# OFSEP

**Observatoire Français
de la Sclérose en Plaques**

## FROM LIFE TO SCIENCE
## MS DATA IS OUR COMMITMENT

# OFSEP,
# the French MS registry

## ECTRIMS 2023

# OFSEP scientific presentations

# at ECTRIMS 2023

## Wednesday 11 October

### Poster session 1

**P023** Late-onset MOGAD : a French multicenter retrospective study. Julie Pique (France)

**P062** Evidence of disease activity during pregnancy and post-partum in MS patients treated with high-efficacy therapies: a monocentric retrospective study. Oussama Sahloul (France)

**P063** Assessing the risk of relapse after in vitro fertilization in women with multiple sclerosis. Marie Mainguy (France)

**P125** Identification of new NMOSD and MOGAD genetic associations. Nicolas Vince (France)

**P269** Can we accurately assess disease activity using automated methods in large real-life MRI databases? Insights from the OFSEP HD database. Arthur Masson (France)

### Free communications 2 - Real world evidence (RWE) – Treatment

☉ 14:45-14:55 - Room Brown 3

**O043 - Silent Progression Activity Monitoring in MS despite an early highly active treatment: the SPAM study.** Christine Lebrun-Frenay (France)

## Thursday 12 October

### Poster session 2

**P462** Pregnancy and birth outcomes in MS women : comparison of the RESPONSE cohort to the general French population. Elisabeth Maillart (France)

**P464** RESPONSE, a French cohort of pregnant women with MS and related disorders and their children until the age of 6. Protocol and baseline characteristics. Sandra Vukusic (France)

**P670** PRIMUS: a clinical decision support system for precision medicine in multiple sclerosis contextualizing patients evolutions in multi-source reference data. Stanislas Demuth (France)

**P1546** Impact of lesions detection support system on the therapeutic strategy proposed by the neurologist to Multiple Sclerosis patients. Anne Kerbrat (France)

## Friday 13 October

### Educational Session 13 - MOGAD - phenotypes and management

🕐 8:50-9:05 - Room Silver

**MOGAD in adults**

Romain Marignier (France)

### Scientific Session 15: Paediatric MS - updates on diagnosis, prognostic and treatment

🕐 10:42-10:49  - Room Gold

**Highly effective therapies as first-line treatments for pediatric onset multiple sclerosis in a French nationwide cohort**

Nail Benallegue (France)

# The French MS registry

## Collected data

# Clinical data collection

**FROM LIFE ...**

Physician visit or hospitalization

Collection

Data collection during patient visit

**Clinical**

**Imaging**

**Biology**

Standardized minimal data

+ additional data for specific projects

Gathering

- Data reconciliation
- Control
- Queries
- Statistical analyses
- Reports

Data gathered in the OFSEP common database

Data available for researchers

Projects

**... TO SCIENCE**

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# Clinical data collection

- Clinical data collected during routine follow-up visits, usually at least once a year, retrospectively at the first visit and prospectively thereafter

- Minimal mandatory data set:
  - demographic and socioeconomic characteristics
  - neurological episodes
  - disability
  - brain and spinal cord MRI reports
  - disease-modifying treatments
  - serious adverse events

- Patients with RIS, CIS, MS, NMOSD or MOGAD followed up in a participating centre are eligible

- All French MS expert centers and several peripheral centers participate in data collection

# Clinical data collection

About

**80,000**
patients all around France

**20,000**
patients followed-up
every year

1,100,000 person-years of disease

> 500,000 person-years of prospective follow-up

# Imaging data collection (MRI)

**FROM LIFE ...**

Physician visit or hospitalization

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Data collection during patient visit

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# MRI

**OFSEP cerebral and spinal cord MRI acquisition protocol\*,**
a consensus within the scientific community, feasible on all equipment and compatible with clinical acquisition times

**Recommended sequences:**

- **Brain:** 3D FLAIR, 3D T1, DWI, 3D T1 gado *(if necessary)*
- **Spine:** T2 SAG, T1 gado SAG *(if necessary)*

