

# ICPerMed Best Practice Recognition 2022

## Data Sharing in Personalised Medicine Clinical Research

### Databases and registers towards Barcoding Multiple Sclerosis

on behalf of Barcoding MS network

Pamplona, Navarra (Spain)

17-18<sup>th</sup> January 2023

Prof. Mario Alberto Battaglia

President Italian Multiple Sclerosis Foundation – FISM

Professor of Hygiene and Public Health – University of Siena

No conflict of interest to declare

# ITALIAN MS SOCIETY (AISM) AND ITS FOUNDATION (FISM)

## THE PATH TO IMPACT

- 55 years in research, services and advocacy (<https://www.aism.it>) ;
- To apply a multistakeholder governance and patient engagement innovative model (EU Responsible Research & Innovation MULTI-ACT project: <https://www.multiact.eu/> );
- Clinical centers and researchers network of excellence committed to contribute with high quality data to study different aspects of the disease; (<https://www.aism.it> - <https://www.neuro.it>)
- To promote and finance the development of registries and databases infrastructures;

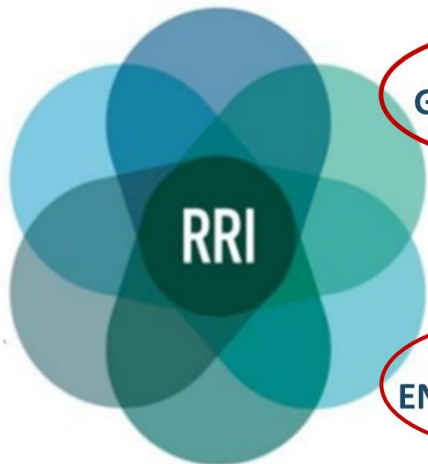
# MULTISTAKEHOLDER INITIATIVES EMBRACING THE MULTI-ACT MODEL

SCIENCE EDUCATION

GENDER EQUALITY

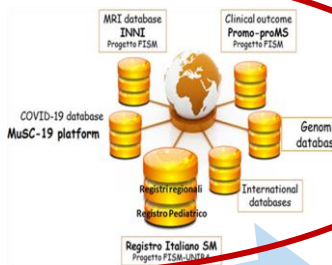
ETHICS

OPEN ACCESS



GOVERNANCE

PUBLIC ENGAGEMENT



INTERNATIONAL PROGRESSIVE MS ALLIANCE  
CONNECT TO END PROGRESSIVE MS



MS Initiatives



# 2020 MS AGENDA

## The Agenda of People with MS in Italy 2015-2020

#7

*“I would like a research committed to finding answers for any phase of disease that improves my present and it reassure me for the future.”*

### THE PRIORITY

7.1 | Definition of a common global agenda and public institutions' commitments to MS research through the collaboration with the national MS scientific community and in line with the specific international strategies

7.2 | Involvement of all research stakeholders, each for their own role and potential of contributions

7.3 | Data sharing among public institutions, research facilities, reference Clinical MS Centers together with the Italian MS Society and its Foundation, for epidemiological, clinical and social-health research

7.4 | Promoting a concrete impact of scientific research on the National Health Service clinical practice

7.5 | Promoting research towards personalized medicine

7.6 | Progressive MS dedicated resources for concrete results on care and quality of life

7.7 | Development of strategic research infrastructures and networks to guarantee effective and timely return of research investment

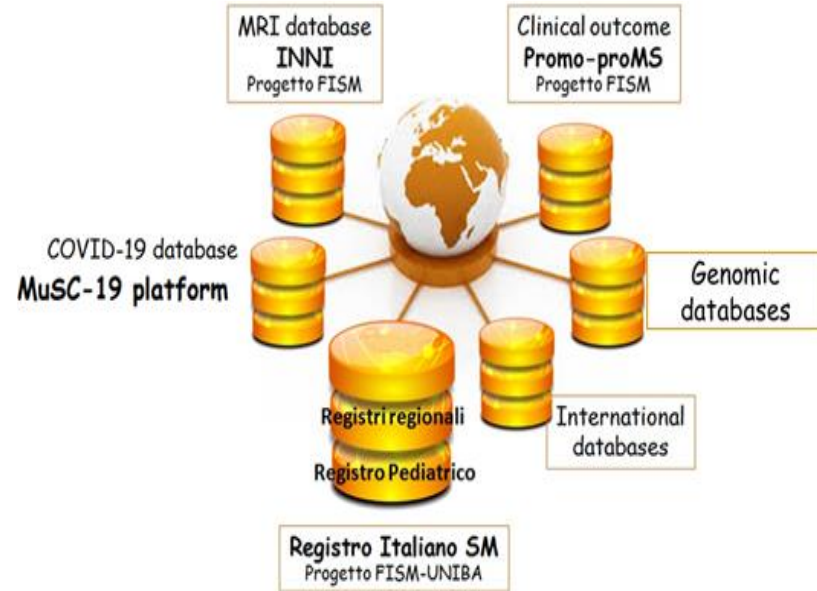
7.8 | To assure dedicated training and career paths for researchers in strategic areas

7.9 | To assure adequate financial resources dedicated to specific research, at national and international level

7.10 | Italian MS Society and its Foundation will play a key role in the MS research system at the national and international level

**SCLE  
ROSI  
MULT  
IPLA**  
associazione  
italiana

un mondo  
libero dalla SM



AI SM. INSIEME, UNA CONQUISTA DOPO L'ALTRA

# The numbers of Italian Multiple Sclerosis & Related Disorders Register data



171

- Centers enrolled (70% of all Italian MS Centers )

200

- Clinicians/Researchers involved

18

- Research Assistants

12

- Staff members

# The numbers of Italian Multiple Sclerosis & Related Disorders Register data



>80,000

- MS cases (~60% Italian MS population)

44.642

- MS cases treated with DMTs (60%)

24.912

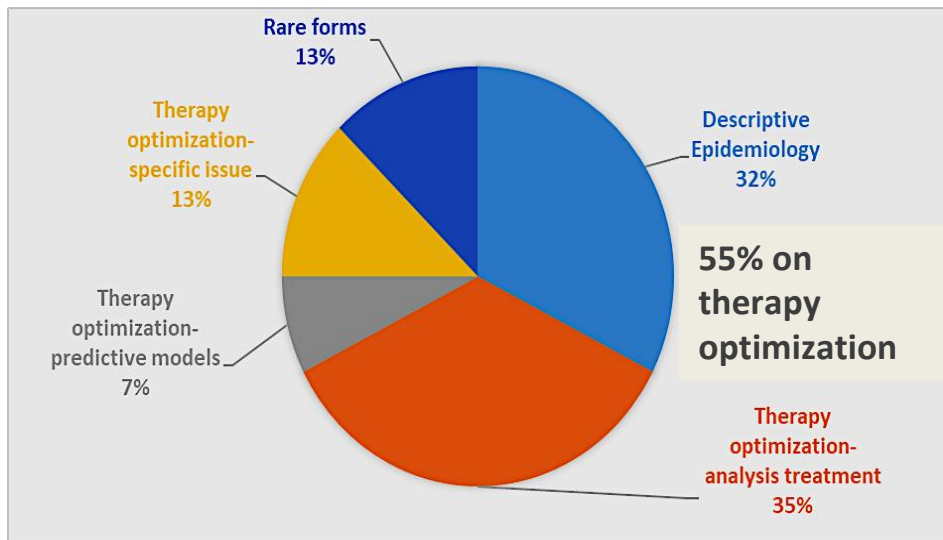
- MS cases treated with Moderate Effective DMTs (56 %)

19.730

- MS cases treated with HIGH Effective DMTs (44 %)

# Research Projects based on Italian Multiple Sclerosis & Related Disorders Register data

≈ 50 projects approved



> 20 papers published  
2018-2022

> 30 projects are ongoing

Main areas of the projects



# International data-sharing initiatives

## BigMSData Network



The Danish Multiple Sclerosis Registry



### The Italian Multiple Sclerosis Register

Translating Research Into Health



UNIBA/FISM



### Mission

To be a catalyst for MS research for the member registries and external partners such as the life sciences industry



