The first & second Pan-European Multi-Stakeholder Colloquia

Brussels, Belgium, May 2014 & 2015

Exploring opportunities and challenges for improving Multiple Sclerosis management – Calls to Action

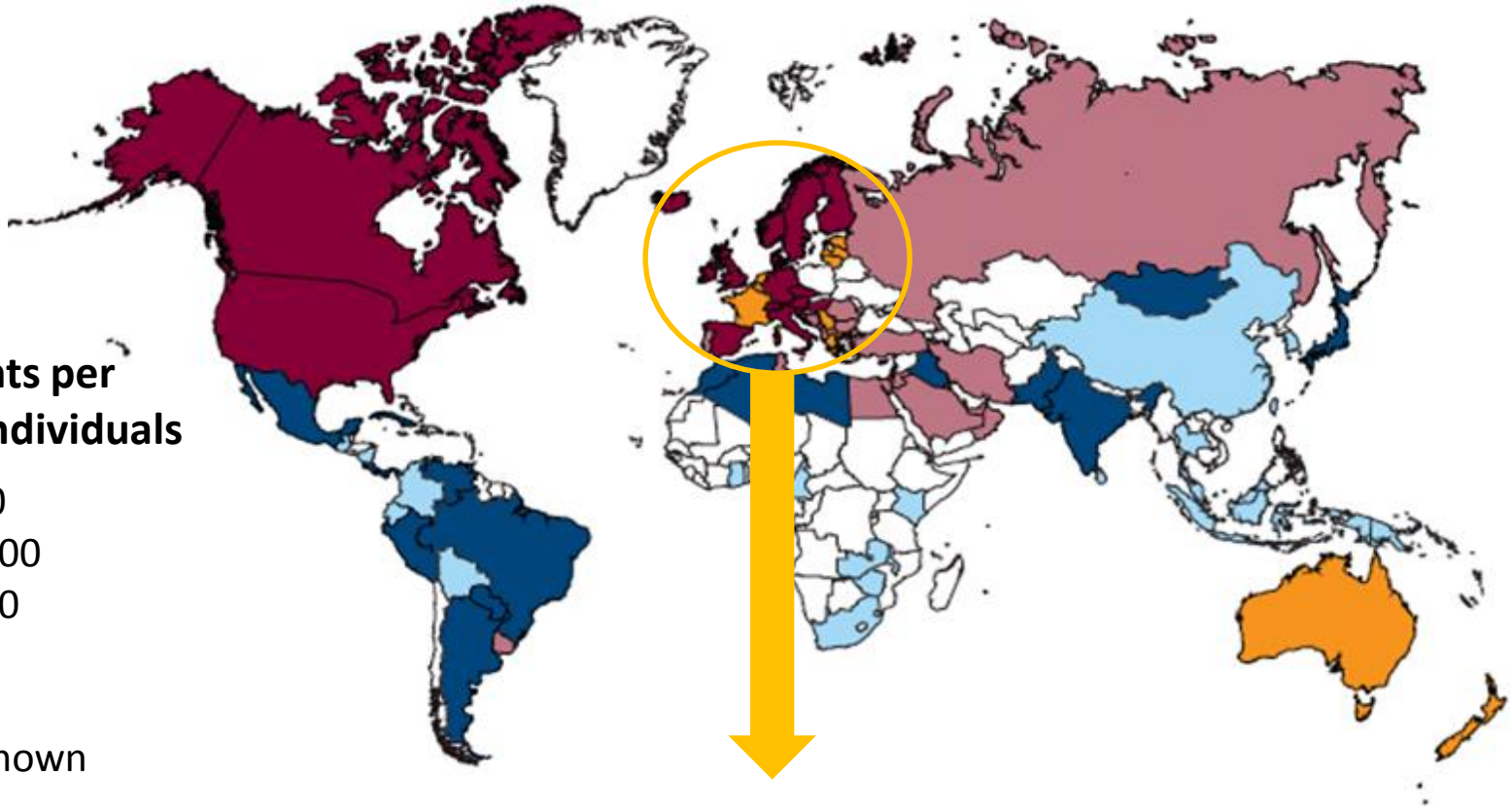
Prof. Patrick Vermersch
Chair of the scientific committee of the Multi-Stakeholder Colloquia on MS

Conflicts of interests/financial support

- Consulting fees and honoraria from Bayer Schering, Biogen Idec, Merck-Serono, Novartis, Teva, Genzyme-Sanofi and Almirall

- Research support from Bayer Schering, Biogen Idec, Merck-Serono, and Teva

Prevalence of Multiple Sclerosis (MS)

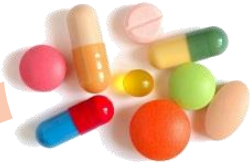


- Leading cause of non-traumatic disability in young adults
  - Europe: 600,000 MS patients and 1,000,000 caregivers
- Diagnosed in the peak of their productive life, with >50% becoming unemployed within 3 years

