Supplementary Material

ANNEX I: MSCU QUESTIONNAIRE

General information

- Name of the organization (Hospital/University/Centre)
- Country [selection window]
- Indicate the type of organization There must be an explanation on this point
    - Healthcare organization
    - Hospital
    - Regional authority
    - Research centre
    - Private practitioner

MS in your country

Epidemiology / who gets MS?

- Prevalence rates per 100.000 [Possible responses to select 1 from predefined list:]
    a. <25
    b. 25-50
    c. 51-100
    d. 101-150
    e. 151-200
    f. >200
- Incidence rates per 100.000 [Possible responses to select 1 from predefined list:]
    a. < 1
    b. 1-2
    c. 3-5
    d. 6-10
    e. >10

In your country which proportion of MS patients are cared for?

- MS clinics in University Hospitals [Possible responses to select 1 from predefined list:]
    - < 10%
    - 10-25%
    - 25-50%
    - 50-75%
- MS clinics in Non-academic Hospitals [Possible responses to select 1 from predefined list:]
    - < 10%
    - 10-25%
    - 25-50%
    - 50-75%
- Non-academic hospitals without specific MS clinic [Possible responses to select 1 from predefined list:]
    - < 10%
    - 10-25%
    - 25-50%
    - 50-75%
- Practising Neurologists [Possible responses to select 1 from predefined list:] Eliminate from the general analysis. Not UNITS
    - < 10%
    - 10-25%
    - 25-50%
    - 50-75%

MS care experience

- Number of patients of MS attended in one year
    - < 500
    - 500-1000
    - 1000-1500
    - 1500-2000
    - 2000-2500
    - 2500-3000
    - 3000-3500
    - 3500-4000
    - 4000-4500
    - 4500-5000

- Processes in MS patients: (access to, routinely used) – This is important. We should know the completeness of the so call units in every geographic area.
    - CSF studies (cerebrospinal fluid)
    - MRI
    - Evoked potentials (EP)
    - OCT (optic coherence tomography)
    - Blood tests

Other activities carried out in your centre
Possible responses to select from and then provide also the quantitative measure. This is important. We should know the completeness of the so call units in every geographic area.

- Teaching [% of overall working activity]
- Continuous Medical Education [% of overall working activity]
- Research [% of overall working activity]
- Publications [Number of publications/year]
- Is previous experience needed when entering the unit
    a. Yes
    b. No

MSCU specific resources
Health care professionals needed for the adequate assistance of MS patients. This is important. We should know the completeness of the so call units in every geographic area.
Possible responses to select from and then provide also the quantitative measure.

- Neurologists [number of Neurologists]
- Nurses [number of Nurses]
- Physiotherapists [number of Physiotherapists]
- Additional health care professionals [Possible responses to select from:] This is important. We should know the completeness of the so call units in every geographic area.
    - Occupational therapist
    - Neuropsychologist
    - Speech therapist
    - Clinical psychologists
    - Rehabilitation neurologist-physician

MSCR specific equipment This is important. We should know the completeness of the so call units in every geographic area.

- Day hospital integrated in the MSCU or available at the centre [Possible responses to select from:]
    - None
    - Yes
    - No
- Area for extraction and manipulation of body fluids (blood, CSF) [Possible responses to select from:]
    - None
    - Yes
    - No
- Area of outpatient assistance [Possible responses to select from:]
    - None
    - Yes
    - No
- System of communications with patients [Possible responses to select from:]
    - E-mail
    - Telephone
    - Mobile (SMS)
    - Web page
    - Other…
- Banking facilities for Sera/CSF [Possible responses to select from:]
    - Yes
    - No
- Resources of other units or services apart from the MSCU, necessary for the adequate provision of care for MS patients [Possible responses to select from:]
    - Service/Unit of Neuroradiology with MRI 1.5 tesla or more
    - Service/Unit of Neurophysiology, with the possibility to perform EP (visual, brainstem, somatosensory and motor)
    - Service/Unit of Nuclear Medicine, with SPECT or PET available, needed in some cases for differential diagnosis
    - Service/Unit of Immunology that can perform IgG oligoclonal bands
    - Service/Unit of Immunology that can perform Neurofilament Light in blood (Simoa)
    - Service/Unit of Rehabilitation with experience in the management of MS patients
    - Service/Unit of Ophthalmology, able to perform OCT and with experience in the management of MS patients

- Service/Unit of Urology, with experience in the management of MS patients
- Service/Unit of Genetics, with possibility for banking of DNA/RNA samples
- Availability of a Haematology Unit for autologous hematopoietic stem cell transplantation (aHSCT)

Indicators of processes and clinical results of the MSCU/year

- Number of treatments administered in the day hospital/outpatient clinic. (Oral or IV) [Possible responses to select from:]
  - 0-200
  - 200-400
  - 400-600
  - 600-800
  - 800-1000
  - 1000-1200
  - 1200-1400
  - 1400-1600
  - 1600-1800
  - 1800-2000
  - 2000 -2200
  - 2200-2400
  - 2400-2600
  - 2600-2800
  - 2800-3000
- Number of treated exacerbations (relapses) [Possible responses to select from:]
  - 0-50
  - 50-100
  - 100-150
  - 150-200
  - 200-250
  - 250-300
  - 300-350
  - 350-400
  - 400-450
  - 450-500

- Number of severe adverse events [Possible responses to select from:]

  - 0-50
  - 50-100
  - 100-150
  - 150-200
- Use of disability progression, expanded disability status scale (EDSS) [Possible responses to select from:]
  - Yes
  - No
- Assessment of degree of satisfaction of users [Possible responses to select from:]
  - Yes
  - No
- Administrative data [Possible responses to select from:]
  - Yes
  - No
- Do you have cost accountability? [Possible responses to select from:]
  - Yes
  - No
  -

MSCU registry

- Does MSCU have a registry of patients with MS? [Possible responses to select from:]
  - None
  - Yes
  - No

[If Yes] Minimal data set requirement - data type collected [Possible responses to select from:]

i. Number of patient identification
ii. Date of birth
iii. Sex
iv. Autonomous community-state -province of residence
v. Date of diagnosis and date of exacerbations (relapses)
vi. Other diagnosis (icd-9-mc)

vii. Diagnostic procedures used in the patient (ICD-9-MC) types of procedures and date of same [Possible responses to select from:]
   a) Clinical assessment [Possible responses to select from:]
      a. EDSS
      b. MSFC
      c. Nhpt
      d. T25FW
      e. SDMT
      f. Cognition
      g. Neuropsychological tests
      h. BICAMS
   b) Patient Reported Outcome assessment [Possible responses to select from:]
      a. Qol MEASURE
      b. FATIGUE: MODIFIED FATIGUE IMPACT SCALE OR OTHER
      c. ANXIETY/DEPRESSION: HOSPITAL ANXIETY AND DEPRESSION SCALE
      d. Other
   c) Blood tests [Possible responses to select from:]
      a. AQ4A
      b. NfL
      c. Immunology serological profile
   d) CSF studies (cerebrospinal fluid) [Possible responses to select from:]
      a. IgG OB
      b. IgM OB
      c. IT Synthesis of IgG
   e) Evoked potentials (EP) [Possible responses to select from:]
      a. Visual EP
      b. Somatosensory EP
      c. Auditory EP
      d. Motor EP

Hospital admissions [Possible responses to select from:]
   a) Date of hospitalization
   b) Date hospital discharge
   c) Type of hospitalization
      - Urgent
      - Programmed
   d) Type of hospital discharge
   e) MRI
      - Yes
      - No
   f) OCT (optic coherence tomography)
      - Yes
      - No
   g) X-Ray
      - Yes
      - No
   h) Date of visit
   i) Type of visit
   j) Reason for visit
      - Relapse
      - Initiation or monitoring of disease modifying therapy
      - Diagnostic
      - Follow up
      - Regular annual follow-up in patients not treated with DMTs
      - Infusion
      - MRI
      - Differential Diagnosis

   k) Clinical assessment
   l) Patient reported outcome assessment
   m) Blood tests
   n) CSF studies (cerebrospinal fluid)

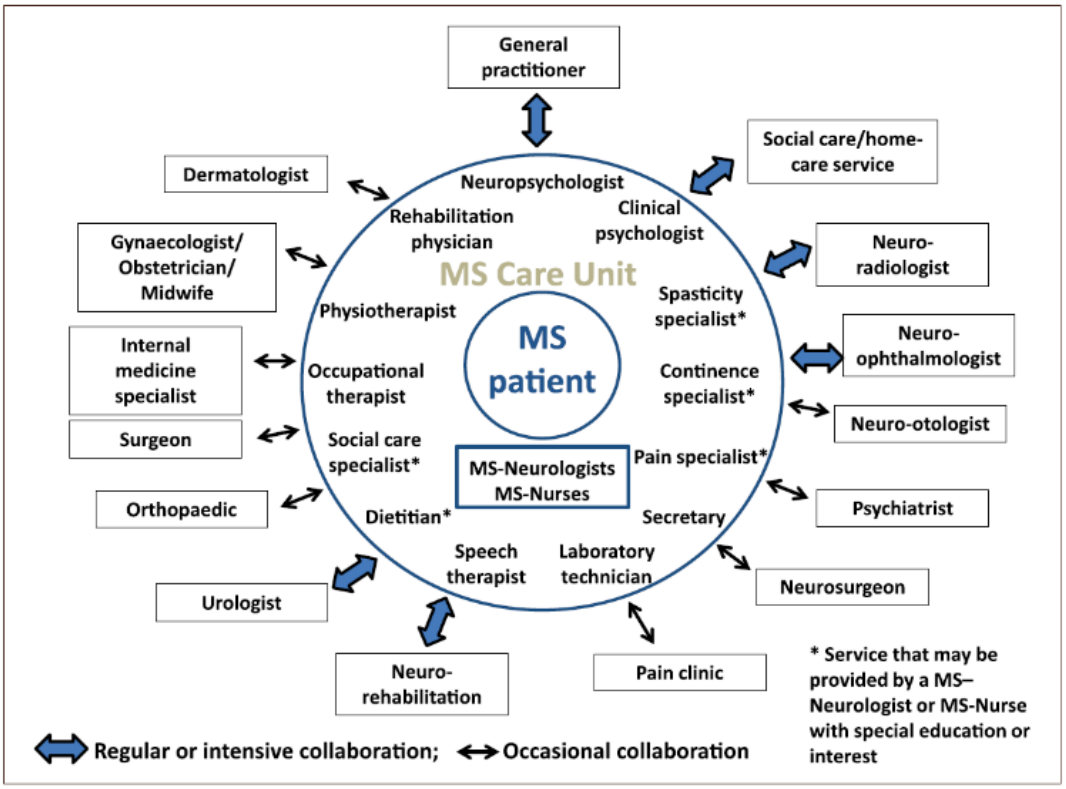
Treatments available

- Immunomodulator treatment
- Immunosuppressant treatment

- Autologous hematopoietic stem cell transplantation (ASCT)
- Other therapeutic procedures
    - Please specify
- Adverse effects

ANNEX II

I. Definition of the needed requirements to be designated as a complete multidisciplinary MSCU (MSCU-I)



❖ **ACTIVITY:**

- **Number of patients of MS who must be attended per year to ensure adequate care:**
  - 1,000-2,000 patients (new and revisions) per year, of these at least 25-30 new patients/year.
- **Number of procedures that must be performed per year:**

- Similar to those for which the designation is requested.