### Vision

To allow pooling of MS data at a scale that raises MS research to a new level (>300.00 MS patients)

**AISM. INSIEME, UNA CONQUISTA DOPO L'ALTRA**

# The EMA Initiative for Patient Registries

1 5 November 2018  
2 EMA/763513/2018  
3  
4  
5  
6  
7



8 **Discussion paper:**  
9 **Use of patient disease registries for regulatory purposes –**  
10 **methodological and operational considerations**  
11  
12  
13 The Cross-Committee Task Force on Patient Registries  
14

## Aims:

- **To optimise and facilitate** the use of existing Patient Registries for the benefit-risk monitoring of new drugs
- **To promote** dialogue between regulators, companies and registry holders

## European Post Authorization Safety Study (PASS)

**BIOGEN** - to estimate the risk of progressive multifocal leukoencephalopathy (PML) and other serious opportunistic infections among patients who were exposed to an MS DMT prior to treatment with **Tysabri**

**ROCHE** - Long-term surveillance of **Ocrelizumab** treated patients with Multiple Sclerosis

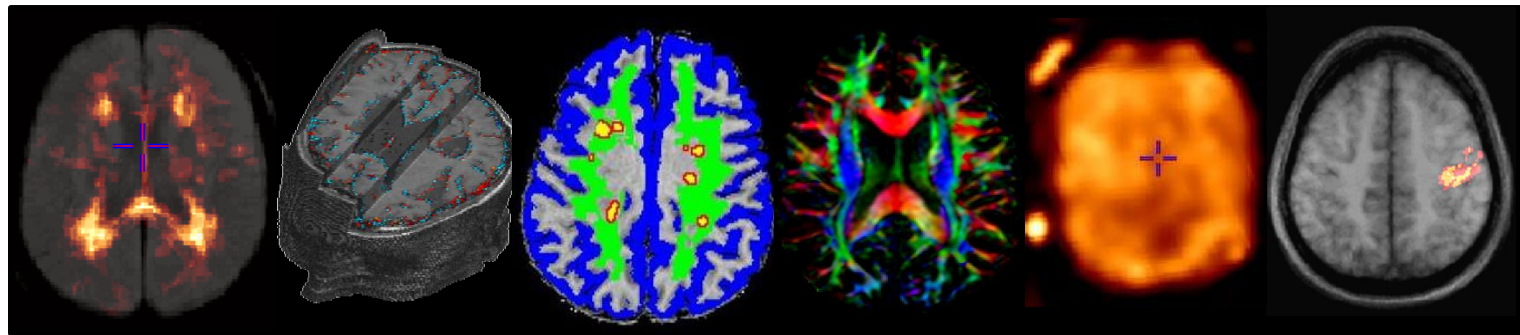
**MERCK** - Long-term surveillance (CLARION study) of **oral Cladribine** in patients with highly active RMS

**3 more PASS studies to come in 2023**

**BMSD** – A joint core protocol allows to collect specific SAEs (coded by **MedDRA**), **Pregnancy outcomes** (classified by **EUROCAT**) and **effectiveness outcomes** for each new approved DMT

## ... But what else?

- Most of clinical MS registries include MRI information, but MRI data collection is usually limited to conventional measures (T2 and T1 lesion numbers/volumes) and **original Digital Imaging and Communications in Medicine data are not included**
- **Advanced MRI techniques are not included** in these initiatives



MRI-LV

Atrophy

MTR

DTI

MRSI

fMRI

# The Italian Neuroimaging Network Initiative (INNI) to optimize the use of advanced MRI techniques in patients with MS



## The Italian Neuroimaging Network Initiative (INNI): enabling the use of advanced MRI techniques in patients with MS

M. Filippi<sup>1,2</sup> · G. Tedeschi<sup>3,4</sup> · P. Pantano<sup>5,6</sup> · N. De Stefano<sup>7</sup> · P. Zoratti<sup>8</sup> ·

M. A. Rocca<sup>1,2</sup> · For the INNI Network *Neurol Sci* 38, 1029–1038 (2017). <https://doi.org/10.1007/s10072-017-2903-z>

*Journal of Neurology* (2019) 266:2848–2858  
<https://doi.org/10.1007/s00415-019-09000-0>

ORIGINAL ARTICLE

MRI quality  
moving target

Loredana Storelli · Gioacchino Tedeschi · Patrizia Pantano · Massimo Filippi · For the INNI Network

Received: 26 June 2019 / Revised: 12 August 2019 / Accepted: 13 August 2019 / Published online: 17 August 2019  
© Springer-Verlag GmbH Germany, part of Springer Nature 2019

### INNI Academy

## The Italian Neuroimaging Network Initiative (INNI): towards the standardization of the use of MRI in the patient with Multiple Sclerosis at the national level

functional  
MRI with

Silvia Tommasin<sup>1</sup> · Viktoriia Iakovleva<sup>1</sup> | Maria Assunta Rocca<sup>2,3,4</sup> · Costanza Gianni<sup>1,5</sup> · Gioacchino Tedeschi<sup>6</sup> | Nicola De Stefano<sup>7</sup> | Carlo Pozzilli<sup>1</sup> · Massimo Filippi<sup>2,3,4,8,9</sup> | Patrizia Pantano<sup>1,5</sup> | the INNI Network

MULTICENTER · DATA · HARMONIZATION · FOR · REGIONAL · BRAIN · ATROPHY · IN · MULTIPLE · SCLEROSIS

<sup>1</sup>Elisabetta Pagani, MSc, <sup>1</sup>Loredana Storelli, PhD, <sup>2,3</sup>Patrizia Pantano, MD, <sup>2</sup>Nikolaos Petsas, MD, PhD, <sup>4</sup>Gioacchino Tedeschi, MD, <sup>4</sup>Antonio Gallo, MD, PhD, <sup>5</sup>Nicola De Stefano, MD, PhD, <sup>5</sup>Marco Battaglini, PhD, <sup>1,6,7</sup>Maria A. Rocca, MD, <sup>1,6,7,8,9</sup>Massimo Filippi, MD, for the INNI Network

*J Neurol* 270, 446–459 (2023). <https://doi.org/10.1007/s00415-022-11387-2>



AISM. INSIEME, UNA CONQUISTA DOPO L'ALTRA

# PROgnostic GENetic factors in Multiple Sclerosis

- The PROGEMUS Consortium was established in 2005, coordinated by Maurizio Leone (IRCSS Casa Sollievo della Sofferenza, San Giovanni Rotondo, FG) and Sandra D'Alfonso (Università del Piemonte Orientale, Novara)
- **23 Italian MS Centers** that collected DNA samples and well-characterized phenotypes of more than **3,500 incident and prevalent MS patients**. This genetic database is currently one of the largest in Europe.