Multiple Sclerosis International Federation (MSIF) Atlas of MS 2013

Different stakeholders…different platforms

Pharmaceutical industry



Regulators

- EU: EMA with CHMP
- National

Patients

- EMSP

Stakeholders

Payers

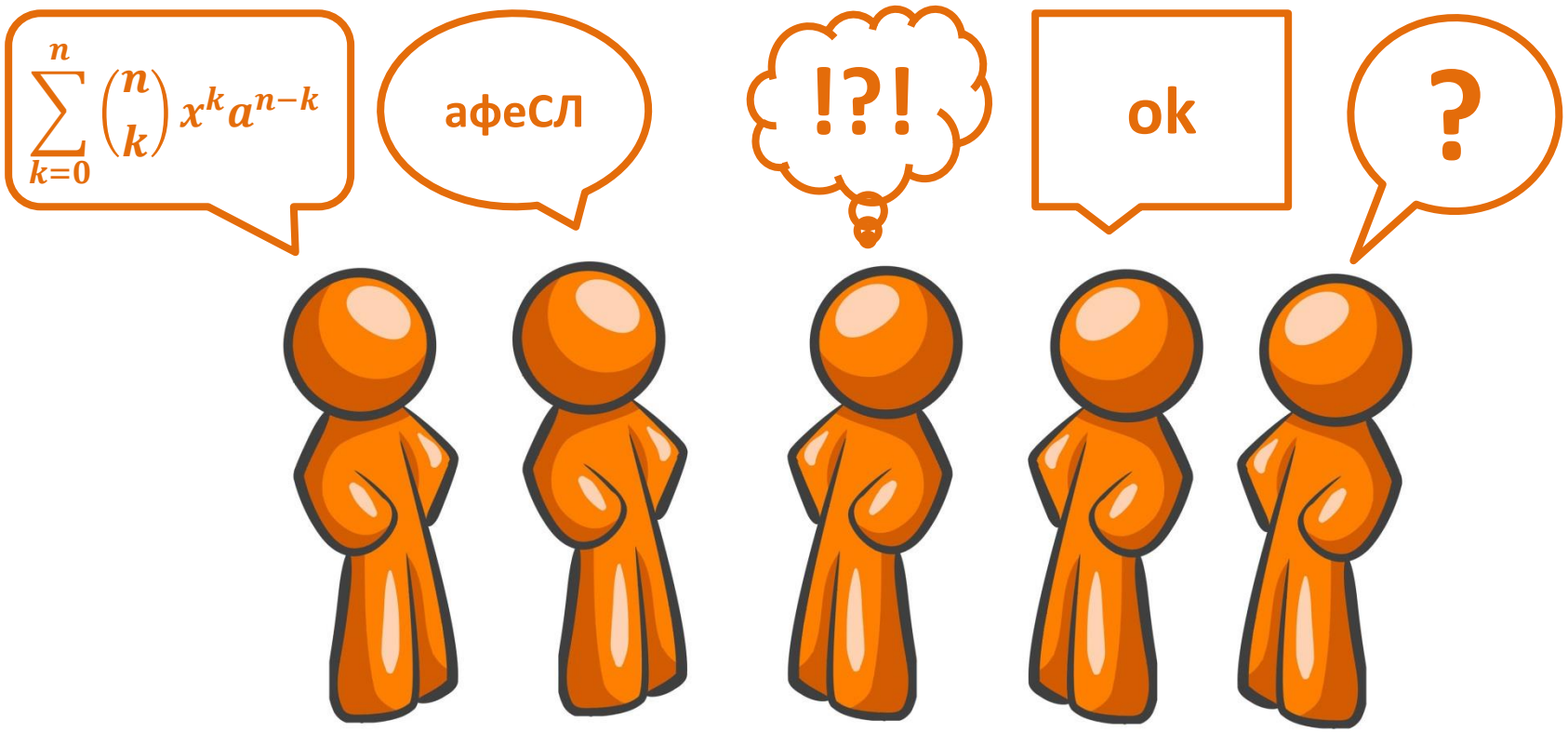
- Responsible for funding of approved medicines (National)
- Advised by national HTA

Healthcare professionals

- Neurologists: ECTRIMS, ECP…
- Radiologists: MAGNIMS
- Rehabilitation therapists: RIMS
- MS nurses, psychotherapists,…

EMSP= European Multiple Sclerosis Platform; ECTRIMS= European Committee for Treatment and Research in MS; ECF= European Charcot Foundation; MAGNIMS= Magnetic Resonance Imaging in MS; RIMS= Rehabilitation in MS; EMA= European Medicines Agency; CHMP= Committee for Medicinal Products for Human Use; HTA= Health technology assessments

Different stakeholders…different language?

