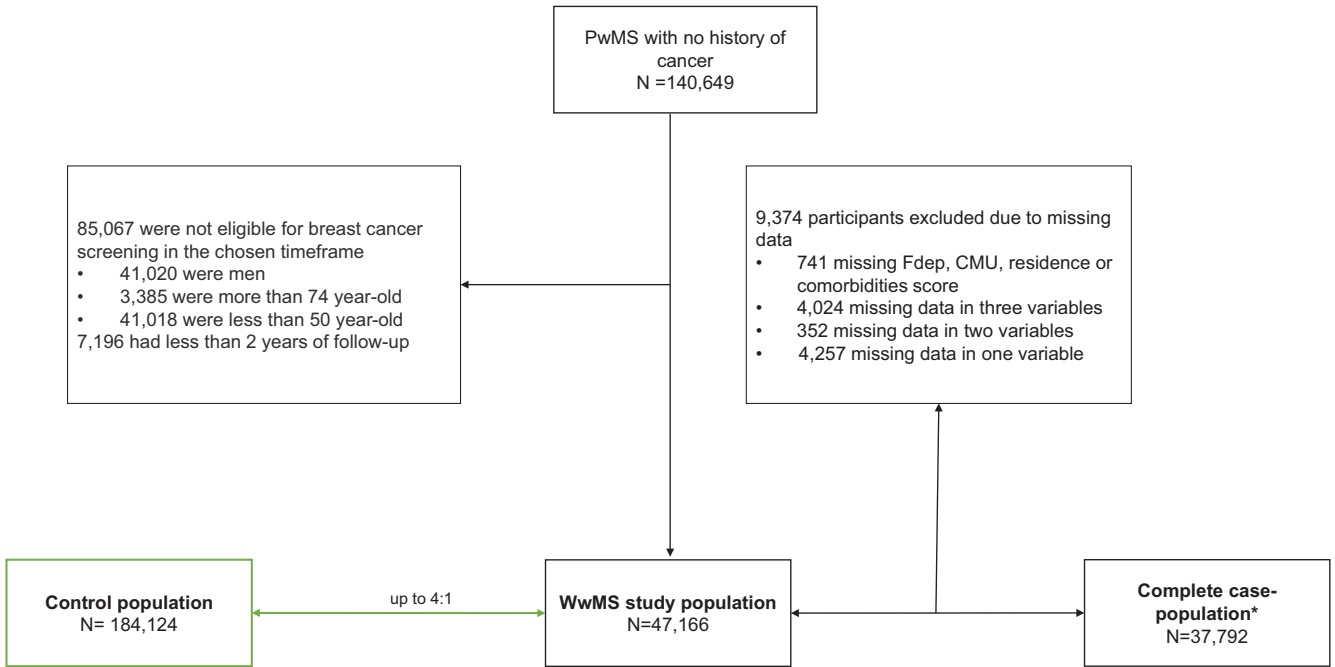
<sup>c</sup>Index year corresponds to the calendar year of the index date (i.e., date of entry in cohort).

status (FDep quintile), rates decreased as the FDep (deprivation) increased in both groups, and rates were consistently lower (−10% to −15%) in WwMS across all quintiles (Figure 3). The yearly mammography rates from 2012 to 2021 (Figure 3) showed stable rates in WwMS until 2019 (oscillating between 0.56 [0.56–0.57] and 0.58 [0.57–0.58]) and COVID-related fluctuations in 2020–2021). Mammography rates were consistently lower (−10% to −15%) in WwMS throughout the period. In each region except overseas departments, mammography rates were lower in WwMS (−8.1% to −15.0%) (Figure S1). In