**DICOM files** stored on a centralized neuroimaging platform

*\* Brisset JC, Kremer S, Hannoun S, et al. New OFSEP recommendations for MRI assessment of multiple sclerosis patients: special consideration for gadolinium deposition and frequent acquisitions. J Neuroradiol. 2020;47(4):250-258.*

**Last year** > **2,500** new patients | > **18,000** exams | > **130,000** sequences

**9,134** patients with at least one MRI scan

| | |
|---|---|
| **33,485** brain exams | **312,476** brain sequences |
| **14,629** spinal cord exams | **80,499** spinal cord sequences |

# Brain MRI
## Main sequences
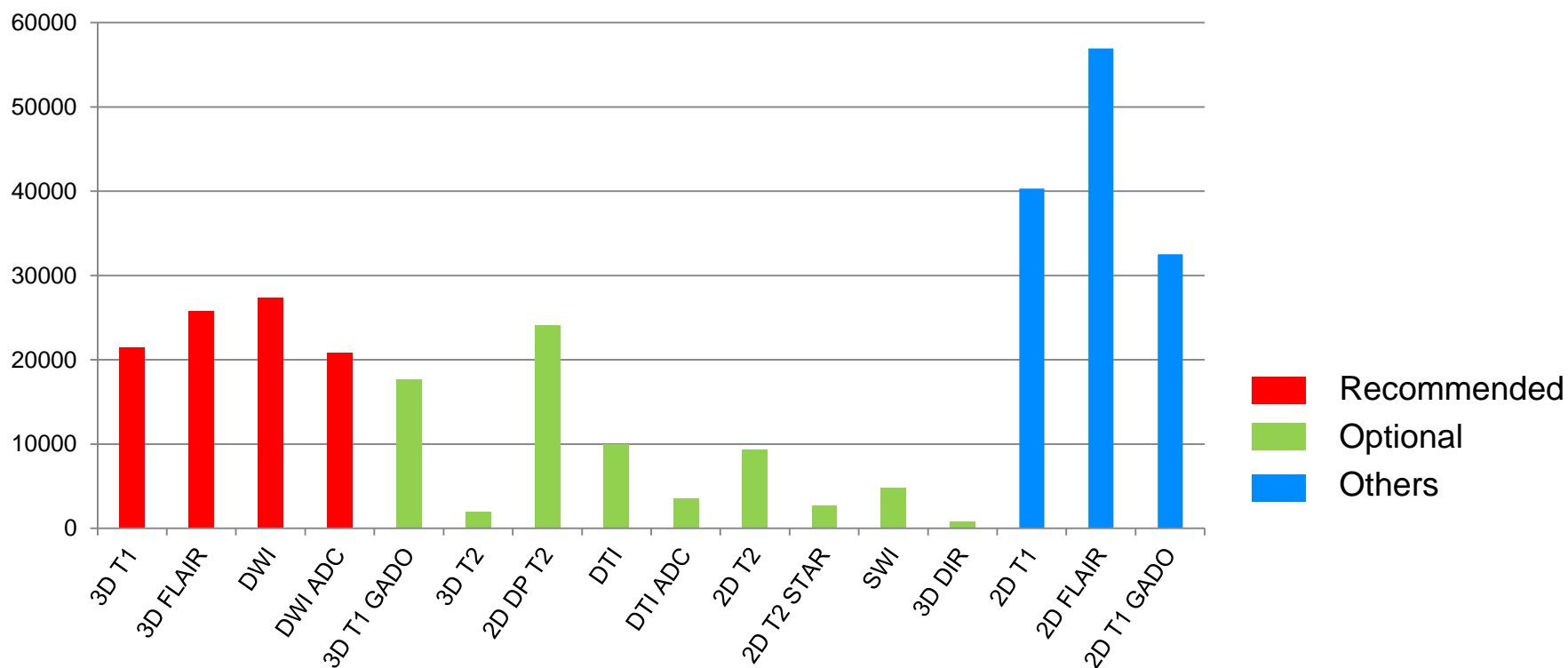
**33,485** brain exams

**312,476** brain sequences

Legend:
- Recommended (red)
- Optional (green)
- Others (blue)