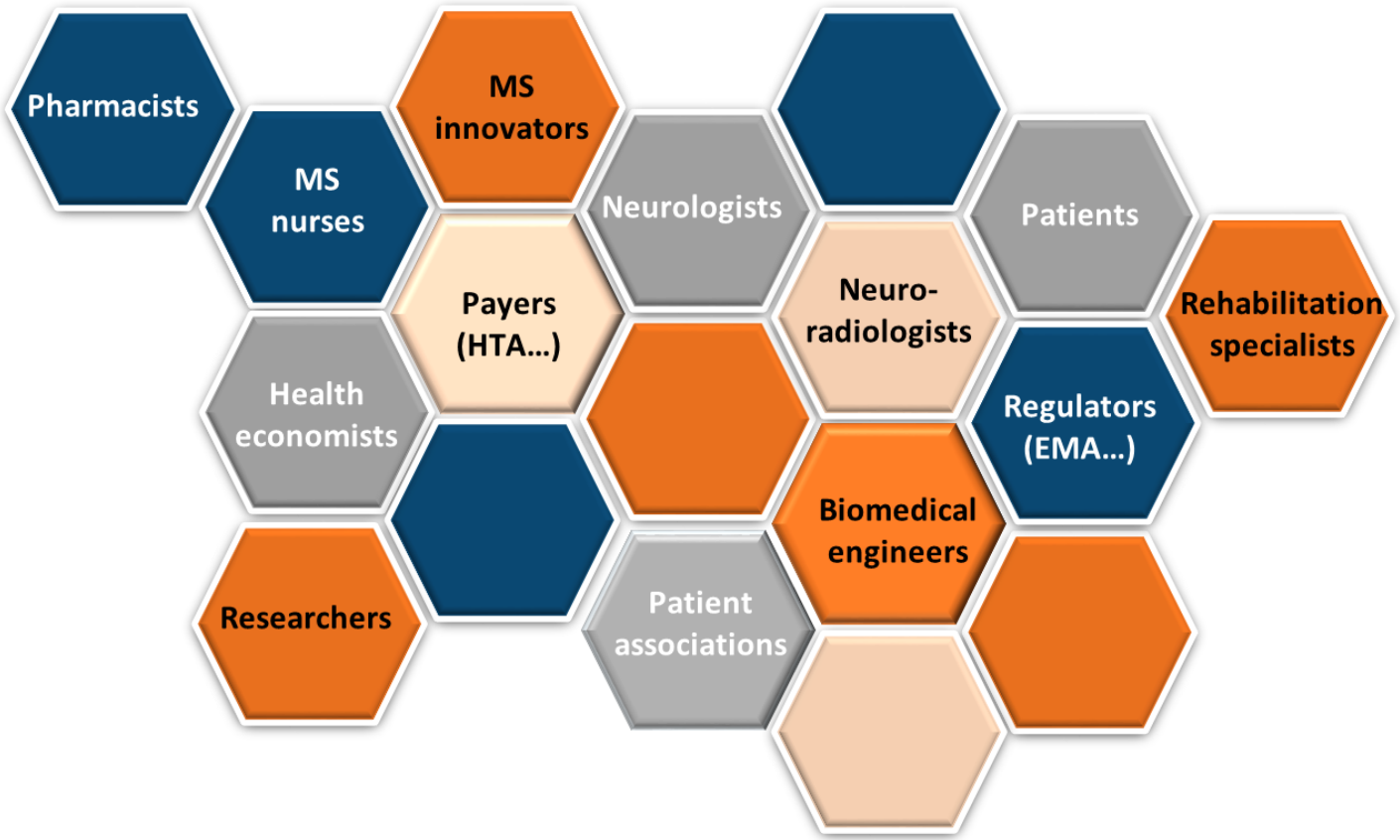


Multiple voices towards Commission

Goal of the Multi-Stakeholder Colloquia

Improve cross-talk

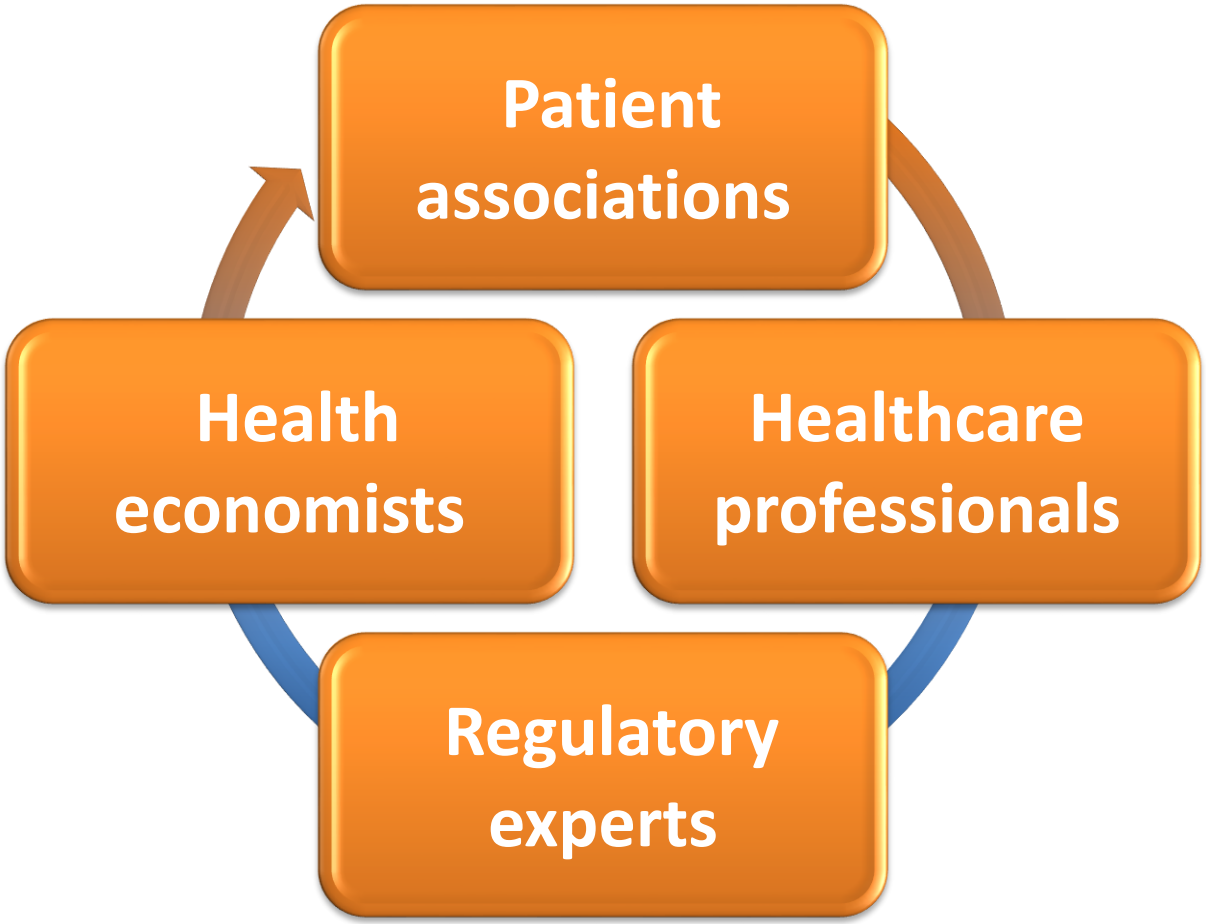
Explore and provide **integrated solutions for better care** of MS, by bridging the viewpoints of different stakeholders