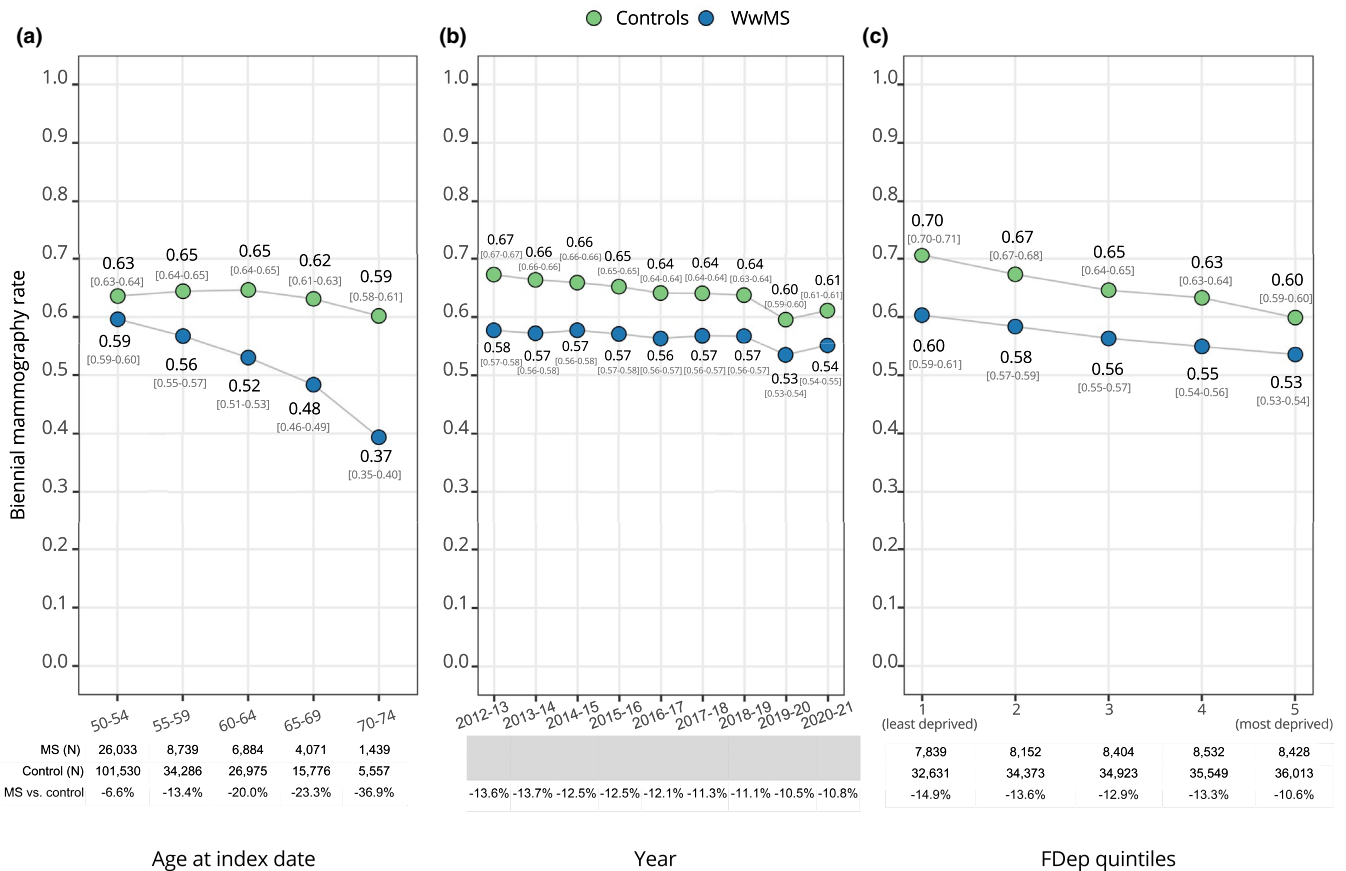
conclusion, mammography rates were lower in WwMS than in the general population, regardless of age, region of residence, socioeconomic status, and year. This difference became more pronounced in the older age groups.