PROGEMUS Centers

# Projects of deeply genetically profiled Sardinian individuals (ProgeNIA)

Study of Multiple Sclerosis & Type 1 Diabetes

SardiNIA general population cohort study on QTLs

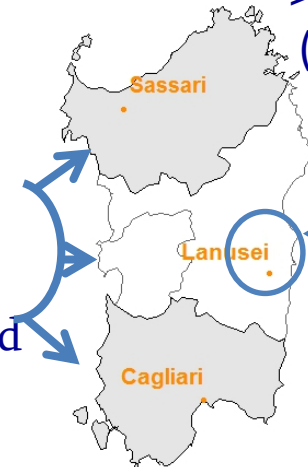
~2000 T1D patients  
~5000 MS patients  
~5000 Controls

~8,000 individuals  
1257 families  
>1000 quantitative traits (QTLs)

Affected individuals and matched controls from all over the island

enrollment from 4 towns in a small area of the Island

(only 50 samples enrolled in both studies)



## Overexpression of the Cytokine BAFF and Autoimmunity Risk

M. Steri, V. Orrù, M.L. Idda, M. Pitzalis, M. Pala, I. Zara, C. Sidore, V. Faà, M. Floris, M. Deiana, I. Asunis, E. Porcu, A. Mulas, M.G. Piras, M. Lobina, S. Lai, M. Marongiu, V. Serra, M. Marongiu, G. Sole, F. Busonero, A. Maschio, R. Cusano, G. Cuccuru, F. Deidda, F. Poddie, G. Farina, M. Dei, F. Viridis, S. Olla, M.A. Satta, M. Pani, A. Delitala, E. Cocco, J. Frau, G. Coghe, L. Lorefine, G. Fenu, P. Ferrigno, M. Ban, N. Barzzone, M. Leone, F.R. Guerini, M. Piga, D. Firinu, I. Kockum, I. Lima Bomfim, T. Olsson, L. Alfredsson, A. Suarez, P.E. Carreira, M.J. Castillo-Palma, J.H. Marcus, M. Congia, A. Angius, M. Melis, A. Gonzalez, M.E.A. Riquelme, B.M. da Silva, M. Marchini, M.G. Danieli, S. Del Giacco, A. Mathieu, A. Pani, S.B. Montgomery, G. Rosati,\* J. Hillert, S. Sawcer, S. D'Alfonso, J.A. Todd, J. Novembre, G.R. Abecasis, M.B. Whalen, M.G. Marrosu, A. Meloni, S. Sanna, M. Gorospe, D. Schlessinger, E. Fiorillo, M. Zoledziewska, and F. Cucca

THE NEW ENGLAND JOURNAL of MEDICINE

### EDITORIALS



#### A BAFFing Association between Malaria Resistance and the Risk of Multiple Sclerosis

Thomas Korn, M.D., and Mohamed Oukka, Ph.D.

### ARTICLES

<https://doi.org/10.1038/s41588-020-0684-4>

nature  
genetics

Check for updates

## Complex genetic signatures in immune cells underlie autoimmunity and inform therapy

Valeria Orrù<sup>1,2</sup>, Maristella Steri<sup>1,2</sup>, Carlo Sidore<sup>1,2,3</sup>, Michele Marongiu<sup>1</sup>, Valentina Serra<sup>1</sup>, Stefania Olla<sup>1</sup>, Gabriella Sole<sup>1</sup>, Sandra Lai<sup>1</sup>, Mariano Dei<sup>1</sup>, Antonella Mulas<sup>1</sup>, Francesca Viridis<sup>1</sup>, Maria Grazia Piras<sup>1</sup>, Monia Lobina<sup>1</sup>, Mara Marongiu<sup>1</sup>, Maristella Pitzalis<sup>1</sup>, Francesca Deidda<sup>1</sup>, Annalisa Loizedda<sup>1</sup>, Stefano Onano<sup>1,2</sup>, Magdalena Zoledziewska<sup>1</sup>, Stephen Sawcer<sup>3</sup>, Marcella Devoto<sup>4,5</sup>, Myriam Gorospe<sup>6</sup>, Gonçalo R. Abecasis<sup>7</sup>, Matteo Floris<sup>1,2</sup>, Mauro Pala<sup>1</sup>, David Schlessinger<sup>8</sup>, Edoardo Fiorillo<sup>1</sup> and Francesco Cucca<sup>1,2,3,20</sup>

Cell

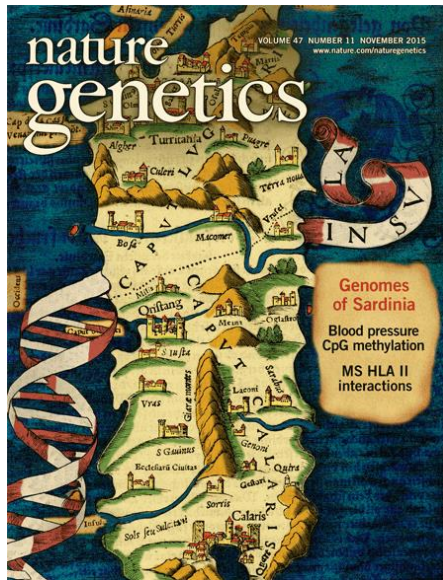
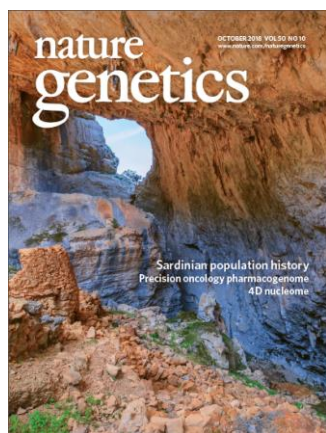
Resource

## Genetic Variants Regulating Immune Cell Levels in Health and Disease

Valeria Orrù<sup>1,2</sup>, Maristella Steri<sup>1,2</sup>, Gabriella Sole<sup>1</sup>, Carlo Sidore<sup>1,2,3</sup>, Francesca Viridis<sup>1</sup>, Mariano Dei<sup>1</sup>, Sandra Lai<sup>1</sup>, Magdalena Zoledziewska<sup>1</sup>, Fabio Busonero<sup>1</sup>, Antonella Mulas<sup>1</sup>, Matteo Floris<sup>1</sup>, Wierdava I. Mentzen<sup>1</sup>, Silvana A.M. Urru<sup>1</sup>, Stefania Olla<sup>1</sup>, Michele Marongiu<sup>1</sup>, Maria G. Piras<sup>1</sup>, Monia Lobina<sup>1</sup>, Andrea Maschio<sup>1,2</sup>, Maristella Pitzalis<sup>1</sup>, Maria F. Urru<sup>1</sup>, Marco Marcellì<sup>1</sup>, Roberto Cusano<sup>1</sup>, \*Francesca Deidda<sup>1</sup>, \*Valentina Serra<sup>1,2</sup>, \*Manuela Oppo<sup>1</sup>, \*Rosella Pili<sup>1</sup>, \*Frederic Reiner<sup>1</sup>, \*Riccardo Beretti<sup>1</sup>, \*Luca Pirodda<sup>1</sup>, \*Seria Zaza<sup>1</sup>, \*Eleonora Porcu<sup>1,2</sup>, \*Alan Kovacs<sup>1</sup>, \*Christine Brennan<sup>1</sup>, \*Brendan Tierney<sup>1</sup>, \*Robert Lyons<sup>1</sup>, \*Hyun M. Kang<sup>1</sup>, \*Sergio Uzzau<sup>1</sup>, \*Rossano Azzari<sup>1</sup>, \*Marta Valentini<sup>1</sup>, \*Davide Pirina<sup>1</sup>, \*Lidia Leon<sup>1</sup>, \*Gianluca Potta<sup>1</sup>, \*Silvia Naitza<sup>1</sup>, \*Andrea Angius<sup>1,2</sup>, \*Mauro Congia<sup>1</sup>, \*Michael B. Whalen<sup>1</sup>, \*Chris M. Jones<sup>1</sup>, \*David Schlessinger<sup>12</sup>, \*Gonçalo R. Abecasis<sup>12</sup>, \*Edoardo Fiorillo<sup>1,12</sup>, \*Serena Sanna<sup>1,12</sup> and \*Francesco Cucca<sup>1,1,12</sup>