EMA= European Medicines Agency; HTA= health technology assessment

Key faculty of the Multi-Stakeholder Colloquia (1)

Participation from:



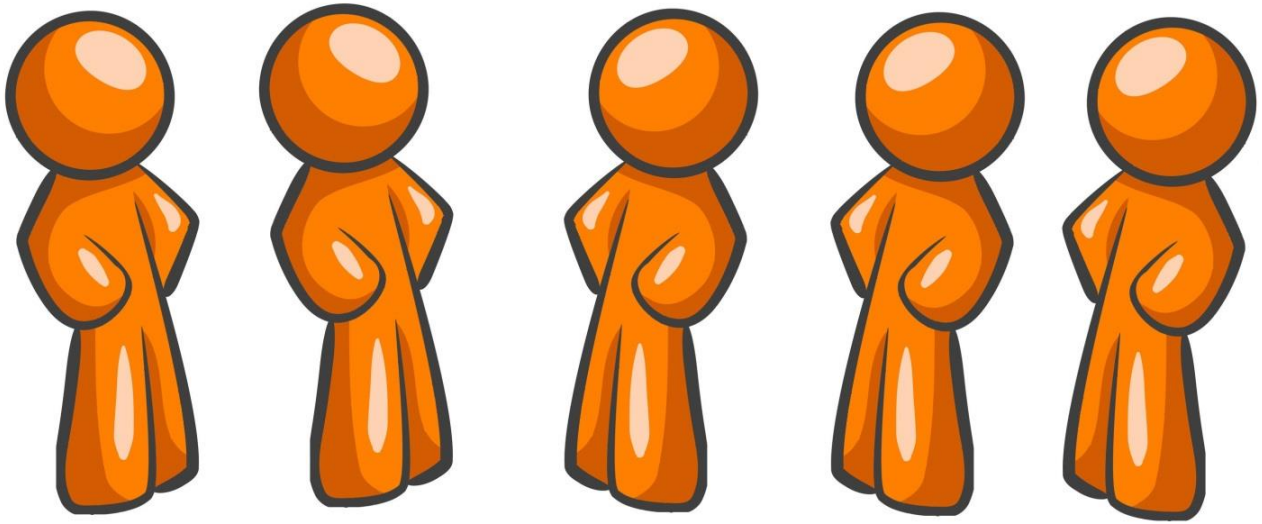
Key faculty of the Multi-Stakeholder Colloquia (2)