### 3.1.2 | BCS According to DMT Use

When computing age-standardized biennial mammography rates according to DMT use, either a small or no difference was



**FIGURE 2** | Population flowchart.



**FIGURE 3** | Biennial mammography rates according to (a) age at index date, (b) year, (c) deprivation status (FDep quintiles).

observed in WwMS that had received at least two DMT reimbursements over follow-up compared to their matched controls (high efficacy: 0.61 [0.60–0.63] vs. 0.64 [0.63–0.65]; moderate efficacy: 0.64 [0.63–0.65] vs. 0.64 [0.63–0.64]; MS vs. controls, respectively). However, age-standardized biennial mammography rates were much lower in the non-treated group (0.51 [0.51–0.52] vs. 0.64 [0.64–0.64]).

### 3.1.3 | Factors Associated With BCS in WwMS

Table 2 shows the estimates from the adjusted logistic and negative binomial regression models and Table S1 summarizes the crude estimates from the univariate analyses. Factors associated with lower mammography rates in WwMS, independently of age, year, and region of residence were living in a city with higher deprivation (most deprived vs. least deprived; IRR 0.88 [0.86–0.91]), CMU beneficiary (0.76 [0.72–0.80]), MS duration  $\geq 16$  years (16–25 years vs.  $\leq 5$  years: 0.91 [0.89–0.94];  $\geq 26$  years vs.  $\leq 5$  years: 0.87 [0.83–0.91]), and hospitalization 12 months before inclusion (MS-related hospitalization: 0.85 [0.82–0.88]; non-MS-related hospitalization: 0.92 [0.89–0.94]), comorbidity status at baseline (1 vs. 0: 0.91 [0.89–0.93]). Conversely, being treated for MS was associated with higher mammography rates for both high- and moderate-efficacy DMTs ( $\geq 1$  high-efficacy DMT vs. no DMT: 1.17 [1.14–1.21]; only moderate-efficacy vs. no DMT: 1.18 [1.16–1.20]). Similar findings were observed in the adjusted logistic models for the binary outcomes.

### 3.1.4 | Missing Data

Table 1 compares baseline characteristics between the complete-case population ( $n = 37,792$ ) and the study population including missing data ( $n = 47,166$ ). No missingness pattern was noted, and it was assumed that data were missing at random. Data imputation yielded similar results as the complete-case analysis (Table S2).

## 3.2 | Qualitative Component

Twenty semistructured interviews (duration: 20–40 min) were conducted with WwMS eligible to the organized BCS (mean age: 62 years, range: 50–74; mean MS duration: 26 years, range: 1–46). Twelve of these women reported walking limitations, including needing a cane ( $n = 4$ ) and using a wheelchair ( $n = 4$ ) (Table S3). Seventeen (85%) reported undergoing BCS and following the national BCS recommendations. The identified barriers and facilitators and the corresponding quotes are summarized in Table 3.

### 3.2.1 | MS Effect on the Perception of Preventive Care

Participants said that MS influenced their relationship to preventive care. Two opposing points of views were identified. Some women reported that MS increased their health awareness: “I’ve already got MS, so if we can avoid the rest, that would be good” (Cécile). For others, MS left no room for other care types: “Everything revolves around MS. So after that, there’s not much room for anything else” (Chantale). Some women reported

feelings of over-medicalization, such as Valerie who felt “overwhelmed” by the “overdose of medical appointments.”

### 3.2.2 | Accessibility

Physical accessibility of the screening center and procedure was a major concern for participants, especially those with reduced mobility. Magalie mentioned: “the people who developed these machines did not realize that not everyone can stand.” Lack of proper accessibility led to uncomfortable situations: “There had to be two persons holding me [...] At some point I was on the floor” (Martine). Conversely, adjustments by the healthcare personnel and the screening center were seen as facilitators. Sylvie reported no difficulties because “the screening center adapts to [her] disability.”

To bypass accessibility issues and travel-related fatigue, WwMS often had to rely on an informal caregiver, mainly the partner. However, this created inequities for those without one; for example, Laurence thought that others in her situation would have already given up: “I am sick of being told to bring someone to my appointments. I don’t know anyone who can carry me. Some give up but I don’t!”. Some women expressed worry about MS progression and how this would affect their ability to adhere to the BCS program: “It’s going to be hard to get screened at some point” (Agnès).