- Procedures in patients with multiple sclerosis:

- 100-200 Lumbar punctures/cerebrospinal fluid.
- 500-1,000 MRIs

- **Other data needed on activity:**

- Teaching: Accredited postgraduate teaching: participation of the Unit in the Center's specialist training program. Yes/no (Yes to qualify)
- Participation in Research projects Yes/no (Yes to qualify)
- Publications in the field of MS. (>10/year)
- Continous Medical Education

- Continous training program standardized and authorized by the center's management. Yes/no (Yes to qualify)
- Multidisciplinary clinical sessions, at least monthly, for clinical decision making and treatment coordination). Yes/no (Yes to qualify)

❖ **MSCU SPECIFIC RESOURCES:**

- **Human resources necessary for adequate care of multiple sclerosis patients**

- 3-5 neurologists: Yes/no (Yes to qualify)
- 2-8 Nursing staff: Yes/no (Yes to qualify)
- 1-2 clinical psychologist or daily collaboration: Yes/no (Yes to qualify)
- 1-2 Neuropsychologist or daily collaboration: Yes/no (Yes to qualify)
- 1 Physiotherapist in the MSCU or daily collaboration with physiotherapist: Yes/no (Yes to qualify)

- **Basic training of team members**

- Neurologists with accredited experience of at least 3 years in the care of patients with multiple sclerosis.
- Clinical psychologist accredited with experience of at least 3 years in the care of patients with multiple sclerosis.
- Nursing staff with accredited experience in caring for patients with multiple sclerosis.

❖ **Specific equipment necessary for adequate care of multiple sclerosis.**

- Day hospital integrated into the unit or available in the center, for outpatient IV immunomodulatory/immunosuppressant treatments. Yes/no (Yes to qualify)
- Local for extractions and manipulation of body fluids (blood, CSF). Yes/no (Yes to qualify)
- External consultation exclusive to the unit. Yes/no (Yes to qualify)
- CSF/serum bank: -70ºC, aliquoted, serum and plasma samples. Necessary for immunology, genetic studies, etc. Yes/no (Yes to qualify)
- Communication system with patients, for extraordinary consultations in case of a relapse or complications (telephone, e-mail, website). Yes/no (Yes to qualify)

❖ **ACCESS TO RESOURCES FROM OTHER UNITS OR SERVICES (in addition to those of the MSCU itself are necessary for adequate care of multiple sclerosis)**

- Radiodiagnosis Service/Unit, which has neuroradiology, MRI of 1.5 Tesla or higher. Yes/no (Yes to qualify)
- Neurophysiology Service/Unit, which performs visual, auditory, somatosensory and motor evoked potentials. Yes/no (Yes to qualify)
- Nuclear medicine service/unit, which has SPECT, necessary for differential diagnosis. Yes/no (Yes to qualify)
- Immunology Service/Unit, which performs detection of oligoclonal bands of IgG and/or KFLC index, markers of intrathecal immunoglobulin synthesis that aids in the diagnosis of multiple sclerosis (MS). Routine use of Blood tests (NfL?, AQ4A) . Yes/no (Yes to qualify)
- Rehabilitation Service/Unit with experience in the management of patients with multiple sclerosis. (Physiotherapy, Speech Therapy, Occupational Therapy) Yes/no (Yes to qualify)
- Ophthalmology Service/Unit, which performs optical coherence tomography (OCT) and with experience in the management of patients with multiple sclerosis. Yes/no (Yes to qualify)
- Urology Service/Unit with experience in the management of patients with multiple sclerosis. Yes/no (Yes to qualify)
- Genetics Service/Unit, with the possibility of saving DNA samples for genetic studies. Yes/no (Yes to qualify)
- Hematology Service (AHSCT) Yes/no (Yes to qualify)

Access to all approved DMTs: Yes/no (Yes to qualify)

❖ **PROCEDURE INDICATORS PER YEAR AND CLINICAL RESULTS OF THE MSCU**

- Number of treatments administered in the Day Hospital. >200
- Number of relapses treated > 50
- Disability progression, Expanded Disability Scale (EDSS). Yes/no (Yes to qualify)
- Degree of user satisfaction. Yes/no (Yes to qualify)
- Quality of life measurement (PROs) Yes/no (Yes to qualify)
- Number of complications and their severity: Adverse events, WHO scale: Quantitative variable (number of cases), Qualitative variable (severity). Yes/no (Yes to qualify)

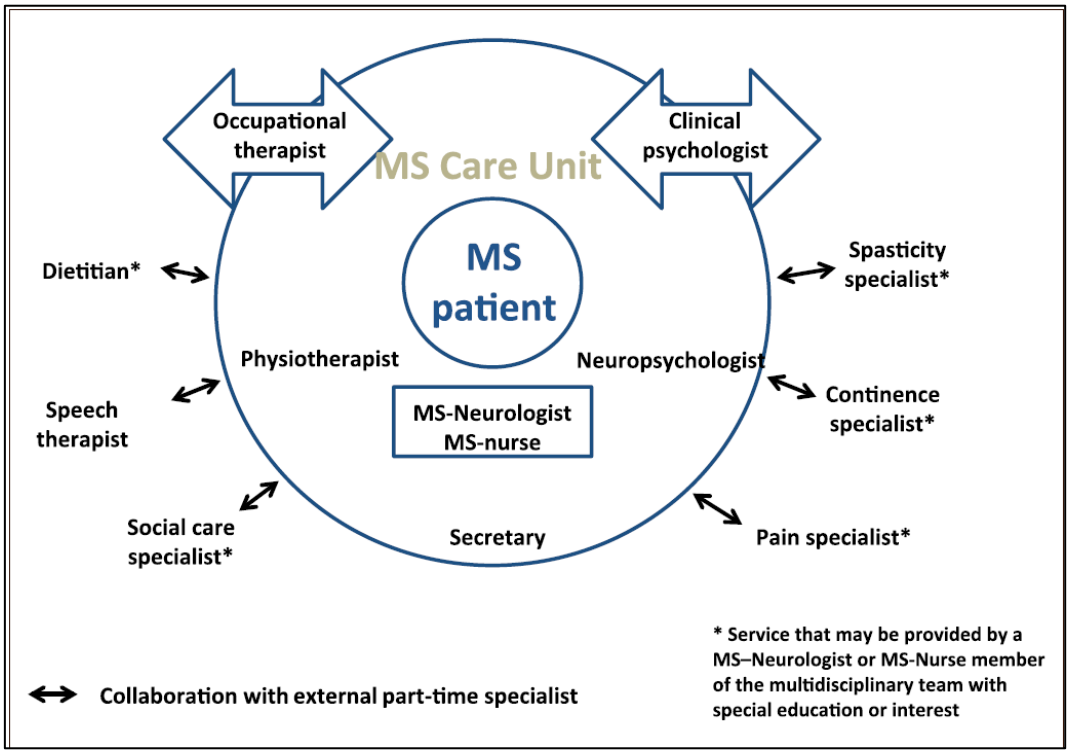
❖ **EXISTENCE OF AN ADEQUATE INFORMATION SYSTEM. (Type of data that the information system must contain to allow knowledge of the activity and evaluation of the quality of the services provided)**

- Completion of the BMDS (basic minimum data set) for hospital discharge in its entirety.
- The Unit must have a record of patients with multiple sclerosis that must include at least: Yes/no (Yes to qualify)
  - Medical History Number.
  - Date of birth.
  - Sex.
  - Address of habitual residence of the patient.
  - Date of admission and date of discharge.
  - Type of admission (Urgent, scheduled, others).
  - Type of discharge (Home, transfer to hospital, voluntary discharge, death, transfer to social and health center, others).
  - Service responsible for patient discharge.
  - Main diagnosis (ICD-9-CM): Date of diagnosis and date of outbreaks.
  - Other diagnoses (ICD-9-CM).
  - Diagnostic procedures performed on the patient (ICD-9-CM): Types of procedures and date of performance.
  - Therapeutic procedures performed on the patient (ICD-9-CM): Types of procedures and dates of performance. Immunomodulatory treatment. Immunosuppressive treatment. Bone marrow transplant. Other therapeutic procedures.

- Complications (ICD-9-CM).
- Follow-up: Number of relapses. Progression of disability,
- QoL evaluation

The unit must have the precise data that it must send to the National Health System for the annual monitoring of the reference unit.

II. Definition of the minimum requirement to be designated as a multidisciplinary MSCU (MSCU-II)



❖ **ACTIVITY:**

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- **Number of procedures that must be performed per year:**

- Similar to those for which the designation is requested.