Siemens: 56%
Philips: 25%
GE: 18%

1.5T: 47%
3T: 53%

16

# Brain MRI

| | | |
|---|---|---|
| **33,485** brain exams | **312,476** brain sequences | |

| Number of patients | | | | | | |
|---|---|---|---|---|---|---|
| | 1 TP* | 2 TP | 3 TP | 4 TP | 5-10 TP | > 10 TP |
| Brain IRM | 2,168 | 1,377 | 956 | 751 | 1,535 | 202 |

\* Time point

| Disease form at the first MRI | N |
|---|---|
| RIS | 128 |
| First attack | 2,423 |
| RRMS | 4,469 |
| SPMS | 856 |
| PPMS | 648 |
| NMOSD | 155 |
| MOGAD | 112 |
| Not currently identified | 177 |

# Spinal cord MRI
## Main sequences

**14,629** spinal cord exams | **80,499** spinal cord sequences
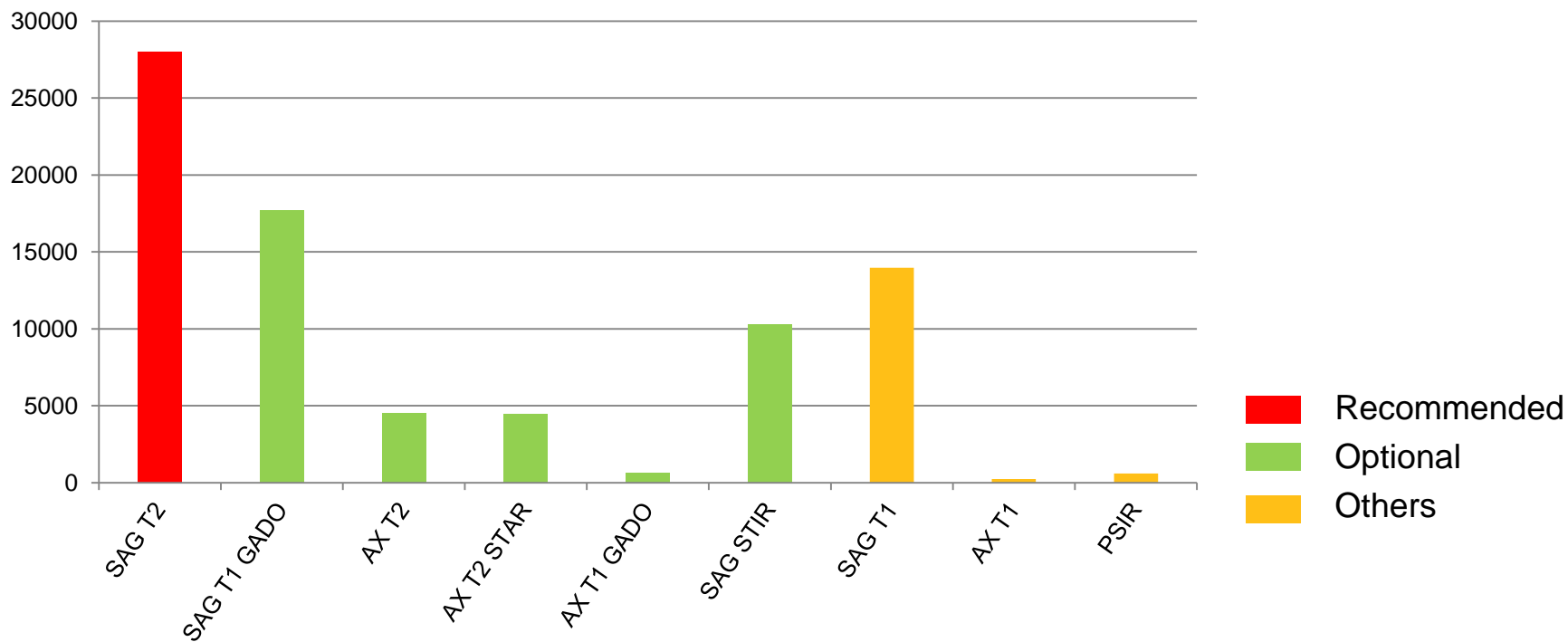
Siemens: 67%    1.5T: 69%
Philips: 19%    3T: 31%
GE: 13%