Lastly, concerns about the popularization of online medical appointment services were raised. Indeed, some centers can no longer be reached by phone to obtain information on specific accommodation for their disability. As WwMS “need [...] to know if the place is accessible”, they call in advance to “put in some safeguards” and “make sure [they]’re not going for nothing” (Murielle).

### 3.2.3 | Organizational Difficulties

Additional sources of organizational difficulties were mentioned, such as the lack of appointments and work-related schedule issues. As BCS appointments are difficult to find, one might have to use a vacation day from work to attend, which adds to the vacation days used for MS-related healthcare. Frederique stated that she “cannot afford” to do that because she “take[s] enough days off work for the MS treatment.”

Moreover, fatigue, a common MS symptom, was reported as a barrier to BCS especially concerning travel: “Not only is it tough to get an appointment, but it’s also super far. I’m tired from traveling” (Marjorie). Fatigue exacerbates every other challenge that WwMS may be facing when trying to access BCS: “All this seems a bit overwhelming to me, with the fatigue, the pre-organization. It’s complicated” (Magalie).

### 3.2.4 | BCS Facilitators

The most mentioned facilitator was the perception of BCS as a routine procedure that is part of a “woman’s journey” (Estelle). They compared mammography to “going to the

**TABLE 2** | Factors associated with mammography use by women with multiple sclerosis, results of the adjusted negative binomial and logistic models ( $n = 37,792$ ).

|                                                                                | Biennial mammography rate |          | ≥ 1 mammography during follow-up |          | ≥ 1 mammography every 3 years |          |
|--------------------------------------------------------------------------------|---------------------------|----------|----------------------------------|----------|-------------------------------|----------|
|                                                                                | IRR (95% CI)              | <i>p</i> | OR (95% CI)                      | <i>p</i> | OR (95% CI)                   | <i>p</i> |
| Socio-demographic characteristics                                              |                           |          |                                  |          |                               |          |
| Age, years                                                                     |                           |          |                                  |          |                               |          |
| 50–55                                                                          | Ref.                      |          | Ref.                             |          | Ref.                          |          |
| 56–60                                                                          | 0.99 (0.96–1.01)          | 0.251    | 0.90 (0.84–0.96)                 | 0.001    | 1.28 (1.19–1.37)              | <0.001   |
| 61–65                                                                          | 0.93 (0.90–0.95)          | <0.001   | 0.74 (0.69–0.79)                 | <0.001   | 1.18 (1.08–1.28)              | <0.001   |
| 66–70                                                                          | 0.89 (0.86–0.93)          | <0.001   | 0.64 (0.58–0.69)                 | <0.001   | 1.12 (0.99–1.26)              | 0.073    |
| 71–74                                                                          | 0.72 (0.66–0.79)          | <0.001   | 0.30 (0.26–0.34)                 | <0.001   | 5.23 (3.46–7.92)              | <0.001   |
| Deprivation index—FDep, quintiles                                              |                           |          |                                  |          |                               |          |
| 1st (least deprived)                                                           | Ref.                      |          | Ref.                             |          | Ref.                          |          |
| 2nd                                                                            | 0.95 (0.93–0.98)          | 0.002    | 0.91 (0.84–0.99)                 | 0.021    | 0.95 (0.87–1.03)              | 0.214    |
| 3rd                                                                            | 0.92 (0.90–0.95)          | <0.001   | 0.83 (0.76–0.90)                 | <0.001   | 0.96 (0.88–1.06)              | 0.434    |
| 4th                                                                            | 0.90 (0.87–0.93)          | <0.001   | 0.79 (0.73–0.86)                 | <0.001   | 0.90 (0.83–0.99)              | 0.031    |
| 5th (most deprived)                                                            | 0.88 (0.86–0.91)          | <0.001   | 0.74 (0.68–0.80)                 | <0.001   | 0.90 (0.82–0.99)              | 0.033    |
| MS duration, years                                                             |                           |          |                                  |          |                               |          |
| 0–5                                                                            | Ref.                      |          | Ref.                             |          | Ref.                          |          |
| 6–10                                                                           | 0.97 (0.94–0.99)          | 0.007    | 0.94 (0.87–1.00)                 | 0.068    | 0.95 (0.88–1.02)              | 0.164    |
| 11–15                                                                          | 0.98 (0.95–1.00)          | 0.052    | 0.95 (0.88–1.02)                 | 0.131    | 0.95 (0.88–1.02)              | 0.179    |
| 16–25                                                                          | 0.91 (0.89–0.94)          | <0.001   | 0.81 (0.76–0.86)                 | <0.001   | 0.87 (0.80–0.93)              | <0.001   |
| 26+                                                                            | 0.87 (0.83–0.91)          | <0.001   | 0.75 (0.67–0.84)                 | <0.001   | 0.78 (0.68–0.90)              | 0.001    |
| CMU beneficiary                                                                | 0.76 (0.72–0.80)          | <0.001   | 0.58 (0.51–0.65)                 | <0.001   | 0.55 (0.47–0.65)              | <0.001   |
| Healthcare use                                                                 |                           |          |                                  |          |                               |          |
| ≥ 1 inpatient hospitalization related to MS during index year <sup>a</sup>     | 0.85 (0.82–0.88)          | <0.001   | 0.74 (0.68–0.81)                 | <0.001   | 0.70 (0.63–0.78)              | <0.001   |
| ≥ 1 inpatient hospitalization not related to MS during index year <sup>a</sup> | 0.92 (0.89–0.94)          | <0.001   | 0.80 (0.75–0.85)                 | <0.001   | 0.90 (0.83–0.97)              | 0.009    |
| DMT use over follow-up                                                         |                           |          |                                  |          |                               |          |
| None                                                                           | Ref.                      |          | Ref.                             |          | Ref.                          |          |
| ≥ 1 high efficacy                                                              | 1.17 (1.14–1.21)          | <0.001   | 1.68 (1.54–1.82)                 | <0.001   | 1.14 (1.05–1.24)              | 0.003    |
| Only moderate efficacy                                                         | 1.18 (1.16–1.20)          | <0.001   | 1.67 (1.58–1.76)                 | <0.001   | 1.26 (1.19–1.34)              | <0.001   |