Leo Ayerakwa	George C. Ebers	Carsten Lukas	Conor Devine
Yoram Baram	Piet Eelen	Stine Lykke Andersen	Mondher Toumi
Thomas Berger	Andre Elferink	Jana Lizrova Preiningerova	Maria Trojano
Karl Broich	Andreas Faller	Jacqueline Palace	Frauke Zipp
Diego Centonze	Peter Feys	Jean-Louis Prugnaud	Gisela Kobelt
Declan Chard	Emer Fogarty	Alex Rovira	Wim Van Hecke
Manuel Comabella	Gavin Giovannoni	M. Beatriz Silva-Lima	Patrick Vermersch
Daan JA Crommelin	Ralf Gold	Christoph Thalheim	Wil Toenders
Josep Darbà	Chris Holleway	Susan Tilley	Matthijs Versteegh
Luiza Wieckzynska			

Outcomes of the Multi-Stakeholder Colloquia

10 Calls to Action

for improving MS management in Europe



Calls addressing the need for increased funding of both research and education to estimate and communicate the total burden of MS

Call 1: Increase awareness/understanding about the burden of MS, from the patient & caregiver perspective

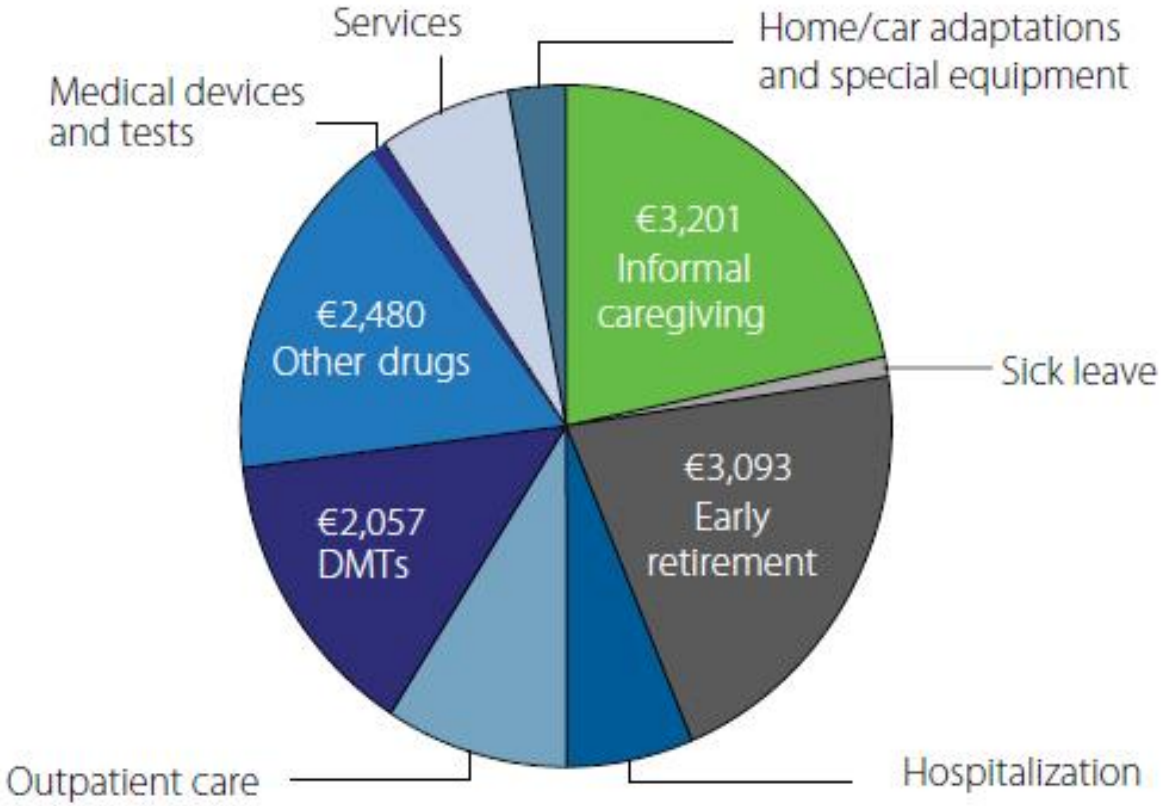
Wheelchair-bound at older age

- Young people
- Afraid of their future
- Loss of mobility
- Loss of energy
- Decrease in cognitive function
- Dependency on caregivers
- Unemployment
- Social isolation
- Reduced quality of life