- Procedures in patients with multiple sclerosis:

- 50-100 Lumbar punctures/cerebrospinal fluid.
- 100-500 MRIs
- **Other data needed on activity:**
- Publications in the field of MS. (>5/year)
- Continous Medical Education

- Continous training program standardized and authorized by the center's management. Yes/no (Yes to qualify)
- Multidisciplinary clinical sessions, at least monthly, for clinical decision making and treatment coordination). Yes/no (Yes to qualify)
-

❖ **MSCU SPECIFIC RESOURCES:**

- **Human resources necessary for adequate care of multiple sclerosis patients**
- 2-3 neurologists: Yes/no (Yes to qualify)
- 2-4 Nursing staff: Yes/no (Yes to qualify)
- 1 clinical psychologist or daily collaboration: Yes/no (Yes to qualify)
- 1 Neuropsychologist or daily collaboration: Yes/no (Yes to qualify)
- 1 Physiotherapist in the MSCU or daily collaboration with physiotherapist: Yes/no (Yes to qualify)
- **Basic training of team members**
- Neurologists with accredited experience of at least 3 years in the care of patients with multiple sclerosis.
- Clinical psychologist accredited with experience of at least 3 years in the care of patients with multiple sclerosis.
- Nursing staff with accredited experience in caring for patients with multiple sclerosis.

❖ **Specific equipment necessary for adequate care of multiple sclerosis.**

- Day hospital integrated into the unit or available in the center, for outpatient IV immunomodulatory/immunosuppressant treatments. Yes/no (Yes to qualify)
- Local for extractions and manipulation of body fluids (blood, CSF). Yes/no (Yes to qualify)
- External consultation exclusive to the unit. Yes/no (Yes to qualify)
- Communication system with patients, for extraordinary consultations in case of a relapse or complications (telephone, e-mail, website). Yes/no (Yes to qualify)

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- Immunology Service/Unit, which performs detection of oligoclonal bands of IgG and/or KFLC index, markers of intrathecal immunoglobulin synthesis that aids in the diagnosis of multiple sclerosis (MS). Routine use of Blood tests (NfL?, AQ4A) . Yes/no (Yes to qualify)
- Rehabilitation Service/Unit with experience in the management of patients with multiple sclerosis. (Physiotherapy, Speech Therapy, Occupational Therapy) Yes/no (Yes to qualify)
- Ophthalmology Service/Unit, which performs optical coherence tomography (OCT) and with experience in the management of patients with multiple sclerosis. Yes/no (Yes to qualify)
- Urology Service/Unit with experience in the management of patients with multiple sclerosis. Yes/no (Yes to qualify)
- Genetics Service/Unit, with the possibility of saving DNA samples for genetic studies. Yes/no (Yes to qualify)
- Hematology Service (AHSCT) Yes/no (Yes to qualify)
- Access to all approved DMTs: Yes/no (Yes to qualify)

❖ **PROCEDURE INDICATORS PER YEAR AND CLINICAL RESULTS OF THE MSCU**

- Number of treatments administered in the Day Hospital. >50
- Number of relapses treated > 20
- Disability progression, Expanded Disability Scale (EDSS). Yes/no (Yes to qualify)
- Degree of user satisfaction. Yes/no (Yes to qualify)
- Quality of life measurement (PROs) Yes/no (Yes to qualify)
- Number of complications and their severity: Adverse events, WHO scale: Quantitative variable (number of cases), Qualitative variable (severity). Yes/no (Yes to qualify)

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  - Medical History Number.
  - Date of birth.
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  - Address of habitual residence of the patient.
  - Date of admission and date of discharge.
  - Type of admission (Urgent, scheduled, others).
  - Type of discharge (Home, transfer to hospital, voluntary discharge, death, transfer to social and health center, others).
  - Service responsible for patient discharge.
  - Main diagnosis (ICD-9-CM): Date of diagnosis and date of outbreaks.
  - Other diagnoses (ICD-9-CM).
  - Diagnostic procedures performed on the patient (ICD-9-CM): Types of procedures and date of performance.
  - Therapeutic procedures performed on the patient (ICD-9-CM): Types of procedures and dates of performance. Immunomodulatory treatment. Immunosuppressive treatment. Bone marrow transplant. Other therapeutic procedures.
  - Complications (ICD-9-CM).
  - Follow-up: Number of relapses. Progression of disability.

Supplementary Tables

Table S1: Distribution of Participating MS-Centers per Country (N=198)

Country	Orgs	Country	Orgs	Country	Orgs	Country	Orgs	Country	Orgs
Argentina	21	Colombia	7	Honduras	1	Paraguay	2	Sweden	3
Australia	1	Denmark	5	Hungary	3	Poland	10	Switzerland	7
Austria	2	Estonia	1	Israel	2	Portugal	10	Tunisia	1
Belgium	4	Finland	4	Italy	10	Romania	2	Turkey	2
Brazil	3	France	25	Japan	1	Russia	3	United Kingdom	4
Bulgaria	3	Germany	5	Lebanon	1	Serbia	2	United States	4
Canada	5	Greece	1	Lithuania	3	Slovenia	5	Uruguay	3
Chile	9	Guatemala	3	Norway	5	Spain	19		
TOTAL Countries	38	TOTAL Orgs	198						

Table S2. Patient Volume per Year Attended by Region and Type of Hospital (N=168).

Region	Non-Academic Hospitals (N=124) (Mean ± SD)	Academic Hospitals (N=44) (Mean ± SD)
Western Europe	1426 ± 853	2228 ± 901
Other European Countries	1301 ± 603	1875 ± 704
North America	918 ± 329	2000 ± 894
Latin America	860 ± 745	1133 ± 854
Rest of World	772 ± 412	1011 ± 320

Table S3. MS-Center Academic Activities by Region and Hospital Type (N=168)

Region	Type	Teaching _Total	CME _Total	Research _Total	Mean Publications	p-value
Western Europe	Academic	23	23	23	26.41	0.0007
Western Europe	Non-Academic	75	75	75	14.14	0.0007
Other Europe	Academic	13	13	13	11.73	0.1037
Other Europe	Non-Academic	15	15	15	7.08	0.1037
Latin America	Academic	5	5	5	13.50	0.0673
Latin America	Non-Academic	27	27	27	8.68	0.0673

Table S4. Availability and utilization of diagnostic resources (Blood tests, CSF studies, evoked potentials, MRI, OCT) across regions and differences by type of hospitals (Non-Academic and Academic hospitals) (N=168)

Region	Process	Non-Academic (%)	Academic (%)	Difference (%)	p-value
Western Europe	BloodTests	70.7	95.7	-25.0	0.012
Western Europe	CSFStudies	78.7	91.3	-12.6	0.227
Western Europe	EvokedPotentials	76.0	91.3	-15.3	0.145
Western Europe	MRI	90.7	95.7	-5.0	0.676
Western Europe	OCT	90.7	95.7	-5.0	0.676
Other European Countries	BloodTests	66.7	69.2	-2.5	1.0
Other European Countries	CSFStudies	73.3	69.2	4.1	1.0
Other European Countries	EvokedPotentials	53.3	69.2	-15.9	0.46
Other European Countries	MRI	73.3	69.2	4.1	1.0
Other European Countries	OCT	73.3	69.2	4.1	1.0
North America	BloodTests	50.0	0.0	50.0	0.467
North America	CSFStudies	50.0	0.0	50.0	0.467
North America	EvokedPotentials	50.0	0.0	50.0	0.467
North America	MRI	100.0	50.0	50.0	0.333
North America	OCT	100.0	50.0	50.0	0.333
Latin America	BloodTests	63.3	100.0	-36.7	0.157
Latin America	CSFStudies	60.0	100.0	-40.0	0.141
Latin America	EvokedPotentials	53.3	100.0	-46.7	0.069
Latin America	MRI	80.0	100.0	-20.0	0.561
Latin America	OCT	80.0	100.0	-20.0	0.561
Rest of the World	BloodTests	33.3	50.0	-16.7	1.0
Rest of the World	CSFStudies	33.3	50.0	-16.7	1.0
Rest of the World	EvokedPotentials	33.3	50.0	-16.7	1.0
Rest of the World	MRI	66.7	50.0	16.7	1.0
Rest of the World	OCT	66.7	50.0	16.7	1.0

Table S5. Use of Immunomodulatory Treatments by Hospital Type (N=168)

Treatment	Academic Hospital	Non-Academic Hospital	p-value (Academic vs Non-Academic)
Avonex	45	122	1.0
Betaseron	44	107	0.1442
Copaxone	46	116	0.1952
Extavia	27	71	0.9507
Generic Glatiramer	34	87	0.7112
Plasmapheresis	45	109	0.0993
Plegridy® (PEG-Interferon)	43	108	0.3347
Rebif® (interferon beta-1a)	45	124	1.0
Vumerity ® (Diroximel fumarate)	14	43	0.7686

Table S6. Use of Immunomodulatory Treatments by Region (N=168)

Treatment	Western Europe	Other European Countries	North America	Latin America	Rest of the World	p-value (Academic vs Non-Academic)
Avonex	103	28	9	51	6	1.0
Betaseron	97	29	9	36	6	0.1442
Copaxone	102	30	9	40	4	0.1952
Extavia	83	14	6	2	0	0.9507
Generic Glatiramer	79	18	9	41	3	0.7112
Plasmapheresis	96	23	7	45	5	0.0993
Plegridy® (PEG-Interferon)	102	28	9	29	5	0.3347
Rebif® (interferon beta-1a)	103	29	9	53	5	1.0
Vumerity ® (Diroximel fumarate)	47	5	5	5	3	0.7686

Table S7. Use of Immunosuppressant Treatments by Hospital Type (N=168)

Treatment	Academic Hospital	Non-Academic Hospital	p-value (Academic vs Non-Academic)
Aubagio® (teriflunomide)	46	118	0.3068
Azathioprine	38	110	0.5555
Cyclophosphamide	33	101	0.3163
Gilenya® (fingolimod)	47	120	0.1782
IgIV	1	1	1.0
Kesimpta (ofatumumab)	1	1	1.0
Lemtrada® (alemtuzumab)	39	98	0.4804
Mavenclad® (cladribine)	43	122	0.5496
Methotrexate	33	97	0.581
Mycophenolate Mofetil	0	1	1.0
Novantrone® (mitoxantrone)	35	87	0.5197
Ponesimod (Ponvory)	1	0	0.6005

Table S8. Use of Immunosuppressant Treatments by Region (N=168)