(Continues)

TABLE 2 | (Continued)

|                         | Biennial mammography rate |        | ≥ 1 mammography during follow-up |        | ≥ 1 mammography every 3 years |        |
|-------------------------|---------------------------|--------|----------------------------------|--------|-------------------------------|--------|
|                         | IRR (95% CI)              | p      | OR (95% CI)                      | p      | OR (95% CI)>                  | p      |
| Comorbidities           |                           |        |                                  |        |                               |        |
| MRMI score <sup>b</sup> |                           |        |                                  |        |                               |        |
| 0 (No comorbidity)      | Ref.                      |        | Ref.                             |        | Ref.                          |        |
| 1                       | 0.91 (0.89–0.93)          | <0.001 | 0.89 (0.83–0.95)                 | <0.001 | 0.74 (0.69–0.79)              | <0.001 |
| 2                       | 0.83 (0.80–0.87)          | <0.001 | 0.78 (0.70–0.87)                 | <0.001 | 0.65 (0.57–0.74)              | <0.001 |
| 3+                      | 0.79 (0.74–0.84)          | <0.001 | 0.71 (0.61–0.82)                 | <0.001 | 0.55 (0.45–0.67)              | <0.001 |
| Paraplegia              | 0.72 (0.70–0.75)          | <0.001 | 0.58 (0.54–0.63)                 | <0.001 | 0.58 (0.52–0.64)              | <0.001 |

Note: All models were adjusted for age, FDep, MS duration, CMU, MS-related and non-MS-related hospitalization, DMT use, and region of residence at entry. Logistic models (OR) were additionally adjusted on period and follow-up duration.

Abbreviations: 95% CI, 95% confidence interval; CMU, “Couverture médicale universelle” (i.e., Universal medical coverage); DMT, disease-modifying therapy; FDep, ecological social deprivation index; IRR, Incidence rate ratio; MRMI, mortality-related morbidity index; MS, multiple sclerosis; OR, Odds ratio.