<sup>1</sup>Istituto di Ricerca Genetica e Biomedica (IRGB), CNR, Monastero 09042, Italy  
<sup>2</sup>Center for Statistical Genetics, University of Michigan, Ann Arbor, MI 48109, USA  
<sup>3</sup>Dipartimento di Scienze Biomediche, Università di Sassari, Sassari 07100, Italy  
<sup>4</sup>ORIS, Piano Tecnologico della Sardegna, Pula, Cagliari 09010, Italy  
<sup>5</sup>Università degli Studi di Cagliari, Cagliari 09010, Italy  
<sup>6</sup>Laboratorio di Protomica, Porto Conte Ricerca Srl, Tramariglio, Alghero 07041, Italy  
<sup>7</sup>Dipartimento di Allergologia e Immunologia, Università di Cagliari, Cagliari 09124, Italy  
<sup>8</sup>4D Biosciences Italia, Buccinasco, Milano 20090, Italy  
<sup>9</sup>Dipartimento di Scienze Biomediche e Biotechnologie, Università di Cagliari, Cagliari 09124, Italy  
<sup>10</sup>Laboratory of Genetics, NIA, Baltimore, MD 21224, USA  
<sup>11</sup>University of Michigan Sequencing Core, University of Michigan Medical School, Ann Arbor, MI 48109, USA  
<sup>12</sup>These authors contributed equally to this work  
\*Correspondence: [eduardo.fiorillo@cnr.it](mailto:eduardo.fiorillo@cnr.it) (E.F.), [serena.sanna@irgb.cnr.it](mailto:serena.sanna@irgb.cnr.it) (S.S.), [francesco.cucca@irgb.cnr.it](mailto:francesco.cucca@irgb.cnr.it) (F.C.)  
<https://doi.org/10.1016/j.cell.2013.08.041>

Sardinian population history  
Precision oncology pharmacogenome  
4D nucleome



nature  
genetics

## Genome sequencing elucidates Sardinian genetic architecture and augments association analyses for lipid and blood inflammatory markers

Carlo Sidore<sup>1,2,3,4</sup>, Fabio Busonero<sup>1,2,3,4,5</sup>, Andrea Maschio<sup>1,2,3,4,5</sup>, Eleonora Porcu<sup>1,2,3,4,5</sup>, Silvia Naitza<sup>1,2,3</sup>, Magdalena Zoledziewska<sup>1</sup>, Antonella Mulas<sup>1</sup>, Giorgio Pittis<sup>1,2</sup>, Maristella Steri<sup>1</sup>, Fabrice Dupuis<sup>1</sup>, Alan Kovacs<sup>1</sup>, Vicente Diego Ortega del Vecchio<sup>1</sup>, Charleson W K Chang<sup>1</sup>, Jennifer Bragg-Gresham<sup>1</sup>, Maristella Pitzalis<sup>1</sup>, Ramaiah Nagaraja<sup>1</sup>, Brendan Tierney<sup>1</sup>, Christine Brennan<sup>1</sup>, Sergio Uzzau<sup>1</sup>, Christian Fuchsberger<sup>1</sup>, Rossano Azzari<sup>1</sup>, Frederic Reiner<sup>1</sup>, Riccardo Beretti<sup>1</sup>, Ji Huang<sup>1</sup>, Nicholas J Timmons<sup>1</sup>, Daniela Toniolo<sup>1</sup>, Paolo Gasparini<sup>1,11</sup>, Giovanni Malerba<sup>1</sup>, George Dedousis<sup>11</sup>, Eleonora Zeggini<sup>12</sup>, Nicole Soranzo<sup>12,13</sup>, Chris Jones<sup>12</sup>, Robert Lyons<sup>12</sup>, Andrea Angius<sup>12</sup>, Hyun M Kang<sup>12</sup>, John Novembre<sup>12</sup>, Serena Sanna<sup>12</sup>, David Schlessinger<sup>12</sup>, Francesco Cucca<sup>1,2,3,4,5,6,7,8,9,10,11,12,13</sup> & Gonçalo R. Abecasis<sup>12,13</sup>

## Height-reducing variants and selection for short stature in Sardinia

Magdalena Zoledziewska<sup>1</sup>, Carlo Sidore<sup>1,2,3</sup>, Charleson W K Chang<sup>1,2,3</sup>, Serena Sanna<sup>1,2,3</sup>, Antonella Mulas<sup>1</sup>, Maristella Steri<sup>1</sup>, Fabio Busonero<sup>1</sup>, Joseph H Marcus<sup>1</sup>, Michele Marongiu<sup>1</sup>, Andrea Maschio<sup>1,2,3</sup>, Diego Ortega Del Vecchio<sup>1</sup>, Matteo Floris<sup>1,2,3</sup>, Alessandro Dellalà<sup>1,2</sup>, Maria Pina Concas<sup>1</sup>, Federico Murgia<sup>1</sup>, Ginevra Bittolo<sup>1</sup>, Simona Vaccargiu<sup>1</sup>, Ramaiah Nagaraja<sup>1</sup>, Kirk E Lohmoller<sup>1</sup>, UK10K Consortium<sup>11</sup>, Nicholas J Timmons<sup>11</sup>, Nicole Soranzo<sup>11,12</sup>, Joanna Tachmazidou<sup>11</sup>, George Dedousis<sup>11</sup>, Eleonora Zeggini<sup>12</sup>, The Understanding Society Scientific Group<sup>12</sup>, Sergio Uzzau<sup>12</sup>, Chris Jones<sup>12</sup>, Robert Lyons<sup>12</sup>, Andrea Angius<sup>12</sup>, Gonçalo R. Abecasis<sup>12,13</sup>, John Novembre<sup>12,13</sup>, David Schlessinger<sup>12,13</sup> & Francesco Cucca<sup>1,2,3</sup>

## Genome-wide association analyses based on whole-genome sequencing in Sardinia provide insights into regulation of hemoglobin levels

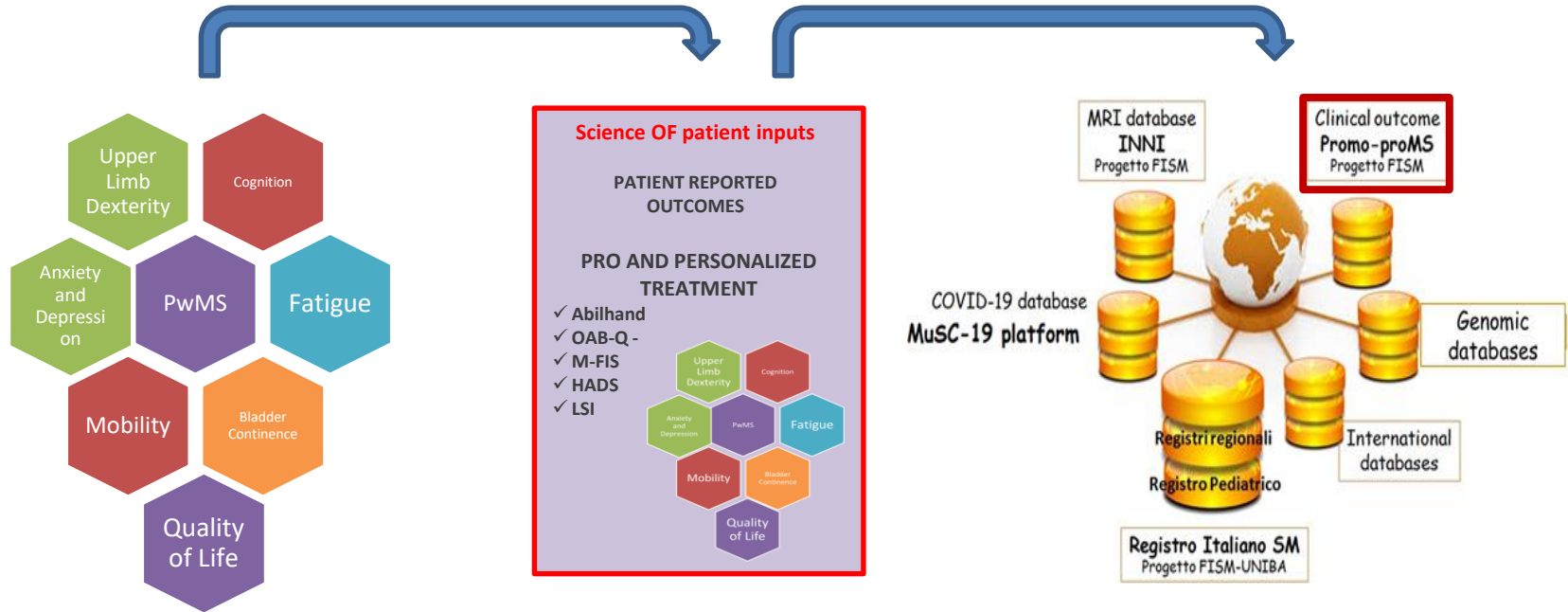
Fabrice Dupuis<sup>1,2,3</sup>, Magdalena Zoledziewska<sup>1,2,3</sup>, Carlo Sidore<sup>1,2,3</sup>, Maristella Steri<sup>1</sup>, Fabio Busonero<sup>1,2,4</sup>, Andrea Maschio<sup>1,2,4</sup>, Antonella Mulas<sup>1</sup>, Lucia Perseu<sup>1</sup>, Susanna Borella<sup>1</sup>, Eleonora Porcu<sup>1,2,4</sup>, Giorgio Pittis<sup>1,2</sup>, Maristella Pitzalis<sup>1</sup>, Mauro Pala<sup>1</sup>, Stephan Menzel<sup>1</sup>, Sarah Mettramy<sup>1</sup>, Timothy D Spencer<sup>1</sup>, Lidia Leon<sup>1</sup>, Andrea Angius<sup>1</sup>, Manuela Uda<sup>1</sup>, Paolo Moa<sup>1</sup>, Sverre Ley Thorgeirsson<sup>1</sup>, Renzo Galanzi<sup>1,12</sup>, Gonçalo R. Abecasis<sup>12,13</sup>, David Schlessinger<sup>12,13</sup>, Serena Sanna<sup>12</sup> & Francesco Cucca<sup>1,2,3</sup>