Most European citizens

Patients with MS and caregivers

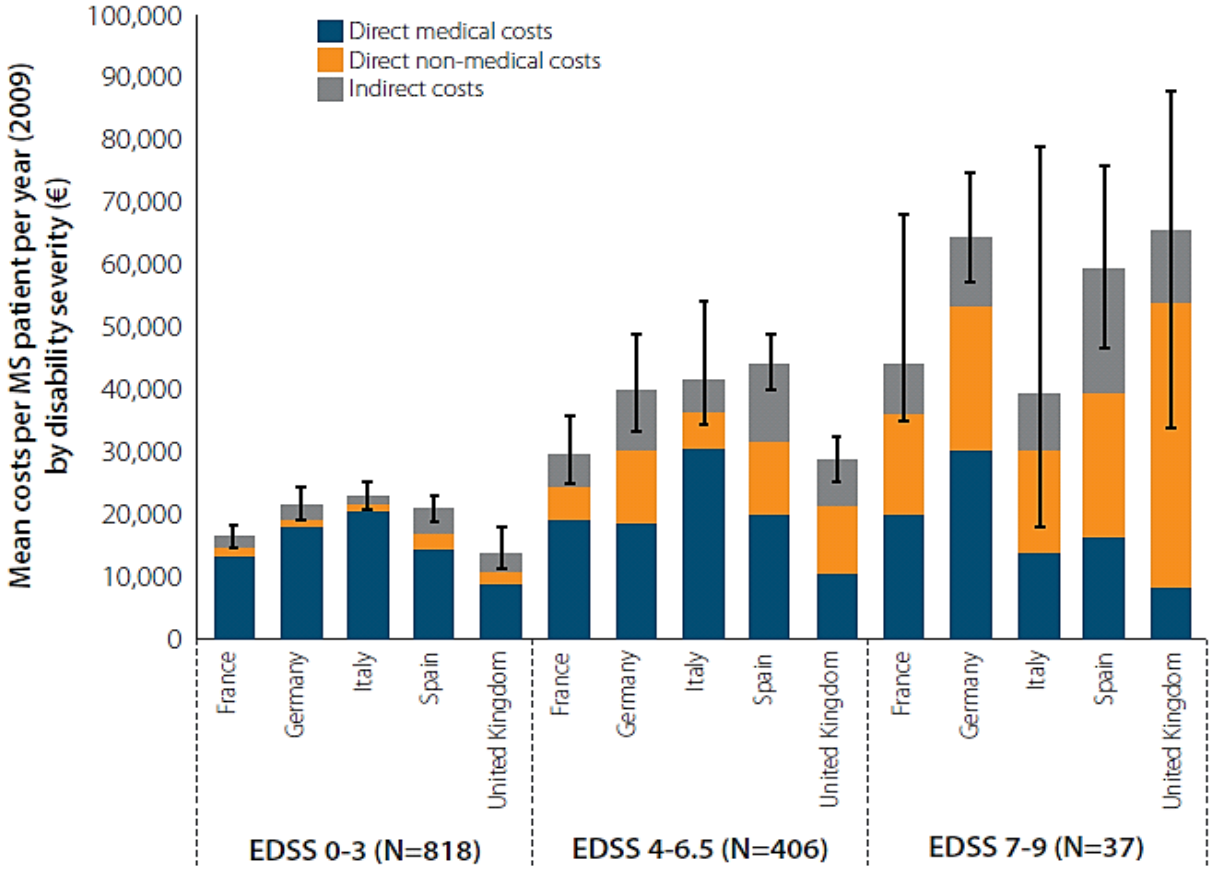
Call 2: Improve communication towards the European community on the cost burden of MS



In Europe, total direct and indirect costs are estimated at **€31,000 per MS patient per year**

Kobelt G, et al. J Neurol Neurosurg Psychiatry 2006;77:918-26

Call 2: Improve communication towards the European community on the cost burden of MS