<sup>a</sup>Index year corresponds to the full calendar year of the index date (i.e., date of entry in cohort).

<sup>b</sup>Unadjusted for age, excluding multiple sclerosis and paraplegia.

dentist” (*Françoise*) or “getting your period every month” (*Estelle*). Healthcare professionals, especially the gynecologist, played a key role in incentivizing women. Many women said that they were mentally prepared by their doctor to receive a BCS invitation by mail on their 50th birthday and according to Chantale: “*It all depends, in the end, on the relationship you have with your general practitioner.*”

Lastly, as WwMS require multiple healthcare appointments, some interviewees suggested to group medical procedures into a single day and location to reduce the feelings of over-medicalization, travel-related fatigue, and work-related scheduling difficulties: “[they] could organize a check-up day. It’d be taken care of, so you don’t have to take days off work, and you do it all at once, so it’s less stressful.” (*Elise*).

#### 4 | Discussion

This mixed-methods study highlights constant suboptimal BCS in WwMS in the last 10 years. Overall, the biennial BCS rate in WwMS was 0.55, meaning 55 mammographies were done per 200-person years, and only 70% of WwMS had at least one mammography during the study period. Mammography rates were consistently lower (by 10%–15%) in WwMS than in controls, regardless of age, period, deprivation index, and region of residence. This difference was mainly driven by non-treated individuals, independently of age.

Combining quantitative and qualitative results allowed identifying key barriers and facilitators to BCS. Long MS duration, hospitalizations (associated or not with MS), comorbidity, not being treated for MS, and older age were all negatively associated with mammography rates. This can be related to the themes of accessibility and the feeling of over-medicalization. Women with more active and degenerative MS face more challenges in accessing BCS. As MS progresses, independence decreases, healthcare needs increase, and preventive care (e.g.,

BCS) becomes less accessible and less important. The interviews suggested that healthcare professionals play a central role in the perception of BCS as a routine procedure and in offering solutions to the specific needs of WwMS. Access to informal support and disability-accessible preventive care were BCS facilitators. Some women reported that they required someone’s assistance to go to the BCS center and during the mammography. However, access to these facilitators was heterogeneous, leaving women with little to no access to informal care with feelings of being overwhelmed and tired.

Some of the identified barriers had been previously reported [23]. However, our study identified new topics. Particularly, some women felt that MS led them to take better care of their health and motivated them to undergo BCS. The previous study only reported that women felt like they had too much to handle with MS and doubted their ability to face another disease. This discrepancy could be explained by a difference in context, period, and health systems, leading to different perceptions and optimism concerning the outcome of a BC diagnosis, and to different views of its financial, physical, and mental burden. Moreover, our interviewees stressed the importance of informal caregivers and healthcare professionals as facilitators.

To our knowledge, this was the first study to formally assess BCS in WwMS and to show disparities compared with a matched sample from the general population associated with qualitative data collection. However, previous quantitative findings from Canadian studies suggested a similar conclusion [20, 21].

One of the main strengths of this mixed-methods approach was the inclusion of population-based estimates of BCS in WwMS and in a matched sample from the general population, and the identification, by statistical analysis, of risk factors of lower mammography rates. Moreover, the qualitative component added context and allowed us to delve deeper into the WwMS’ experiences, attitudes, and perceptions. By combining both approaches, findings could be triangulated, increasing their