Treatment	Western Europe	Other European Countries	North America	Latin America	Rest of the World	p-value (Academic vs Non-Academic)
Aubagio® (teriflunomide)	98	28	6	26	3	0.3068
Azathioprine	88	20	4	28	5	0.5555
Cyclophosphamide	82	13	5	26	5	0.3163
Gilenya® (fingolimod)	96	27	6	30	5	0.1782
IgIV	1	0	0	0	0	0.6005
Kesimpta (ofatumumab)	1	0	0	0	1	0.6005
Lemtrada® (alemtuzumab)	72	25	6	28	3	0.4804
Mavenclad® (cladribine)	98	27	6	29	2	0.5496
Mayzent (siponimod)	0	0	0	0	1	1.0
Methotrexate	82	12	4	24	5	0.581
Mycophenolate Mofetil	1	0	1	0	0	1.0
Novantrone® (mitoxantrone)	82	18	4	14	2	0.5197
HSCT	1	0	0	0	0	1.0
Ponesimod (Ponvory®)	1	0	0	0	0	1.0
Rituximab	95	19	5	35	4	0.085
Tecfidera® (dimethyl fumarate)	98	27	6	26	5	1.0
Tysabri® (natalizumab)	97	28	6	28	5	0.5964
Zeposia (Ozanimod®)	1	0	0	0	0	0.6005
evobrutinib, fenebrutinib	0	1	0	0	0	0.6005
Ocrevus® (ocrelizumab)	92	28	6	32	4	0.3836

Table S9. Use of Immunosuppressant Treatments by Region and Hospital Type (N=168)

Treatment	Western Europe - Academic	Western Europe - Non-Academic	Other European Countries - Academic	Other European Countries - Non-Academic	North America - Academic	North America - Non-Academic	Latin America - Academic	Latin America - Non-Academic	Rest of the World - Academic	Rest of the World - Non-Academic	p-value (Academic vs Non-Academic)
Aubagio® (teriflunomide)	23	75	13	15	2	4	5	21	1	2	0.3068
Azathioprine	20	68	8	12	1	3	5	23	2	3	0.5555
Cyclophosphamide	18	64	4	9	2	3	5	21	2	3	0.3163
Gilenya® (fingolimod)	23	73	13	14	2	4	5	25	2	3	0.1782
IgIV	1	0	0	0	0	0	0	0	0	0	0.6005
Kesimpta (ofatumumab)	0	1	0	0	0	0	0	0	1	0	1.0
Lemtrada® (alemtuzumab)	18	54	12	13	2	4	4	24	1	2	0.4804
Mavenclad® (cladribine)	23	75	12	15	2	4	4	25	0	2	0.5496
Mayzent (siponimod)	0	0	0	0	0	0	0	0	0	1	1.0
Methotrexate	19	63	4	8	1	3	5	19	2	3	0.581
Mycophenolate Mofetil	0	1	0	0	0	1	0	0	0	0	1.0
Novantrone® (mitoxantrone)	20	62	9	9	1	3	3	11	0	2	0.5197
HSCT	0	1	0	0	0	0	0	0	0	0	1.0
Ponesimod (Ponvory®)	0	1	0	0	0	0	0	0	0	0	1.0
Rituximab	22	73	9	10	1	4	5	30	1	3	0.085
Tecfidera® (dimethyl fumarate)	23	75	12	15	2	4	3	23	2	3	1.0
Tysabri® (natalizumab)	23	74	13	15	2	4	4	24	2	3	0.5964
Zeposia (ozanimod®)	1	0	0	0	0	0	0	0	0	0	0.6005
evobrutinib, fenebrutinib	0	0	1	0	0	0	0	0	0	0	0.6005
Ocrevus® (ocrelizumab)	23	69	13	15	2	4	5	27	1	3	0.3836

Table S10. Generic and Commercial Names of MS Therapies

Generic Name	Commercial Name
Glatiramer acetate	Copaxone
Interferón beta-1a	Avonex, Rebif
Interferón beta-1b	Betaferon, Betaseron, Extavia
Peginterferón beta-1a	Plegridy
Teriflunomida	Aubagio
Dimetil fumarato	Tecfidera
Diroximel fumarato	Vumerity
Fingolimod	Gilenya
Siponimod	Mayzent
Ponesimod	Ponvory
Ozanimod	Zeposia
Natalizumab	Tysabri
Cladribine	Mavenclad
Alemtuzumab	Lemtrada
Ocrelizumab	Ocrevus
Ofatumumab	Kesimpta
Mitoxantrone	Novantrone
Autologous stem Cell Transplantation	ASCT

Table S11. MS Therapy Use by Efficacy Level, Region and Hospital Type (N=168) (Including ASCT Separately)

Region	Institution Type	Low Efficacy (%)	Moderate Efficacy (%)	High Efficacy (%)	ASCT (%)
Western Europe	Academic Hospital	90	75	116.5	56.5
Western Europe	Non-Academic Hospital	88	73	119.3	61.3
Other European Countries	Academic Hospital	85	70	93.5	38.5
Other European Countries	Non-Academic Hospital	83	68	93.0	40.0
North America	Academic Hospital	88	78	65.0	0.0
North America	Non-Academic Hospital	86	76	138.0	75.0
Latin America	Academic Hospital	80	68	90.0	40.0
Latin America	Non-Academic Hospital	78	66	59.1	11.1
Rest of the World	Academic Hospital	75	60	95.0	50.0
Rest of the World	Non-Academic Hospital	73	58	43.0	0.0

Note: Percentages by efficacy level are not mutually exclusive. A single MS-Center may report the use of therapies from multiple efficacy categories (e.g., both moderate- and high-efficacy DMTs), and therefore, totals across efficacy levels may exceed 100%.

Table S12. Availability of Core Structural Components in MS-Centers (N=168) by Region and Hospital Type

Region_Organization	Biological Fluids Area	Outpatient Area	Banking Facilities	Day Hospital
Western European Countries - Academic Hospital	1.0	1.0	0.96	0.91
Western European Countries - Non-Academic Hospital	0.95	0.95	0.83	0.92
Other European Countries - Academic Hospital	0.92	1.0	0.92	1.0
Other European Countries - Non-Academic Hospital	1.0	0.87	0.8	0.93
North America - Academic Hospital	0.5	1.0	0.5	0.5
North America - Non-Academic Hospital	1.0	1.0	0.5	0.75
Latin America - Academic Hospital	0.8	1.0	0.6	1.0
Latin America - Non-Academic Hospital	0.87	0.9	0.53	0.63
Rest of the World - Academic Hospital	1.0	1.0	1.0	1.0
Rest of the World - Non-Academic Hospital	1.0	1.0	1.0	1.0

Table S13 – Operational Characteristics of MS-Centers (N=168)

Operational variable	% of centers (N=168)	p (Academic vs Non-Academic)	p (by Region)
Treatments administered (data present)	100.0	<0.001	<0.0001
Treated exacerbations (data present)	100.0	<0.0001	<0.0001
Severe adverse events (data present)	100.0	0.5068	0.2005
Administrative data recorded	81.5	0.6034	0.0015
Cost accountability	53.0	0.0538	<0.0001
MS patient registry	85.7	1.0000	0.0185
Minimal dataset documented	100.0	n.s.	n.s.
Hospital admissions data (any subitem)	100.0	n.s.	n.s.
Type of hospital discharge (any subitem)	100.0	n.s.	n.s.
Date of visit recorded	75.0	0.6198	0.0236
Type of visit recorded	100.0	n.s.	n.s.
Reason for visit recorded	100.0	n.s.	n.s.
Adverse effects classification	100.0	n.s.	n.s.

Table S14. Communication Systems Used in MS-Centers by Hospital Type (N=168)

Communication System	Academic Hospitals	Non-Academic Hospitals
Phone	45	123
E-mail	42	108
SMS	25	62
Website	20	26
Patient Portal	2	1
Social Media	1	2
App	2	1
WhatsApp	0	2
Personal	0	1
Personal Interview	0	1
Digital Mail	0	1
Postal	0	1
Mail, Digital Tool	0	1
Secured Healthcare Network	0	1
Mail	0	1
Through The Electronic Patient Record	0	1
Twitter	1	0
Video Call	1	0
Letter	0	1

Table S15a. Essential and Non-Essential Criteria for MSCU Classification

Criterion	Essential for MSCU-I / MSCU-II	Impact on Classification
MS patient volume	Yes / Yes	Essential
Number of neurologists	Yes / Yes	Essential
Number of nurses	Yes / No	Essential for MSCU-I only
Presence of physiotherapists	Yes / Yes	Essential
Access to MRI	Yes / Yes	Essential
Access to immunology services	Yes / Yes	Essential
Access to neuropsychology	No / Yes	Essential for MSCU-II only
Access to rehabilitation services	Yes / Yes	Essential
Continuing medical education (CME)	Yes / No	Essential for MSCU-I only
Participation in research	Yes / Yes	Essential
Day hospital availability	Yes / Yes	Essential
Access to clinical psychology	Yes / Yes	Essential
Outpatient consultation area	Yes / Yes	Essential
EDSS registry	Yes / Yes	Essential
Patient communication system	No / Yes	Essential for MSCU-II only
Access to DMTs	Yes / Yes	Essential
Area for fluid extraction/handling	No / No	Non-essential
Biobanking (sera/CSF)	No / No	Non-essential
Administrative data system	No / No	Non-essential
Cost accountability system	No / No	Non-essential
MS patient registry	Yes / Yes	Essential
Assessment of patient satisfaction	Yes / Yes	Essential

Table S15b. Summary of MSCU-I / MSCU-II Criteria

Criterion	Response Rate (%)	Included as Primary Criterion
Annual MS patient volume	96.5%	✓
Number of neurologists	93.9%	✓
Number of nurses	91.4%	✓
Presence of physiotherapists	90.4%	✓
Access to MRI	98.0%	✓
Access to immunology services	97.5%	✓
Access to neuropsychology	90.9%	✓
Access to rehabilitation services	91.4%	✓
Continuing medical education (CME)	92.4%	✓
Participation in research	90.9%	✓
Day hospital availability	95.5%	✓
Access to clinical psychology	94.4%	✓
Outpatient consultation area	97.5%	✓
EDSS registry	94.9%	✓
Patient communication system	97.5%	✓
Access to DMTs	100.0%	✓
Area for extraction/manipulation of fluids	90.4%	
Biobanking (Sera/CSF)	91.9%	
Administrative data system	92.4%	
Cost accountability system	90.4%	
MS patient registry	100.0%	✓
Assessment of patient satisfaction	91.4%	✓