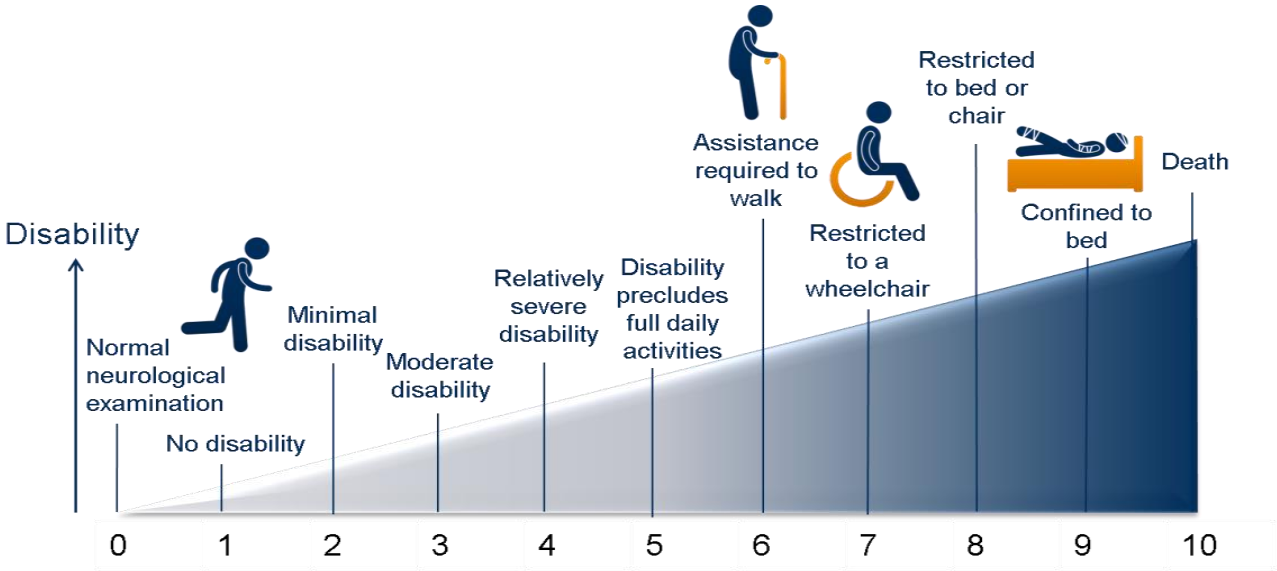


Direct AND indirect costs increase significantly with higher disability levels. It is important to take this information into account when evaluating drug costs.

Naci H, et al. Pharmacoeconomics 2010;28:363-79; Karampampa K, et al. Mult Scler 2012;18:7-15

Call 4: Educate and develop new tools to better capture the total clinical burden of MS

- The EDSS is the most frequently used tool to monitor disability progression in MS but has **several limitations** such as:
  - Poor inter- and intra-rater reliability
  - Too much focus on capturing physical disability/mobility