ISI

L'ALTRA

# Patient reported outcome data

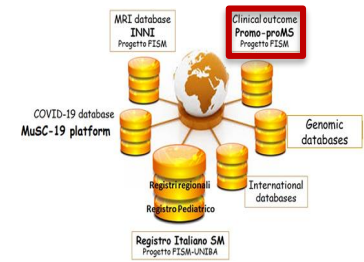
## INTEGRATED FUNCTIONAL DOMAINS EVALUATION



Addressing the patient-reported interdependence of domains



# “A new functional PROfile to MOnitor the PROgression of disability in Multiple Sclerosis” (PROMOPRO-MS data base).




❑ IMPROVING THE DISEASE COURSE DETECTION

❑ PREDICTING THE DISEASE PROGRESSION



Neurological Sciences (2020) 41:459–462  
<https://doi.org/10.1007/s10072-019-04093-x>

## The hidden information in patient-reported outcomes and clinician-assessed outcomes: multiple sclerosis as a proof of concept of a machine learning approach

Giampaolo Brichetto<sup>1,2</sup>  • Margherita Monti Bragadin<sup>1,2</sup> • Samuele Fiorini<sup>3</sup> • Mario Alberto Battaglia<sup>4</sup> • Giovanna Konrad<sup>2</sup> • Michela Ponzio<sup>1</sup> • Ludovico Pedullà<sup>1</sup> • Alessandro Verri<sup>3</sup> • Annalisa Barla<sup>3</sup> • Andrea Tacchino<sup>1</sup>

Annu Int Conf IEEE Eng Med Biol Soc. 2015 Aug;2015:4443-6. doi: 10.1109/EMBC.2015.7319381.

## A Machine Learning pipeline for Multiple Sclerosis course detection from Clinical Scales and Patient Reported Outcomes

Samuele Fiorini<sup>1</sup>, Alessandro Verri<sup>1</sup>, Andrea Tacchino<sup>2</sup>,  
Michela Ponzio<sup>2</sup>, Giampaolo Brichetto<sup>2</sup>, and Annalisa Barla<sup>1</sup>