Table S15c. Summary of Final MSCU Classification Criteria of Hospital MS-Centers (N=168)

Criterion	Response Rate (%)	Primary Criterion
MS patient volume (annual)	96.5	Yes
Number of neurologists	93.9	Yes
Number of nurses	91.4	Yes
Presence of physiotherapists	90.4	Yes
Access to MRI	98.0	Yes
Access to immunology services	97.5	Yes
Access to neuropsychology	90.9	Yes
Access to rehabilitation services	91.4	Yes
Continuing medical education (CME)	92.4	Yes
Participation in research	90.9	Yes
Day hospital availability	95.5	Yes
Access to clinical psychology	94.4	Yes
Outpatient consultation area	97.5	Yes
EDSS registry	94.9	Yes
Patient communication system	97.5	Yes
Access to DMTs	100.0	Yes
Area for extraction/manipulation of fluids	90.4	
Biobanking (Sera/CSF)	91.9	
Administrative data system	92.4	
Cost accountability system	90.4	
MS patient registry	95.5	Yes
Assessment of patient satisfaction	91.4	Yes

Table S15d. Compliance with MSCU Criteria by Hospital type and Region (N=168)

Criterion	Region	Institution Type	MSCU-I (%)	MSCU-II (%)
MS patient volume (annual)	Western Europe	Academic	84.4	79.0
MS patient volume (annual)	Western Europe	Non-Academic	93.3	72.0
MS patient volume (annual)	Other European Countries	Academic	78.9	63.1
MS patient volume (annual)	Other European Countries	Non-Academic	76.5	77.3
MS patient volume (annual)	Latin America	Academic	90.0	74.2
MS patient volume (annual)	Latin America	Non-Academic	75.5	79.4
Number of neurologists	Western Europe	Academic	95.8	64.2
Number of neurologists	Western Europe	Non-Academic	79.5	63.7
Number of neurologists	Other European Countries	Academic	82.6	70.5
Number of neurologists	Other European Countries	Non-Academic	85.8	65.8
Number of neurologists	Latin America	Academic	90.3	62.8
Number of neurologists	Latin America	Non-Academic	82.3	67.3
Number of nurses	Western Europe	Academic	86.4	75.7
Number of nurses	Western Europe	Non-Academic	80.0	70.3
Number of nurses	Other European Countries	Academic	89.8	60.9
Number of nurses	Other European Countries	Non-Academic	90.2	63.4
Number of nurses	Latin America	Academic	76.6	79.0
Number of nurses	Latin America	Non-Academic	99.1	76.2
Presence of physiotherapists	Western Europe	Academic	82.6	62.0
Presence of physiotherapists	Western Europe	Non-Academic	92.1	68.8
Presence of physiotherapists	Other European Countries	Academic	78.1	69.9
Presence of physiotherapists	Other European Countries	Non-Academic	75.9	78.2
Presence of physiotherapists	Latin America	Academic	81.5	73.3
Presence of physiotherapists	Latin America	Non-Academic	82.8	70.4
Access to MRI	Western Europe	Academic	88.7	63.7
Access to MRI	Western Europe	Non-Academic	99.2	75.5
Access to MRI	Other European Countries	Academic	98.5	77.9
Access to MRI	Other European Countries	Non-Academic	89.9	78.4
Access to MRI	Latin America	Academic	77.2	63.9
Access to MRI	Latin America	Non-Academic	76.1	66.5

Table S15e. Summary Table of Criteria for MSCU-I / MSCU-II Classification with Minimum Thresholds

Criterion	Variable Type	Essential for MSCU-I	Indicative Threshold	Essential for MSCU-II	Indicative Threshold
Annual volume of MS patients	Continuous quantitative	Yes	≥1500	Yes	≥1000
Number of neurologists	Discrete quantitative	Yes	≥5	Yes	≥3
Number of nurses	Discrete quantitative	Yes	≥4	No	-
Presence of physiotherapists	Binary (Yes/No)	Yes	-	Yes	-
Access to MRI	Binary	Yes	-	Yes	-
Access to immunology services	Binary	Yes	-	Yes	-
Access to neuropsychology	Binary	No	-	Yes	-
Access to rehabilitation services	Binary	Yes	-	Yes	-
Continuing medical education (CME)	Binary	Yes	-	No	-
Participation in research	Binary	Yes	-	Yes	-
Day hospital availability	Binary	Yes	-	Yes	-
Access to clinical psychology	Binary	Yes	-	Yes	-
Outpatient consultation area	Binary	Yes	-	Yes	-
EDSS registry	Binary	Yes	-	Yes	-
Patient communication system	Binary	No	-	Yes	-
Access to DMTs	Binary	Yes	-	Yes	-
Area for fluid extraction/handling	Binary	No	-	No	-
Biobanking (sera/CSF)	Binary	No	-	No	-
Administrative data system	Binary	No	-	No	-
Cost accountability system	Binary	No	-	No	-
MS patient registry	Binary	Yes	-	Yes	-
Assessment of patient satisfaction	Binary	Yes	-	Yes	-

Note: This scoring model differs from the original classification (120 MSCU-I, 21 MSCU-II) based on proportional fulfillment of 22 criteria, as described in the main Results section.

Table S15f. Automatic Scoring Scheme for MSCU Classification

Criterion	Variable Type	MSCU-I Requirement	MSCU-II Requirement
Total essential criteria	Score threshold	≥14 out of 16	≥14 out of 16
Annual MS patient volume	Continuous quantitative	≥1500	≥1000
Number of neurologists	Discrete quantitative	≥5	≥3
Number of nurses	Discrete quantitative	≥4	Not required
Presence of physiotherapist	Binary (Yes/No)	Yes	Yes
Access to MRI	Binary (Yes/No)	Yes	Yes
Access to immunology services	Binary (Yes/No)	Yes	Yes
Access to neuropsychology	Binary (Yes/No)	Not required	Yes
Access to rehabilitation services	Binary (Yes/No)	Yes	Yes
Continuing medical education (CME)	Binary (Yes/No)	Yes	Not required
Participation in research	Binary (Yes/No)	Yes	Yes
Day hospital availability	Binary (Yes/No)	Yes	Yes
Access to clinical psychology	Binary (Yes/No)	Yes	Yes
Outpatient consultation area	Binary (Yes/No)	Yes	Yes
EDSS registry	Binary (Yes/No)	Yes	Yes
Patient communication system	Binary (Yes/No)	Not required	Yes
Access to DMTs	Binary (Yes/No)	Yes	Yes
MS patient registry	Binary (Yes/No)	Yes	Yes
Assessment of patient satisfaction	Binary (Yes/No)	Yes	Yes

Note: One point is assigned for each essential criterion fulfilled. This scoring system enables an automated and objective classification of MS Care Units (MSCUs) based on the availability of essential clinical, human, and structural resources. This scoring model differs from the original classification (120 MSCU-I, 21 MSCU-II), which was based on proportional fulfilment of 22 predefined criteria (≥80% for MSCU-I; 70–79% for MSCU-II), as detailed in the main Results section.

Table S16. Assessment of User Satisfaction by Region and Type of Hospital (N=168)

Region	Academic Hospital (%)	Non-Academic Hospital (%)
Western European Countries	81.3	75.7
Other European Countries	76.9	73.3
North America	50.0	75.0
Latin America	46.2	55.6
Rest of the World	33.3	50.0

Table S17. Distribution of Patient-Reported Outcome Assessments by Region and Hospital Type (absolute number) (N=168)

Data represents the number of MS-Centers reporting the use of each type of Patient-Reported Outcome (PRO) assessment tool. Values are counts, not percentages.

PRO Assessment (Count)	Western Europe - Academic	Western Europe - Non-Academic	Other Europe - Academic	Other Europe - Non-Academic	North America - Academic	North America - Non-Academic	Latin America - Academic	Latin America - Non-Academic	Rest of World - Academic	Rest of World - Non-Academic
QoL Assessment (Count)	38	34	21	18	6	5	10	14	3	2
Fatigue Assessment (Count)	29	30	17	12	4	4	6	8	2	1
Anxiety/Depression (Count)	17	12	14	11	2	2	3	4	1	1
Other (Count)	14	9	8	6	1	1	2	3	1	1
TOTAL (Count)	98	85	60	47	13	12	21	29	7	5

Table S18. Distribution of Patient-Reported Outcome Assessments by Region and Hospital Type (%) (N=168)

PRO Assessment (%)	Western Europe - Academic	Western Europe - Non-Academic	Other Europe - Academic	Other Europe - Non-Academic	North America - Academic	North America - Non-Academic	Latin America - Academic	Latin America - Non-Academic	Rest of World - Academic	Rest of World - Non-Academic
QoL Assessment (%)	38.8	40.0	35.0	38.3	46.2	41.7	47.6	48.3	42.9	40.0
Fatigue Assessment (%)	29.6	35.3	28.3	25.5	30.8	33.3	28.6	27.6	28.6	20.0
Anxiety/Depression (%)	17.3	14.1	23.3	23.4	15.4	16.7	14.3	13.8	14.3	20.0
Other (%)	14.3	10.6	13.3	12.8	7.7	8.3	9.5	10.3	14.3	20.0
TOTAL (%) (%)	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table S19. GDP and Health Expenditure per Capita by MSCU Type

Variable	MSCU-I (n=120)	MSCU-II (n=21)
GDP per capita (USD)	32,466 ± 14,467	12,802 ± 7,871
Health Exp per capita (USD)	3,639 ± 1,746	1,568 ± 925

Supplementary Figures

Figure S1. Proportional distribution of hospitals and universities across the surveyed geographic regions (N=198).