**TABLE 3** | Breast cancer screening: Barriers and facilitators; quotes.

| BCS Barriers                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | Organizational difficulties: Online appointments and disability                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Organizational difficulties: Lack of available appointments                                                                                                                                                                                                                                                                                                                                             | Work-related organizational difficulties                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Having to rely on someone                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Transportation issues (travel-related fatigue, organization)</b>                                                                                                                                                                                                                                                                                                  | <b>BCS center (current or future) accessibility</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | <b>Feelings of over-medicalization</b>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| (1) "Not only is it tough to get an appointment, but it's also super far. I'm tired from the traveling." (Marjorie)<br>(2) "All of this seems a bit overwhelming to me, with the fatigue, the pre-organization... It's complicated." (Magalie).<br>(3) "I have to drive 50 km to and from because I live in the countryside... I am tired from the trips" (Marjorie) | (1) "The machine is not adapted for wheelchairs" "It will take 15 min for someone who can stand up, but for me it takes an hour... there had to be two persons to hold me ... At some point I was on the floor" (Martine)<br>(2) "The people who developed these machines did not realize that some people cannot stand" "I could not go on the gynecologist table anymore because it could not lower it. [...] I will always get screened for cancer, except for mammography because it is starting to get complicated" (Murielle)<br>(3) "It's complicated because you have to walk and stand; last time it was hard, but now that I can't stand, we will have to find another solution" (Magalie)<br>(4) "I choose places that are accessible by tramway, which I can access with my wheelchair" (Murielle)<br>(5) "The healthcare professionals want me to lay on a bed on which I can't climb as someone with reduced mobility" (Laurence)<br>(6) "It's going to be hard to get screened at some point" (Agnès) | (1) "I spend all my time at the doctor's [...] At some point, it's a bit annoying, you know." (Francoise)<br>(2) "Everything revolves around multiple sclerosis. So after that, there's not much room for anything else." (Chantale)<br>(3) "This year, I postponed them because I was getting tired of seeing doctors, I admit. I was starting to feel a bit overwhelmed, completely overwhelmed. Rather, I felt like it was too much." (Valerie)<br>(4) "Doctors, I have to see this one, I have to see that one, I have to see another one. I can't take it anymore. So I'm certainly not going to go and ask for tests myself." (Veronique)<br>(5) "An over-dose of medical appointments" (Valérie)<br>[...] I'm not afraid of the disease [...] I'm just fed up because I've spent a lot of time there. [...] It's exhausting, actually, to have to organize these appointments in terms of travel, deadlines..." (Marise) | (1) "The time constraints are difficult, with the fatigue and the drive, having to organize with work and trying to put all the appointments together..." (Frédérique)<br>(2) "It's a pain. It's a disaster to find appointments." (Marjorie)<br>(3) "Scheduling appointments can discourage a lot of people" (Agnès)<br>(4) "I call 2 months in advance. It's because there's no appointment." (Elise) | (1) "In relation to my work, [...] I can't afford it. I already take enough days off work with the treatment for multiple sclerosis. I can't afford it." (Frédérique)<br>(2) "I am a lawyer, I have a very busy schedule ... It's very complicated to organize for me" (Maryse)<br>(3) "Everything takes time, for treatments I have to take days off work, it's a bit annoying" (Francoise)<br>(4) "I manage to schedule my appointments because I'm not afraid to organize around work. Health comes first, so I go to my appointments even if I have to take time off. It's not my problem if they're not happy." (Elise) | (1) "I am sick of being told to bring someone to my appointments. I don't know anyone that can carry me. Some give up but I don't! One nurse for each arm for the mammography!" (Laurence)<br>(2) "Someone has to take me" (Magalie)<br>(3) "Well, my husband acts as the chauffeur" "As I have a lot of difficulties for moving around, it's always my partner who drives me in the car, because I can't drive anymore. It's quite heavy." (Chantale)<br>(4) "My husband drives me" (Sylvie)<br>(5) "My husband helps me a lot" (Marjorie) |

(Continues)

TABLE 3 | (Continued)