# Spinal cord MRI

**14,629** spinal cord exams

**80,499** spinal cord sequences

| Number of patients | | | | | | |
|---|---|---|---|---|---|---|
| | 1 TP* | 2 TP | 3 TP | 4 TP | 5-10 TP | > 10 TP |
| Spinal cord MRI | 2,121 | 916 | 494 | 288 | 374 | 15 |

\* Time point

| Disease form at the first MRI | N |
|---|---|
| RIS | 78 |
| First attack | 1,725 |
| RRMS | 3,003 |
| SPMS | 558 |
| PPMS | 483 |
| NMOSD | 143 |
| MOGAD | 90 |
| Not currently identified | 107 |

# Biology samples collection

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Data gathered in the OFSEP common database
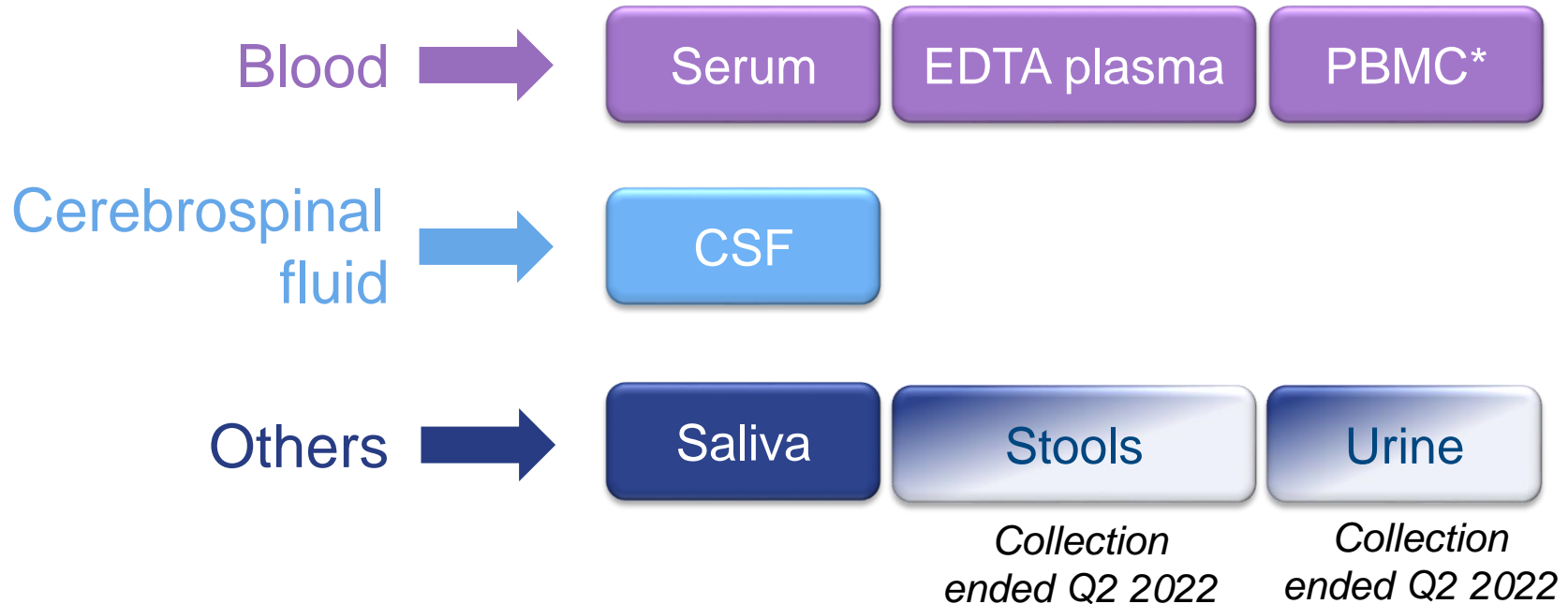
Data available for researchers