# Multiple Sclerosis and Related Disorders

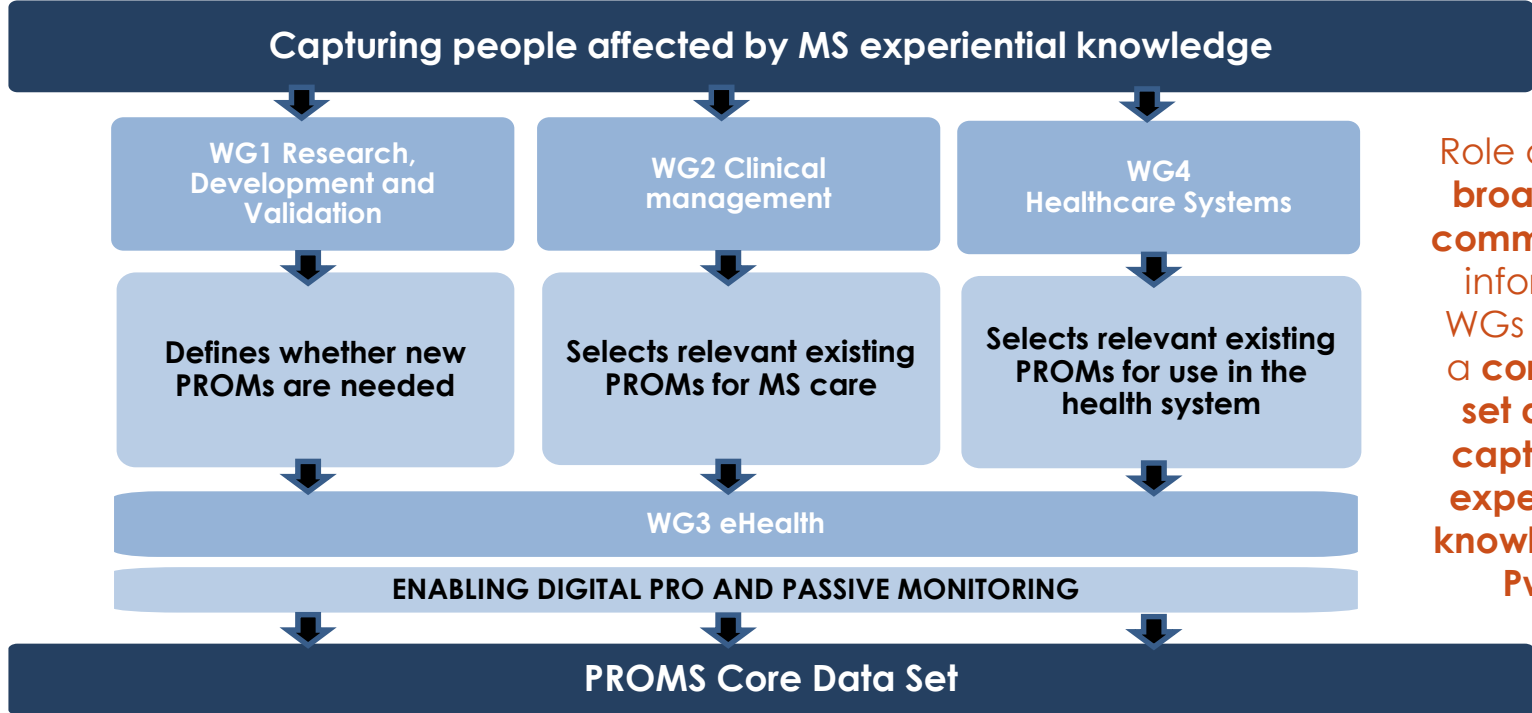
Volume 61, May 2022, 103757



Commentary

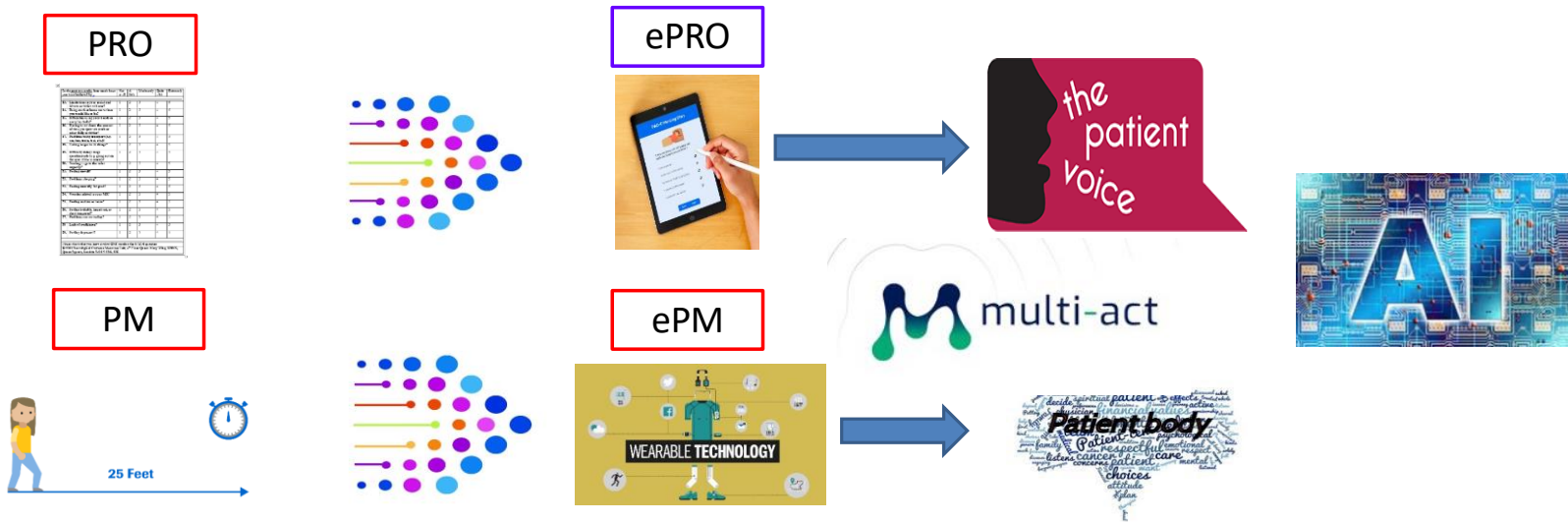
## The agenda of the global patient reported outcomes for multiple sclerosis (PROMS) initiative: Progresses and open questions

Paola Zarin<sup>a, 1</sup> ✉, Patrick Vermersch<sup>b, 1</sup>, Maria Pia Amato<sup>c</sup>, Giampaolo Brichetto<sup>a</sup>, Timothy Coetzee<sup>d</sup>, Gary Cutter<sup>e</sup>, Gilles Edan<sup>f</sup>, Gavin Giovannoni<sup>g</sup>, Emma Gray<sup>h</sup>, Hans Peter Hartung<sup>i, j, k, l</sup>, Jeremy Hobart<sup>m</sup>, Anne Helme<sup>n</sup>, Robert Hyde<sup>o</sup>, Usman Khan<sup>p</sup>, Letizia Leocani<sup>q</sup>, Lorenzo Giovanni Mantovani<sup>r, s</sup>, Robert McBurney<sup>t</sup>, Xavier Montalban<sup>u</sup>, Iris-Katharina Penner<sup>v</sup>, Bernard M.J. Uitdehaag<sup>w</sup>, Pamela Valentine<sup>x</sup>, Helga Weiland<sup>y</sup>, Deborah Bertorello<sup>a</sup>, Mario Alberto Battaglia<sup>z</sup>, Peer Baneke<sup>n</sup>, Giancarlo Comi<sup>q, aa</sup> On behalf of the PROMS Initiative Working Groups



Role of **ECT & broader MS community** to inform the WGs toward a **core-data set** able to capture the experiential knowledge of **PwMS**

# Progress that data integration and interoperability may bring about



- PROMS is conducting a state-of-the-art search to collect information about and analyse the existing tools, devices and methods for digitally enabled collection and assessment of PROMS.
- Digital health companies can help support this effort while making their enterprises and tools visible to the broader MS scientific and industrial community.
- The survey has been developed by PROMS and all rights are reserved.
- MS Data Alliance (MSDA) hosts the meta-data on the MSDA Catalogue.
- Participants have to agree with the general Terms of Use of the MSDA Catalogue and give specific and informed consent to the processing of their personal data as stated in this Privacy Notice.



To join the PROMS eHealth catalogue, vendors are invited to **read the "Invitation Letter" in the QR code** and follow the indications provided until

# Data Sharing in Personalised Medicine

## The COVID-19 emergency





## ALLIANCE COVID-19 in Multiple Sclerosis to help meeting the challenge

- The Italian MS Foundation (FISM), the Italian Neurological Society (SIN), the Italian MS Register (Research Unit FISM-UNIBA) and the Italian Neuroimmunology Association (AINI) have created an Alliance (**Alliance for COVID-19 in MS**).
- The Alliance **aims to promote a non-competitive multi-stakeholder collaboration framework** to study the impact of COVID-19 infection in people with MS (PwMS) and, in particular, the relation between COVID-19 and Disease Modifying Treatments (DMTs). FISM is leading the Alliance and represents the Alliance in the relationship with third parties.
- While epidemiological data are being collected to definitively assess the risk (or protection) in people treated with DMTs, **it is urgent to allocate resources and attention to more mechanistic research, aimed at understanding how DMTs affect SARS-CoV-2 infection in people with MS and how SARS-CoV-2 will affect MS.**



# MuSC-19 international platform: the first data that provided answers to PwMS

## An Italian programme for COVID-19 infection in multiple sclerosis

Italy was the first European country to encounter the effects of the coronavirus disease 2019 (COVID-19) pandemic.<sup>1</sup> For people with multiple sclerosis, the situation carries additional reasons for concern. Although emerging work suggests that some coexisting diseases, such as hypertension, might increase the severity of the COVID-19 infection, how less common conditions, such as multiple sclerosis, effect COVID-19 outcomes is still uncertain. Furthermore, immunosuppressive therapies, the mainstay of treatment for multiple sclerosis, might confer

[www.thelancet.com/neurology](http://www.thelancet.com/neurology) Vol 19 June 2020

Maria Pia Sormani, on behalf of the Italian Study Group on COVID-19 infection in multiple sclerosis  
[mariapia.sormani@unige.it](mailto:mariapia.sormani@unige.it)

## Disease-Modifying Therapies and Coronavirus Disease 2019 Severity in Multiple Sclerosis

Maria P. Sormani, PhD<sup>1,2</sup>, Nicola De Rossi, MD,<sup>3</sup> Irene Schiavetti, PhD,<sup>1</sup> Luca Carmisciano, MD,<sup>1</sup> Cinzia Cordioli, MD,<sup>3</sup> Lucia Moiola, MD,<sup>4</sup> Marta Radaelli, MD,<sup>5</sup> Paolo Immovilli, MD,<sup>6</sup> Marco Capobianco, MD,<sup>7</sup> Maria Trojano, MD,<sup>8</sup> Paola Zaratin, PhD,<sup>9</sup> Gioacchino Tedeschi, MD,<sup>10</sup> Giancarlo Comi, MD<sup>11</sup>, Mario A. Battaglia, MD,<sup>12</sup> Francesco Patti, MD<sup>13,14</sup>, Marco Salvetti, MD,<sup>15,16</sup> and the Musc-19 Study Group

**Objective:** This study was undertaken to assess the impact of immunosuppressive and immunomodulatory therapies on the severity of coronavirus disease 2019 (COVID-19) in people with multiple sclerosis (PwMS).  
**Methods:** We retrospectively collected data of PwMS with suspected or confirmed COVID-19. All the patients had complete follow-up to death or recovery. Severe COVID-19 was defined by a 3-level variable: mild disease not requiring hospitalization versus pneumonia or hospitalization versus intensive care unit (ICU) admission or death. We evaluated baseline characteristics and MS therapies associated with severe COVID-19 by multivariate and propensity score (PS)-weighted ordinal logistic models. Sensitivity analyses were run to confirm the results.  
**Results:** Of 844 PwMS with suspected (n = 565) or confirmed (n = 279) COVID-19, 13 (1.54%) died; 11 of them were in a progressive MS phase, and 8 were without any therapy. Thirty-eight (4.5%) were admitted to an ICU; 99 (11.7%) had radiologically documented pneumonia; 96 (11.4%) were hospitalized.  
**After adjusting for region, age, sex, progressive MS course, Expanded Disability Status Scale, disease duration, body mass index, comorbidities, and recent methylprednisolone use, therapy with an anti-CD20 agent (ocrelizumab or rituximab) was significantly associated (odds ratio [OR] = 2.37, 95% confidence interval [CI] = 1.18–4.74, p = 0.015) with increased risk of severe COVID-19. Recent use (<1 month) of methylprednisolone was also associated with a worse outcome (OR = 5.24, 95% CI = 2.20–12.53, p = 0.001). Results were confirmed by the PS-weighted analysis and by all the sensitivity analyses.**  
**Interpretation:** This study showed an acceptable level of safety of therapies with a broad array of mechanisms of action. However, some specific elements of risk emerged. These will need to be considered while the COVID-19 pandemic persists.