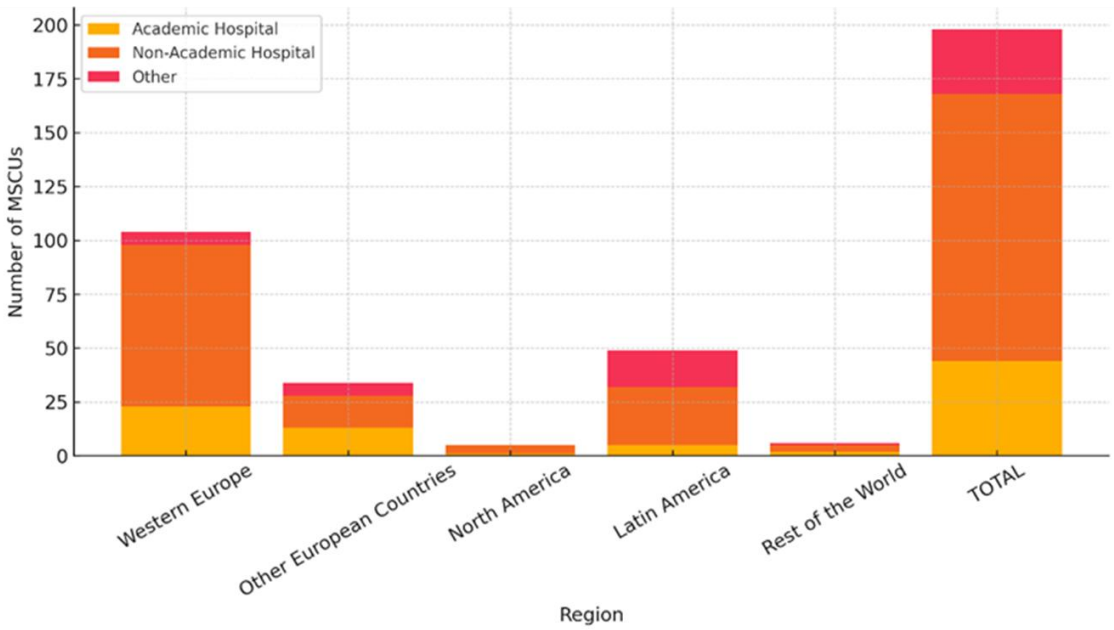


Figure S2. Distribution of MS-Center Staff by Region and Type of Hospital (N=168)

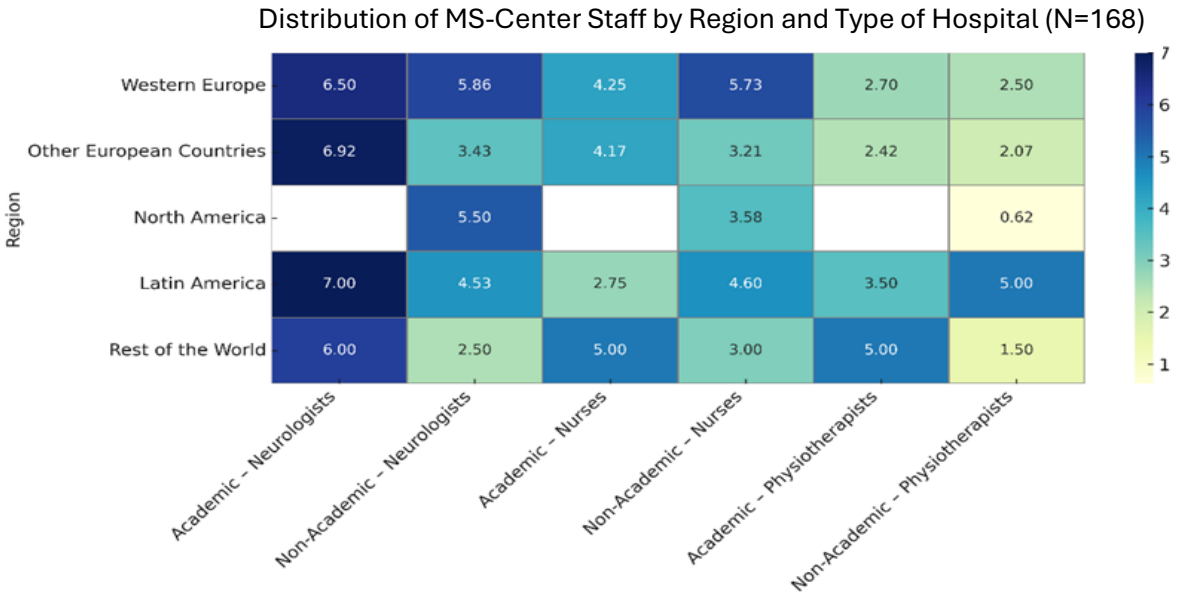
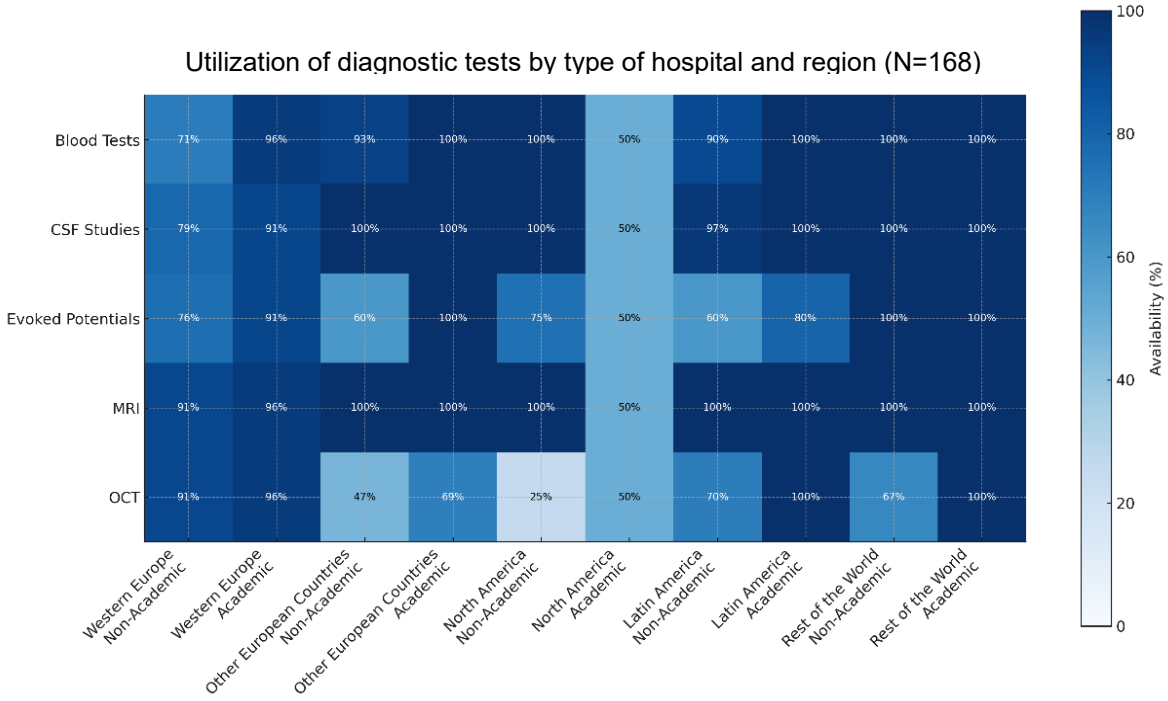
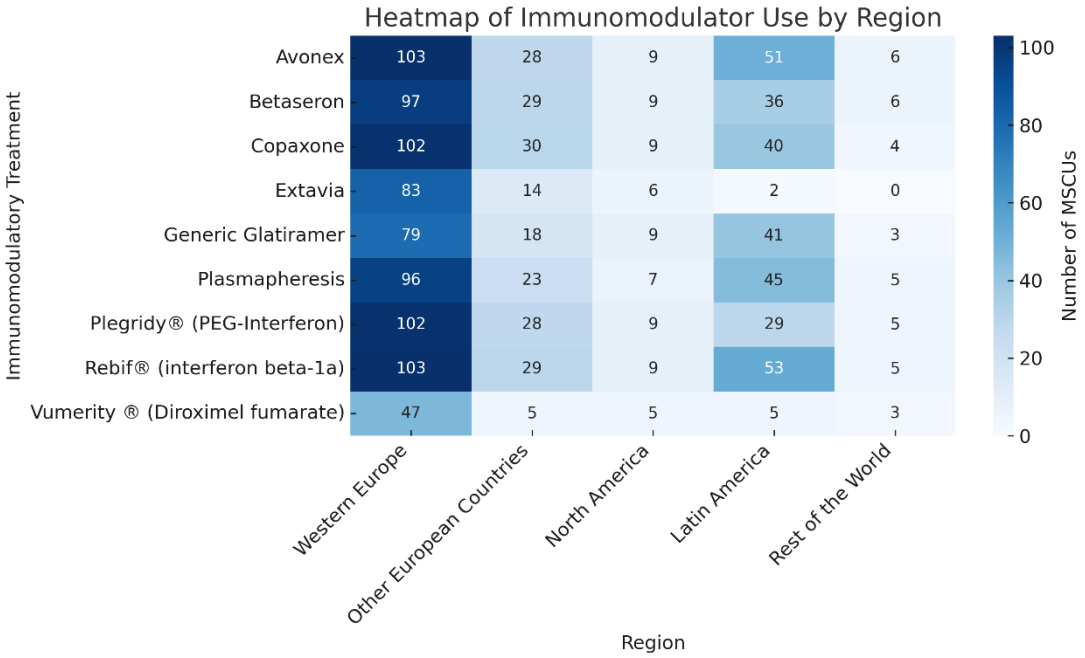


Figure S3. Heatmap illustrating the utilization of diagnostic tests by type of hospital and region (N=168).