Projects

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# Integrated cohorts with biological samples

| Cohort | Iterative sample |
|---|---|
| **Radiologically isolated syndromes (RIS)** | Every year until conversion |
| **Clinical isolated syndromes and relapsing-remitting MS (CIS / RRMS) 'First Attack'**<br>- Sample at less than 6 months of the first inflammatory event of the central nervous system<br>- DMT naive at first sample | At year 1, 3 and 5 and during a relapse |
| **Primary progressive multiple sclerosis (PPMS)**<br>- Less than 6 years disease duration<br>- Untreated patient | No |
| **Neuromyelitis optical spectrum disorders (NMOSD) and Myelin oligodendrocyte glycoprotein-IgG (MOG-IgG) associated disorder (MOGAD) – NOMADMUS cohort** | At year 1, 3 and 5 for patients included after the first relapse and before the second one. Additional sample during a relapse. |
| **Acute Disseminated EncephaloMyelitis (ADEM)** | No |
| **Progressive Multifocal Leukoencephalopathy (PML)** | No |
| **Covid-19**<br>- Sampling within 3 months after biological confirmation of the diagnosis by PCR or onset of symptoms | No |
| **MS patients included in High Definition (HD) cohort** | Every 2 years |

# Biological samples

**Blood** → Serum | EDTA plasma | PBMC*

**Cerebrospinal fluid** → CSF

**Others** → Saliva | Stools | Urine

*Collection ended Q2 2022* | *Collection ended Q2 2022*

*Peripheral blood mononuclear cells

6,001 biological samples collected among 4,688 patients.

| Patients‡ | N. of patients | Blood* | PBMC | CSF** | Saliva | Urine*** | Stools*** | N iterative |
|---|---|---|---|---|---|---|---|---|
| RIS | 170 | 170 | 167 | 79 | 15 | 130 | 5 | 19 |
| First attack | 1,120 | 1,120 | 774 | 535 | 21 | 685 | 33 | 176 |
| RRMS | 2,096 | 2,096 | 268 | 152 | 10 | 215 | 29 | 590 |
| SPMS | 375 | 375 | 22 | 14 | 1 | 21 | 2 | 114 |
| PPMS | 399 | 399 | 261 | 173 | 4 | 225 | 13 | 134 |
| PML | 10 | 10 | 10 | 2 | 0 | 9 | 0 | 0 |
| NMOSD | 320 | 320 | 315 | 26 | 12 | 225 | 3 | 38 |
| MOGAD | 230 | 230 | 227 | 15 | 9 | 172 | 4 | 21 |
| ADEM | 21 | 21 | 21 | 4 | 0 | 15 | 0 | 0 |
| Covid-19*** | 66 | 66 | 65 | 0 | 0 | 21 | 0 | 0 |

‡ some patients could be counted several times if they enter an new cohort during the follow-up (ex : RIS => FA)
* serum, EDTA plasma, DNA
** cerebrospinal fluid
*** closed collection

# Merging with medico-administrative database

## French National Insurance database

# Merging with medico-administrative database

- **French National Insurance database (SNDS)**

  - Reimbursements made by all health insurance plans (consulting, drug dispensing, medical procedures, biological exams, issuance of technical aids, long-term disease)

  - Hospital medical activity (hospitalizations, diagnoses, medical procedures, external consultations)

  - Death causes

- **Allows to access non-specific MS data** including comorbidities, co-prescriptions, recourse to care…

**SNDS extraction**
**2009 ~ 2019**

**>40,000**
patient files

**85%**
successfully merged

**If possible, update every year**

# The French MS registry

## Projects
## and nested cohorts

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# OFSEP HD cohort

- **Diagnosis of multiple sclerosis** according to the most recent criteria

- Age ≥ 15 years

- **Irreversible disability ≤ 7.0 (permanent use of a wheelchair) on EDSS**

- Followed up in one **MS expert center**

- New cases diagnosed after the beginning of the study

  or

- For patients diagnosed before the beginning of the study, **regular follow-up** (at least one visit every two years since the date of the first EDSS assessment) with **prospective collection of minimal dataset in EDMUS since 2011**