ANN NEUROL 2021;89:780-789

# COVID-19 Severity in Multiple Sclerosis

## Putting Data Into Context

Maria Pia Sormani, PhD, Irene Schiavetti, PhD, Luca Carmisciano, MD, Cinzia Cordioli, MD, Massimo Filippi, MD, Marta Radaelli, MD, Paolo Immovilli, MD, Marco Capobianco, MD, Nicola De Rossi, MD, Giampaolo Brichetto, PhD, Eleonora Cocco, MD, Cinzia Scandellari, MD, Paola Cavalla, MD, Ilaria Pesci, MD, Antonio Zito, MD, Paolo Confalonieri, MD, Girolama Alessandra Marfia, MD, Paola Perini, MD, Matilde Inglese, MD, Maria Trojano, MD, Vincenzo Brescia Morra, PhD, Gioacchino Tedeschi, MD, Giancarlo Comi, MD, Mario Alberto Battaglia, MD, Francesco Patti, MD, and Marco Salvetti, MD, on behalf of the MuSC-19 Study Group

*Neurol Neuroimmunol Neuroinflamm* 2022;9:e1105. doi:10.1212/NXI.0000000000001105



### BRIEF COMMUNICATION

## DMTs and Covid-19 severity in MS: a pooled analysis from Italy and France

Maria Pia Sormani<sup>1,2</sup>, Marco Salvetti<sup>3,4</sup>, Pierre Labauge<sup>5</sup>, Irene Schiavetti<sup>1</sup>, Helene Zephir<sup>6</sup>, Luca Carmisciano<sup>1</sup>, Caroline Bensa<sup>7</sup>, Nicola De Rossi<sup>8</sup>, Jean Pelletier<sup>9</sup>, Cinzia Cordioli<sup>8</sup>, Sandra Vukusic<sup>10</sup>, Lucia Moiola<sup>11</sup>, Philippe Kerschen<sup>12</sup>, Marta Radaelli<sup>13</sup>, Marie Théaudin<sup>14</sup>, Paolo Immovilli<sup>15</sup>, Olivier Casez<sup>16</sup>, Marco Capobianco<sup>17</sup>, Jonathan Ciron<sup>18</sup>, Maria Trojano<sup>19</sup>, Bruno Stankoff<sup>20,21</sup>, Alain Créange<sup>22</sup>, Gioacchino Tedeschi<sup>23</sup>, Pierre Clavelou<sup>24</sup>, Giancarlo Comi<sup>25</sup>, Eric Thouvenot<sup>26,27</sup>, Mario Alberto Battaglia<sup>28,29</sup>, Thibault Moreau<sup>30</sup>, Francesco Patti<sup>31,32</sup>, Jérôme De Sèze<sup>33</sup>, Celine Louapre<sup>34</sup>, the Musc-19<sup>a</sup> & the Covisep study groups<sup>a</sup>

Ann Neurol. 2021 Apr;89(4):780-789. doi: 10.1002/ana.26028. Epub 2021 Feb 9. PMID: 33480077; PMCID: PMC8013440.

### Correspondence

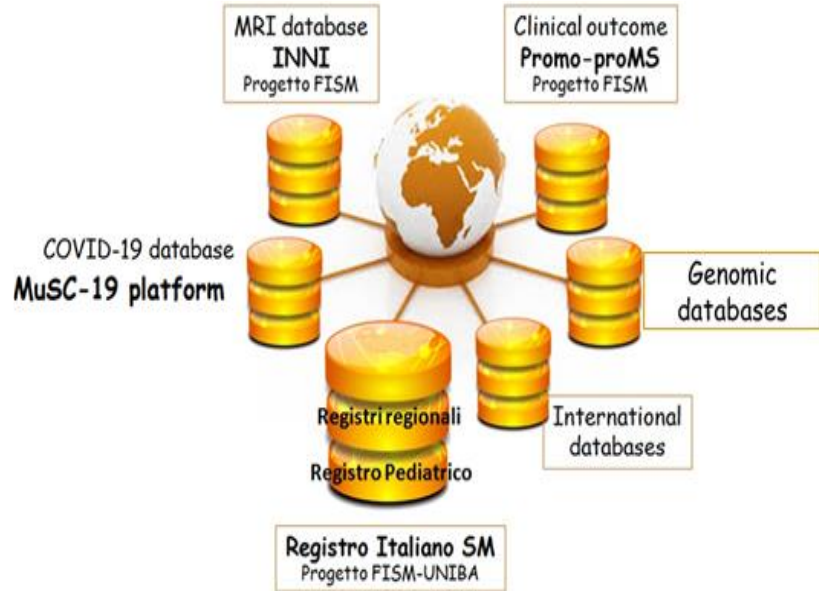
Dr. Salvetti  
[marco.salvetti@uniroma1.it](mailto:marco.salvetti@uniroma1.it)





## Barcoding MS

through a new and integrated research ecosystem: anticipating the pandemic-to-endemic context shift on the shoulders of what we have built





## MISSION LINES

### 3.0 Research in Multiple Sclerosis

- 3.1 Discover the causes of MS and other related disorders (primary prevention)
- 3.2 Stop (block) early the MS and other related disorders (secondary prevention)
- 3.3 Reverse or slow down the progression and symptoms of MS and other related disorders, and promote well-being and quality of life (tertiary prevention)
- 3.4 Direct, promote and finance multi-stakeholder and multidisciplinary research agendas in the priority areas of the mission-oriented research, with a participatory governance
- 3.5 Direct, promote and finance digital platforms for sharing clinical, magnetic resonance, genomic and patient

**3.5 Direct, promote and finance digital platforms for sharing clinical, magnetic resonance, genomic and patient reported data, also promoting the continuous updating of the Italian Multiple Sclerosis and other related pathologies Register towards personalized treatments**

- 3.8 Guarantee adequate resources dedicated to research and to training and career paths of researchers in strategic and scientific priorities. Involvement of the Third Sector, dedicated to MS and related diseases, in the definition of the related strategies and in the development of implementation plans
- 3.9 Promote a unique ecosystem between research and care through the adoption of the approach and principles of Responsible Research Innovation (RRI) with particular attention to the active research participation of the people with MS and other related disorders and their caregivers
- 3.10 Promote the right to scientific citizenship

# BARCODING MS: A NEW AND INTEGRATED RESEARCH ECOSYSTEM



**>80,000 PwMS**



**>4000 PwMS**



**COVID-19  
DATA BASE**

**>3300 PwMS**

**PROMOPRO-MS**



**>1200 PwMS**

**MS PROGEMUS  
>3500 PwMS**



**ProgeNIA  
> 5000 PwMS**

**SCLE  
ROSI  
MULT  
IPLA**  
associazione  
italiana

un mondo  
libero dalla SM

©COPYRIGHT FISM 2022 – ALL RIGHTS RESERVED

**AIMS. INSIEME, UNA CONQUISTA DOPO L'ALTRA**

**BARCODING MS:  
A NEW AND INTEGRATED RESEARCH ECOSYSTEM**

**THE PATH TO IMPACT**

- To develop **an integrated database** of clinical, genetic, imaging and patient-reported measures **capable of producing a “BARCODING”** of all new cases diagnosed with MS in Italy
- To identify an algorithm of factors responsible for disease progression towards personalized pharmacological and rehabilitative treatments