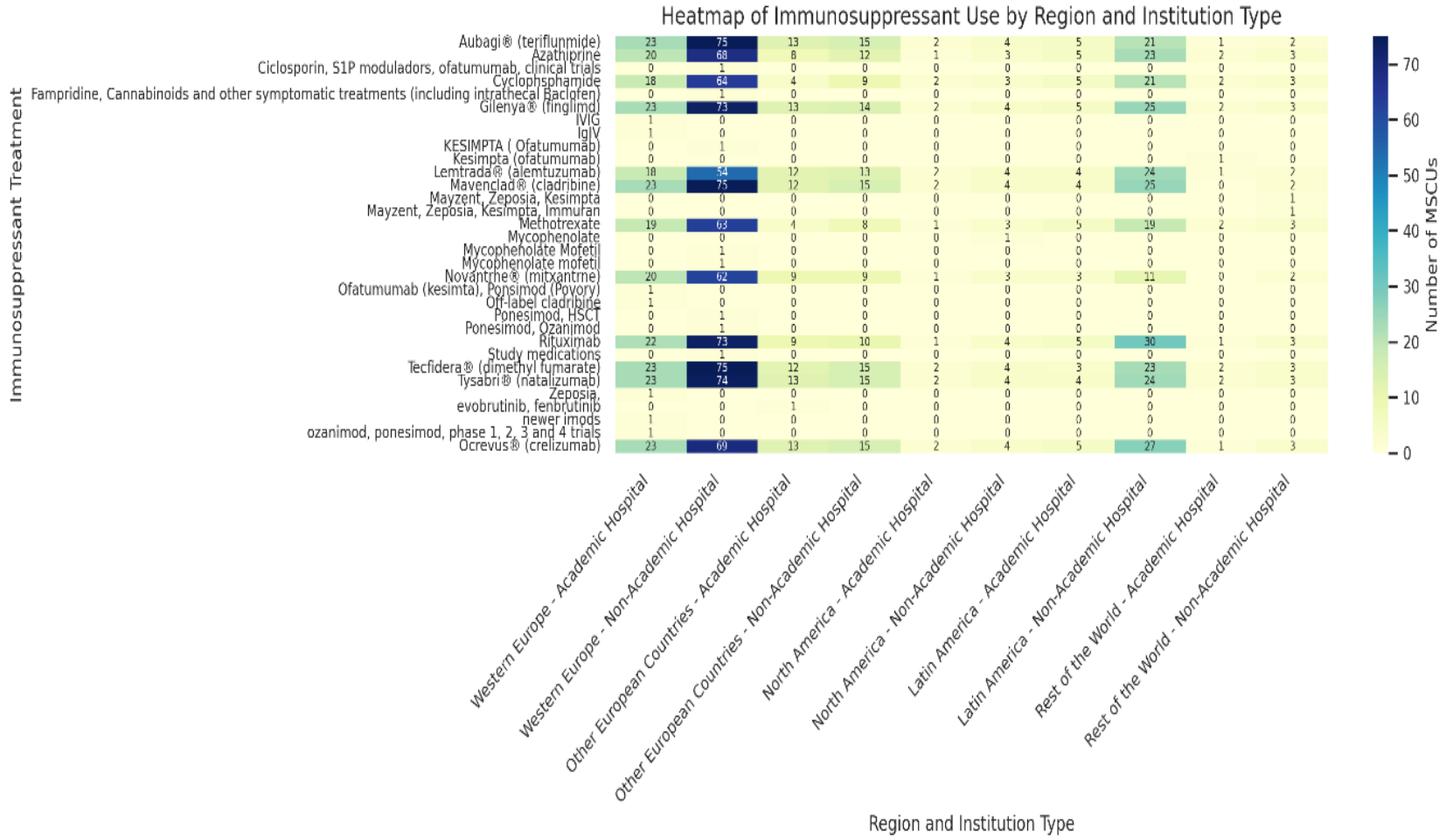
Note: Heatmap showing the availability of key diagnostic tools used in the evaluation of patients with multiple sclerosis, stratified by hospital type (Academic vs Non-Academic) and region. Availability is expressed as the percentage of MS Care Units reporting routine use of each modality: MRI, cerebrospinal fluid (CSF) analysis, evoked potentials (EPs), optical coherence tomography (OCT), and blood tests. Dark blue indicates high availability, while lighter shades indicate more limited use. MRI and blood tests were generally widespread, although not universal, whereas the use of EPs and OCT varied more significantly across regions and organization types.

Figure S4. Use of Immunomodulatory Treatments by Region (N=168)



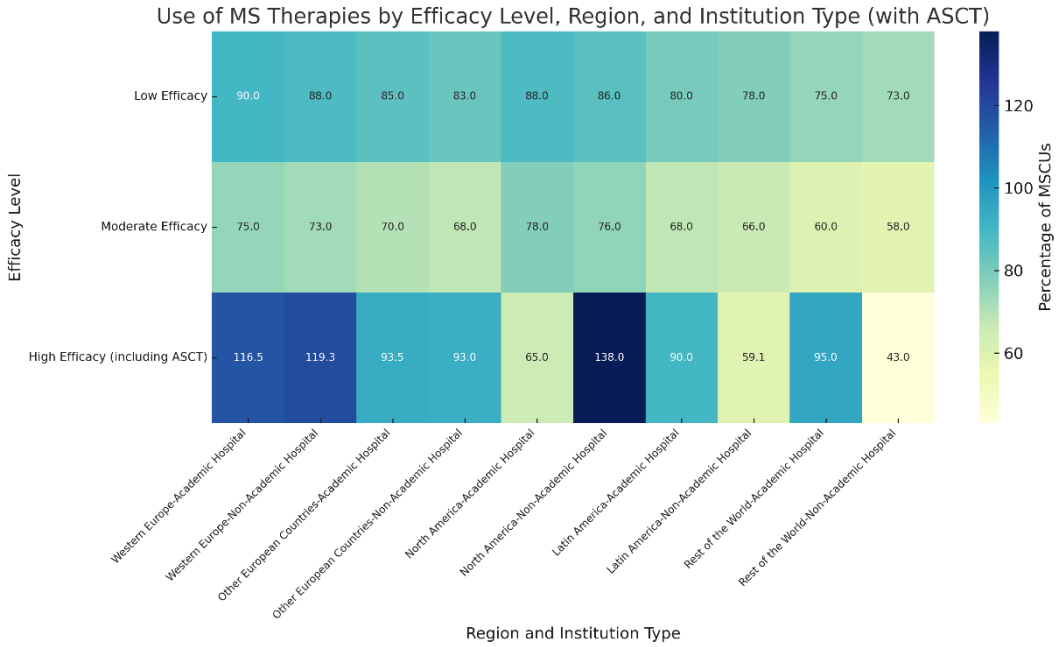
Note: Heatmap showing the number of MS-Centers Care Units (MSCUs) reporting the use of key immunomodulatory treatments across regions. Darker shades indicate more frequent usage. Data represent counts of units reporting each agent.
No statistically significant differences were observed in treatment use between Academic and Non-Academic Hospitals ($p > 0.14$ for all major agents).

Figure S5. Use of Immunosuppressant Treatments by Region and Hospital Type (N=168)



Note: Heatmap showing the number of MS-Centers reporting the use of each immunosuppressant therapy, stratified by region and organization type (Academic vs Non-Academic Hospitals).Darker colors represent higher reporting frequencies.No statistically significant differences in treatment use were observed between academic and non-academic settings (final column in table shows *p*-values from chi-square tests).Frequent therapies included **Aubagio (teriflunomide)**, **azathioprine**, and **cyclophosphamide**, with wide usage across multiple regions.

Figure S6. Distribution of MS Therapy Use by Efficacy Level, Hospital Type, and Region



Note: Percentages by efficacy level are not mutually exclusive. A single MS-Center may report the use of therapies from multiple efficacy categories (e.g., both moderate- and high-efficacy DMTs), and therefore, totals across efficacy levels may exceed 100%.

Figure S7. Availability of External Resources by Region and Hospital Type (Top 9) (N=168)

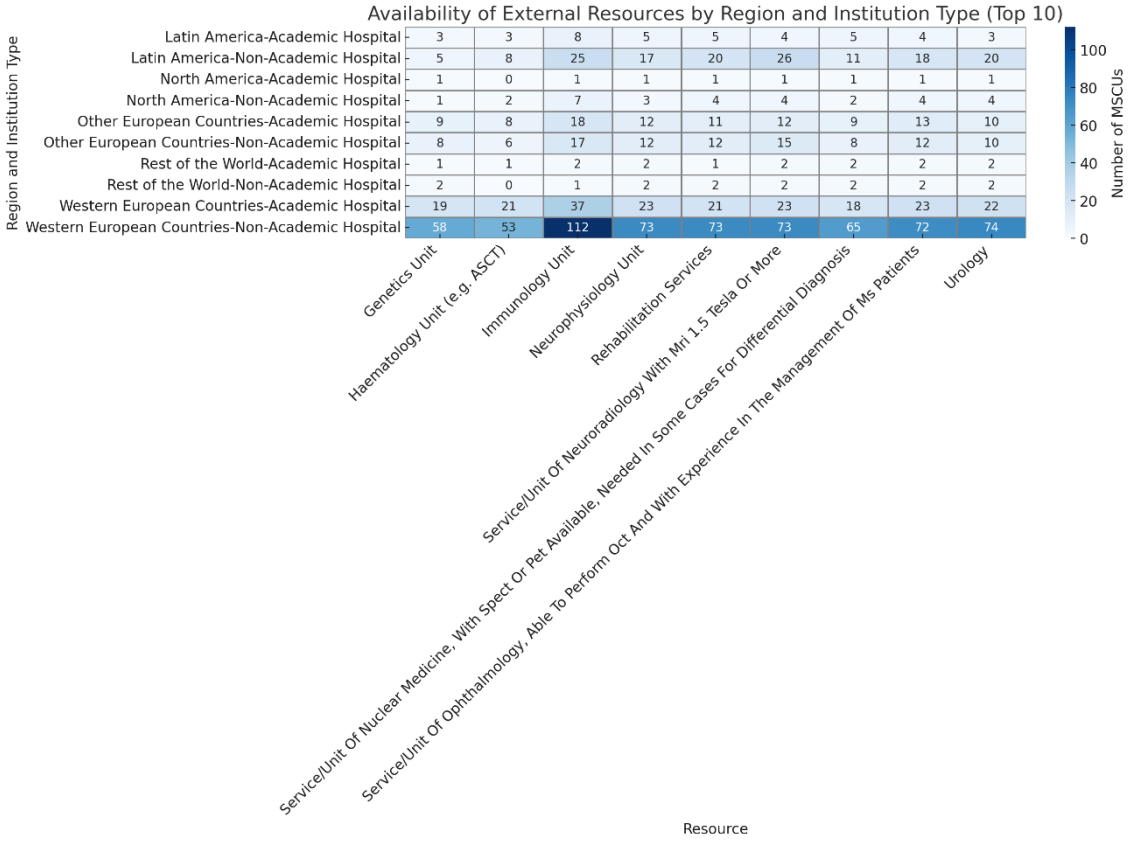


Figure S8. Use of Communication Systems with Patients by Hospital Type (Ordered by Total Usage)(N=168)