*Follow-up*

- Annual follow-up (± 2 months) with rebaseline at the first disease activity
- Continuation of the study at least until the end of 2026

*Specific data every year*

- PRO : sociodemographic data, medical background, quality of life (EQ5D-5L, SF-12, MusiQoL), tobacco, cannabis and alcohol consumption
- Walk test (T25FW), test of upper extremity function (9HPT), test for the detection of information processing speed (CSCT)
- MRI (post-processing) : T2 and new T2 lesions, cerebral volume and atrophy

## *Population*

- 2842 patients included between July 2018 and September 2020.
- At inclusion
  - 73% ♀
  - age = 43 years (± 12)
  - disease duration = 11 years (± 9)
  - prospective follow-up = 8 years (± 7)
  - 80% RRMS, 14% SPMS, 6% PPMS
  - untreated patients or all types of ongoing treatments

## *Biocollection*

- Blood sample and dosages (at inclusion and every two years) : NF-L, GFAP, vitamin D

# NOMADMUS cohort

- **Inclusion criteria**

  Patients meeting the international NMOSD criteria (Wingerchuk criteria 1999 and 2006, IPND 2015) including Aquaporin 4 – IgG positive patients (AQP4+)

  or  Isolated, recurrent or not, acute extensive transverse myelitis

  or  Isolated atypical optic neuritis

  or  Myelin Oligodendrocyte Glycoprotein – IgG positive patients associated disease (MOGAD)

  or  MOGAD-like patients (MOG-IgG negative patients presenting clinical and/or radiological MOGAD features)

- The **NOMADMUS expert group** validates inclusions with a focus on double seronegative (AQP4 and MOG) patients and MOGAD-like patients

- **Minimal mandatory data** set specific to NMOSD/MOGAD

# NOMADMUS cohort

- **2167** patients included

- 1080 patients with biological samples (serum, plasma, PBMC, CSF…) in a dedicated biobank or in the OFSEP biobank

- 1161 patients with at least one MRI in a dedicated imaging bank or in the OFSEP imaging bank

# RIS cohort

# RIS cohort

**Inclusion criteria**

- MRI lesions suggestive of multiple sclerosis according to 2005 and 2017 MS DIS criteria
- EDSS=0
- Index MRI indication not consistent with demyelinating disease

**Exclusion criteria**

- Any focal neurological manifestation prior to the acquisition of the MRI

**Mandatory data set** specific to RIS and RIS conversion

- The **RIS expert group** validates all inclusions
- The RIS expert group is member of the Radiologically Isolated Syndrome Consortium (RISC)

- 528 RIS 2009 patients including 202 MS conversion
- 182 RIS 2023 patients including 60 MS conversion

# Publications

## Reference publications

Confavreux C et Al. **EDMUS, a European database for multiple sclerosis.** J Neurol Neurosurg Psychiatry 1992; 55: 671-676

Vukusic S et Al. **Observatoire Français de la Sclérose en Plaques (OFSEP): A unique multimodal nationwide MS registry in France.** Mult Scler. 2020;26(1):118–22

Brisset JC et Al. **New OFSEP recommendations for MRI assessment of multiple sclerosis patients: Special consideration for gadolinium deposition and frequent acquisitions.** J Neuroradiol. 2020;47(4):250-258. doi:10.1016/j.neurad.2020.01.083

Brocard G et Al. **The biological sample collection of the OFSEP French MS registry: An essential tool dedicated to researchers.** Multiple Sclerosis and Related Disorders. 2023 Sep;77:104872

## **All publications**

OFSEP publications are available on our website:

https://www.ofsep.org/en/publications-en

# Acknowledgement

This work was done within the framework of OFSEP, the French multiple sclerosis registry