# BARCODING MS

- BARCODING MS builds on a solid experience of good practices in the acquisition of **high quality disease data in different areas of expertise**
- BARCODING MS **engages people with MS**, the first to recognize the importance of the circulation of data to provide answers to their unmet needs

# BARCODING MS: A MULTISTAKEHOLDER PLATFORM

## INFRASTRUCTURE ECOSYSTEM

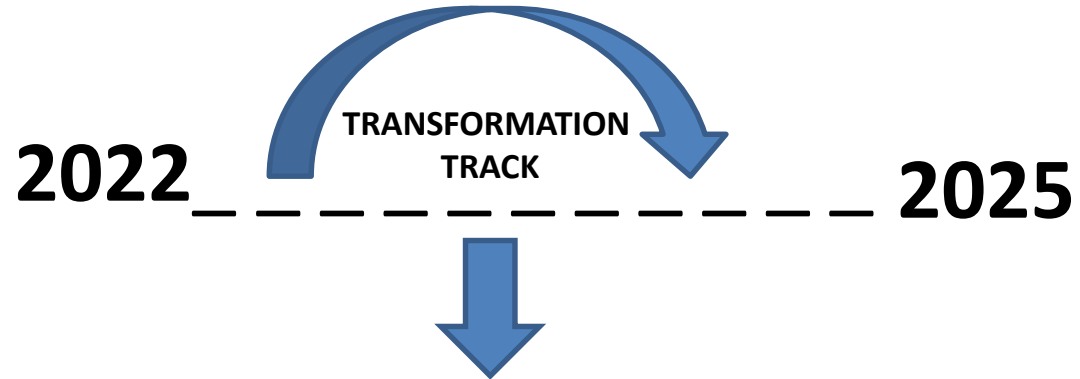
European Health  
data space

GDPR-compatible  
legal for data  
access and use

Technical facilities  
and building block

Capacity building  
program for skills  
and competencies

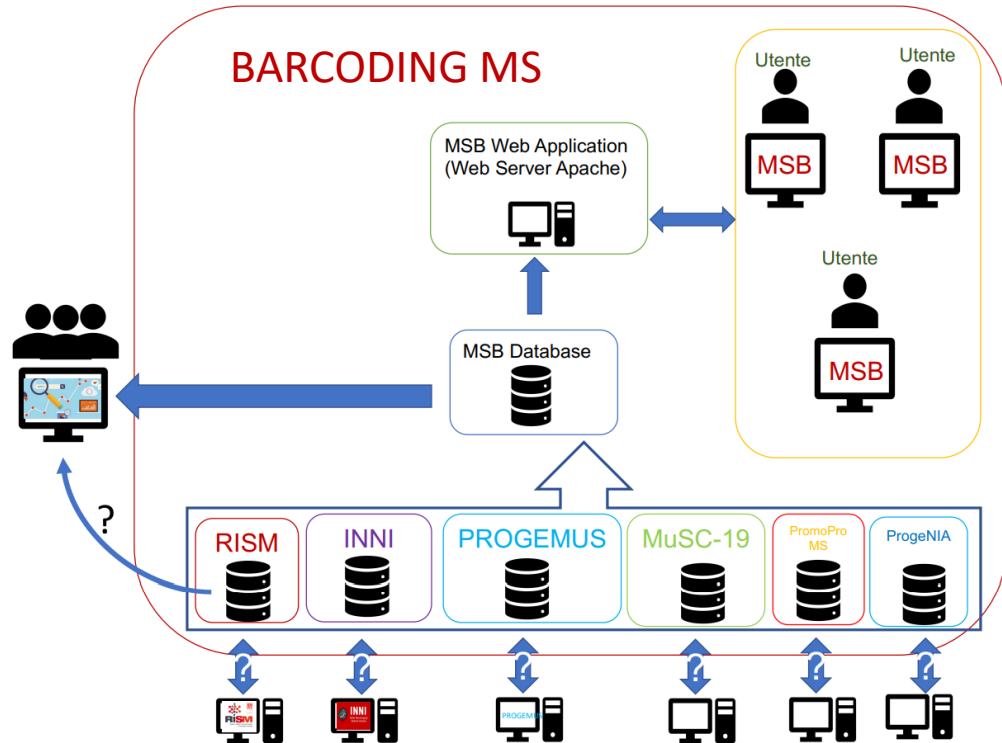
## MS AGENDA STRATEGIC PRIORITIES



## PERSONALIZED MEDICINE



## BARCODING MS





# BARCODING MS PARTNERS

- **Francesco Cucca**, professor of Medical Genetics of the **University of Sassari** and PI of numerous studies like the Sardinia project funded since 2001 by the National Institute of Health (NIH, USA) at the Institute of Genetic and Biomedical Research (IRGB) of the CNR which he has directed for 10 years
- **Sandra D'Alfonso**, professor of Medical Genetics at the Department of Health Science **University of Eastern Piedmont A. Avogadro** and coordinator of the **PROGEMUS consortium** (PROgnostic GENetic factors in MULTiple Sclerosis)
- **Massimo Filippi**, director of the Neurology Unit, of the Neurophysiology service and of the Neurorehabilitation Unit of the **IRCCS San Raffaele Hospital** and full professor of Neurology at the **Vita-Salute San Raffaele University** in **Milan**. Coordinator of the **INNI project database**.

# BARCODING MS PARTNERS

- **Roberto Furlan**, Head of the Clinical Neuroimmunology Unit and Director of the Institute of Experimental Neurology (**INSpe**) of the **IRCCS San Raffaele Hospital** in **Milan**. He is President of the **Italian Society of Neuroimmunology (AINI)**.
- **Claudio Gasperini**, Director of the UOC Neurology and Neurophysiopathology of the “**San Camillo-Forlanini**” hospital in **Rome** as well as coordinator of the SM study group of the **Italian Society of Neurology (SIN)**.
- **Maurizio Lenzerini**, professor of computer engineering, Department of Computer, Automatic and Management Engineering **Sapienza University of Rome**. Co-Founder & President of the **Ontology-based Data Management (OBDA)** System startup of the Sapienza University of Rome, and a company of the Almage Group.

# BARCODING MS PARTNERS

- **Maurizio Leone**, Division of Neurology, **IRCCS Casa Sollievo della Sofferenza Hospital**, Padre Pio **San Giovanni Rotondo** and coordinator of the **PROGEMUS consortium**.
- **Marco Salvetti**, professor of Neurology at the **Sapienza University of Rome** and Director of Neurology at the **S. Andrea University Hospital** in Rome.
- **Mariapia Sormani**, professor of Biostatistics, Department of Health Sciences, **University of Genoa** and coordinator of the **MuSC-19 platform**.
- **Maria Trojano**, professor of Neurology at the "Aldo Moro" **University of Bari** and director of the Neurology Operative Unit of the Bari Polyclinic. Professor Trojano is President of the Scientific Committee of the **Italian Multiple Sclerosis Registry**.

# BARCODING MS PARTNERS: AISM and FISM members

- **Mario Alberto Battaglia**, professor of Hygiene and Public Health at the **University of Siena** and president of **Italian MS Foundation (FISM)**; Executive Committee **Italian MS Registry**; CEO of Italian MS Society (**AISM**).
- **Giampaolo Bricchetto**, coordinator of research in rehabilitation of **FISM**, Medical Director of the **AISM Liguria Rehabilitation Center** and european president of **Rehabilitation in MS (RIMS)**.
- **Paola Zaratin**, Director of Scientific Research of **FISM**; **Coordinator EU Responsible Research & Innovation MULTI-ACT project**.

# BARCODING MS