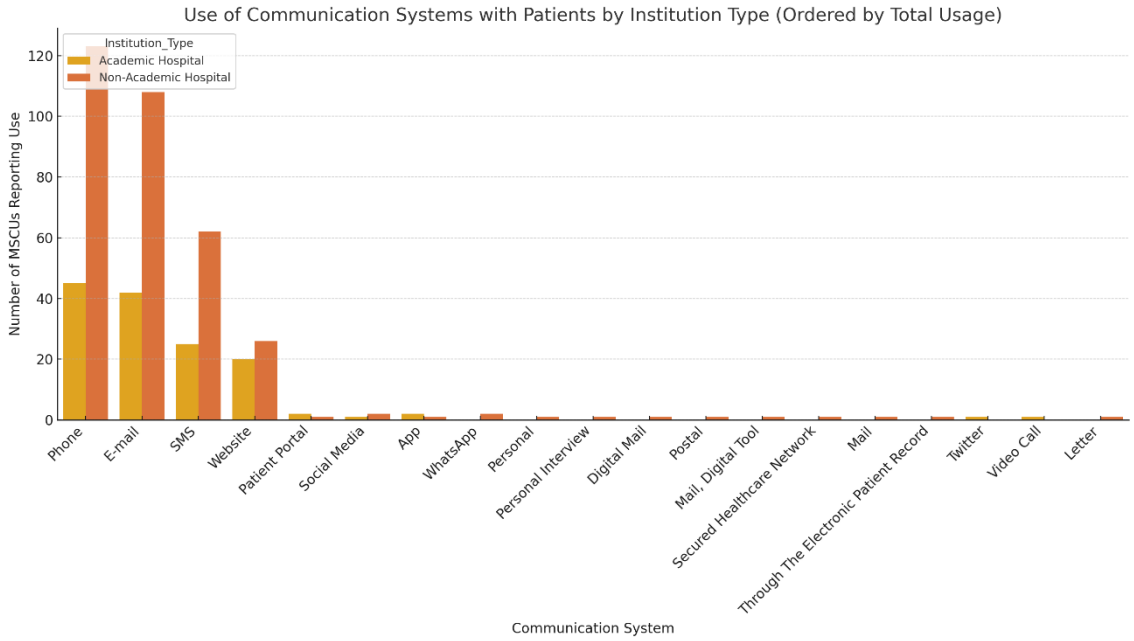
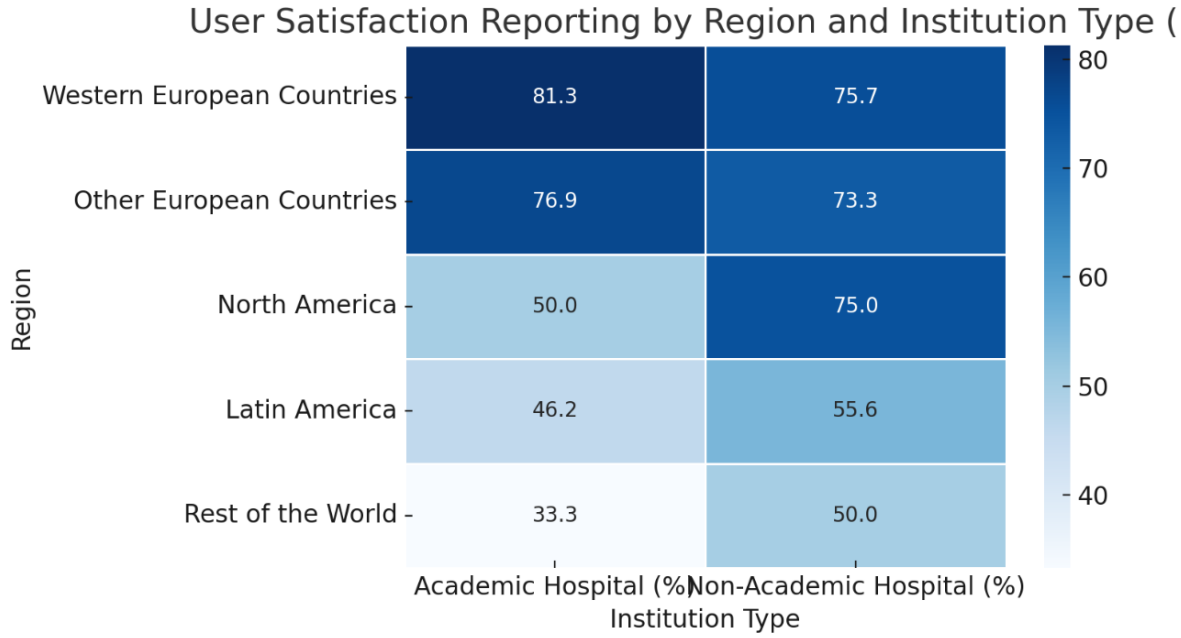


Figure S9. Assessment of User Satisfaction by Region and Hospital Type (N=168)



Heatmap showing the percentage of MS-Centers reporting routine assessment of user satisfaction, stratified by global region and type of organization (Academic vs Non-Academic Hospitals). Darker blue tones represent higher reporting rates. No statistically significant differences were found across settings (p = 0.856, chi-square test).

Figure S10. Distribution of Patient-Reported Outcome Assessments by Region and Hospital Type (N=168)

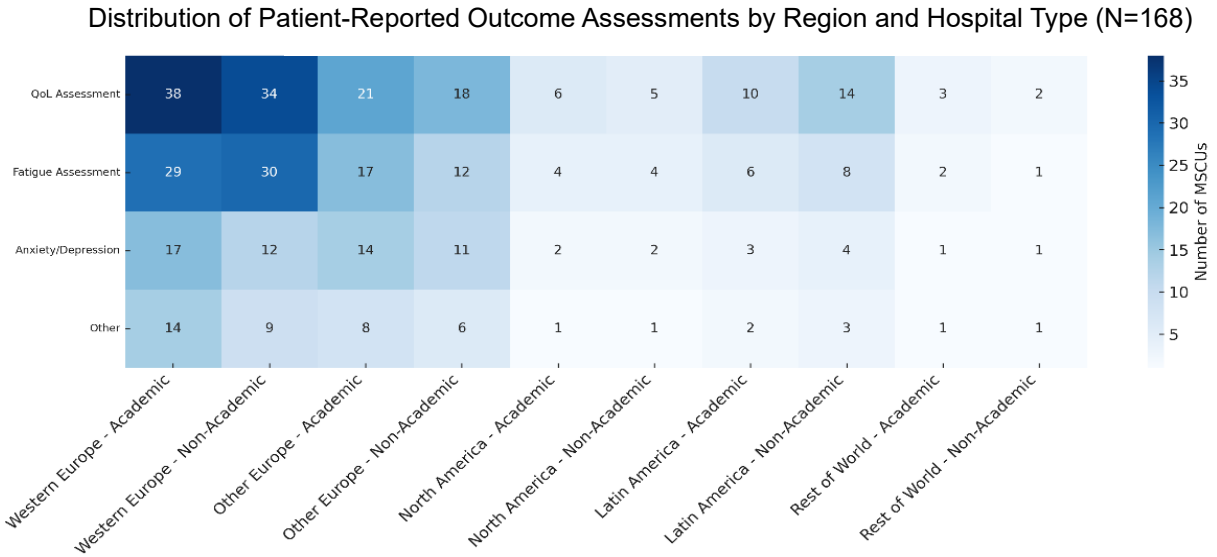


Figure S11. GDP per capita by MSCU Type

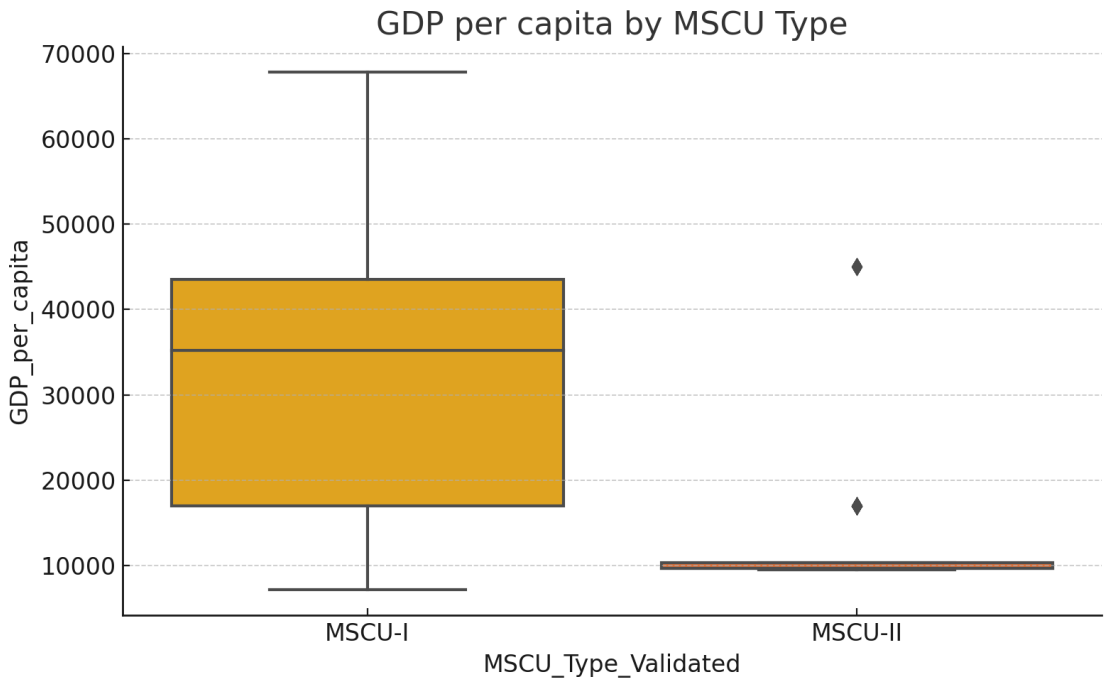


Figure S12. Health Expenditure per capita by MSCU Type