| BCS Facilitators                      |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Heightened health awareness due to the existing chronic condition (MS)                                                                                                                                                                                                                                                                                                                                 | Grouping medical procedures in 1 day                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Adaptability of the BCS center to the disability                                                                                                                                                                                                                                                                                                                                                                                                                                       |
|---------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Routine and BCS seen as a norm</b> | <p>(1) "It's the follow-up with a gynecologist that does everything. It's important to be used to having examination like that, by talking to the gynecologist." (Marjorie)</p> <p>(2) "My gynecologist and my general practitioner Ask me if I follow the recommendations and if I do the tests as recommended. I'm under no obligation to do so, but it's an incentive to do so and it's organized." (Cécile)</p> <p>(3) "I see a gynecologist regularly and I receive breast cancer screening invitations by mail." (Catherine)</p> <p>(4) "Regarding breast cancer, I go to see my gynecologist every 10 months. It's a habit really, I don't question it." (Virginie)</p> | <p>(1) "I've already got MS, so if we can avoid the rest, that would be good. I've already got my burden. I don't want to carry around 36,000 other ones, if we can avoid it." (Cécile)</p> <p>(2) "I did all of it [cancer screening]. I said even though I already have MS, might as well get screened for everything else" (Estelle)</p> <p>(3) "Having MS pushed me to get screened" (Martine)</p> | <p>(1) "I want to make only one trip. So I try to take appointments on the same days [as DMT treatments] because I'm in the area. And the answer is... it's already full" (Frédérique)</p> <p>(2) "I now have the advantage of having a gynecologist and a general practitioner in neighboring offices who share all information on the same server. So, everything's in one place..." (Cécile)</p> <p>(3) "The mammography examination room was at the gynecologist's, so it was on site. So, it was easier, it was all in one place. That's the only time I managed to get screened." (Frédérique)</p> | <p>(1) "They adapt to me, wherever I go. The screening center adapts to my disability" (Sylvie)</p> <p>(2) "With my electric wheelchair and accessible public transportation, I can go where I want in the city [including the BCS center]" (Martine)</p> <p>(3) "I have to ask if the exam can be arranged so that I can stand by holding to something or possibly sit." (Magalie)</p> <p>(4) "Knowing the center well, the nurses, they know it's complicated for me" (Chantale)</p> |

validity and reliability. The mixed-methods approach allowed us to address the research question comprehensively.

Another strength lies in the comprehensiveness of the used population-based database. This database includes all health-care consumption (both public and private) data for, including mammography procedures, on ~99% of the French population [25], leading to little or no selection bias. Moreover, as this database relies on reimbursements and not self-reporting, recall and social desirability bias are minimized. Although a small percentage of identified mammography reimbursements could have been related to diagnosis and not screening, this possibility was minimized by only including individuals without a history of cancer. However, clinician's diagnoses are not available, and an MS identification algorithm is used to define our population. Hence, we cannot exclude that a few individuals with MS-related care consumption that did not have MS were included. To minimize this potential issue, we did not include individuals with only one MS hospitalization and no other MS-related care consumption, as well as individuals with only one MS-specific DMT reimbursement or individuals with neuromyelitis optica spectrum disorder hospitalizations [26].

The quantitative analyses could not be adjusted for physical disability and overall health status, although they were identified as perceived barriers to BCS in our qualitative analysis; therefore, proxy variables (MS disease duration and hospitalization) were used. Similarly, some indications on the participants' socio-economic status were available (e.g., FDep and CMU), but not others (e.g., employment and household income). In the qualitative data, organizational difficulties were mentioned by WwMS with physical disability and by those still in employment. These data were not available in the quantitative dataset for these specific characteristics. Nevertheless, a lower BCS rate was associated with longer disease duration, which could be a proxy for physical disability, independently of age.

To conclude, although most WwMS expressed a positive view on BCS, access to screening was suboptimal, especially for WwMS with worse overall health status and more degenerative or advanced disease. The pivotal role of healthcare professionals in preparing and encouraging women to get screened was highlighted. Working toward a more disability-accessible approach and grouping preventive services together could promote BCS adherence and reduce the WwMS and informal caregivers' burden, thus contributing to decrease inequity in access to preventive care.

#### Author Contributions

**Chloe Pierret:** data curation, formal analysis, writing – original draft, conceptualization, methodology, validation, visualization. **Lou Philippe:** writing – review and editing, formal analysis, data curation, validation, methodology, conceptualization. **Emmanuelle Leray:** conceptualization, funding acquisition, writing – review and editing, methodology, resources, supervision.

#### Conflict of Interest

C. Pierret and L. Philippe declare no conflicts of interests. E. Leray reports consulting and lecture fees or travel grants from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi, not related to the submitted work.

#### Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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### Supporting Information

Additional supporting information can be found online in the Supporting Information section.