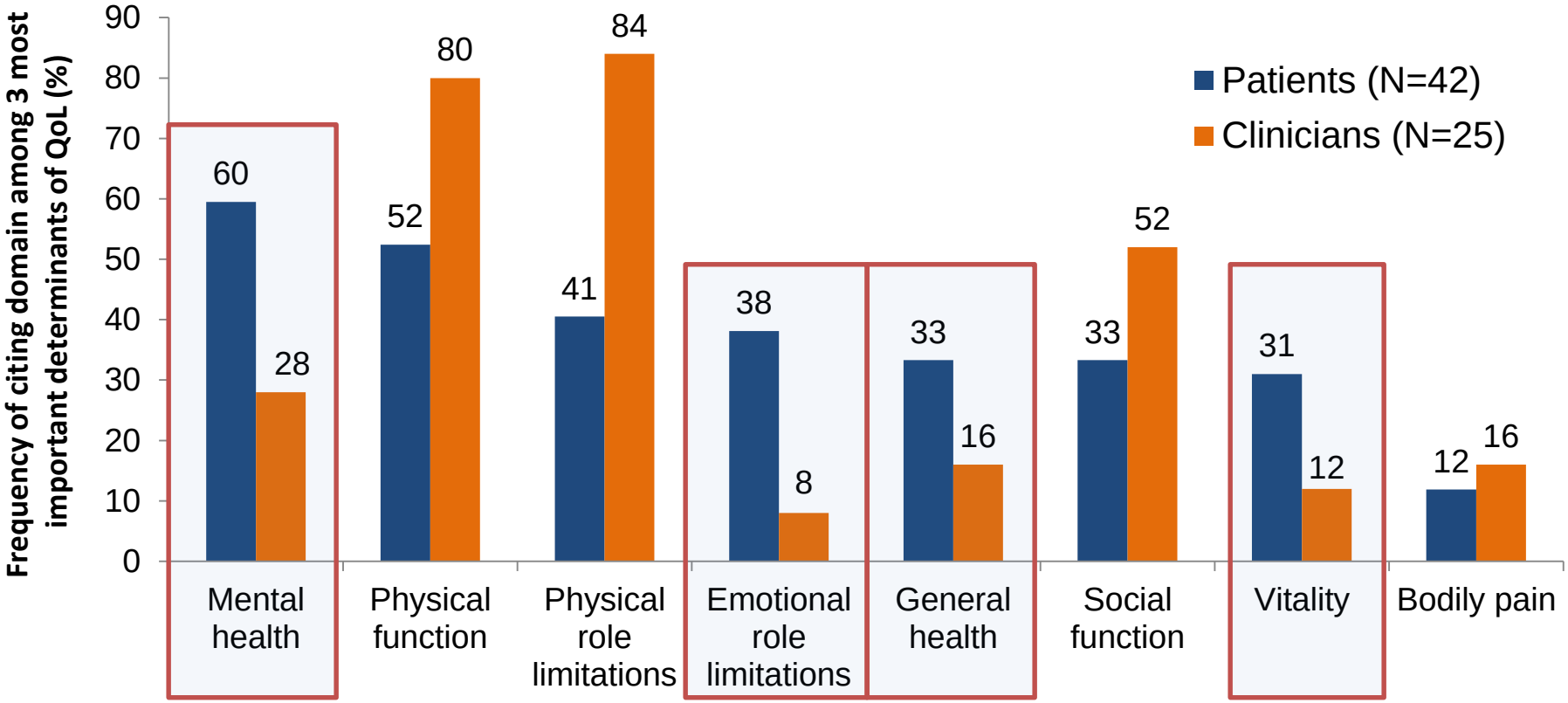


More effort/research should be undertaken to develop a tool which captures less visible but bothersome symptoms

Cohen JA, et al. 2012 Lancet Neurol 2012;11:467-76; Kurtzke JF. Neurology 1983;33:1444-52

Calls addressing the need for increased funding to define patient-centred endpoints and explore and validate biomarkers

Call 3: Perform patient research to (re)define treatment goals and clinical study endpoints



Patient perspectives differ from physician perspectives, with patients giving high value to not only physical but also mental /emotional health

Karampampa K, et al. Mult Scler 2012;18:7-15; Rothwell PM ,et al. BMJ 1997;315:1571-7

Call 3: Perform patient research to (re)define treatment goals and clinical study endpoints

Classical clinical efficacy outcomes

- Relapse
- EDSS
- MRI lesions

Newer clinical efficacy outcomes

- Direct Access File System
- Gait: T25FWT
- Upper extremity motor skills: 9-hole peg test
- MRI whole brain atrophy

Measuring individual treatment success

Risk of adverse events/ Convenience of use

- Mode of administration
- Need for regular monitoring

Outcomes considered important by patients

- Cognition
- Fatigue
- Mobility/activities of daily living
- HRQoL

Patient's perspectives/expectations should be taken into account when evaluating "value for money" during drug approval & HTA decision making

EDSS= Kurtzke Expanded Disability Status Scale; MRI= magnetic resonance imaging; T25FWT= time 25-foot walk test; HRQoL= health-related quality of life ; HTA= health technology assessment

Call 5: Develop a protocol for standardisation of MRI in MS to optimise its use as a marker of disability progression

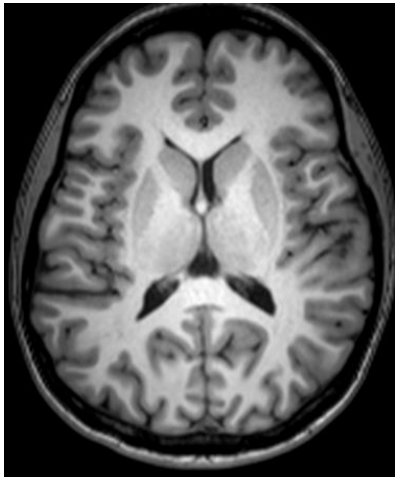
- Clinical indicators of a higher risk of disability progression are
  - Later age at onset
  - Male gender
  - High number of relapses in the first 2 years from onset
  - Incomplete recovery from the first relapse
  - High number of abnormal lesions at the MRI scan
- The rate of disability progression in MS is variable
  - It is currently not possible to predict the disease course in an individual person with MS at onset
  - It is difficult to capture clinically relevant disability progression in clinical trials with disease-modifying drugs of 2 years duration

Research should focus on finding markers, preferably surrogate endpoints, for long-term disability progression

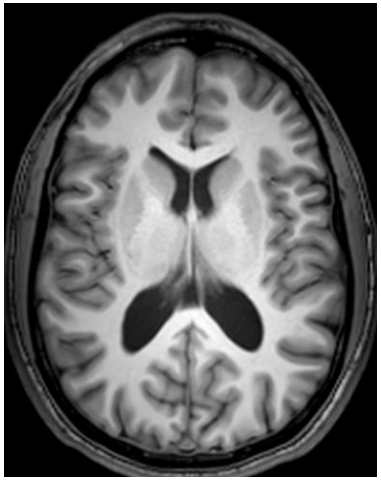
* ≥2 gadolinium-enhancing and ≥9 T2 lesions; MRI= magnetic resonance imaging

Call 5: Develop a protocol for standardisation of MRI in MS to optimise its use as a marker of disability progression

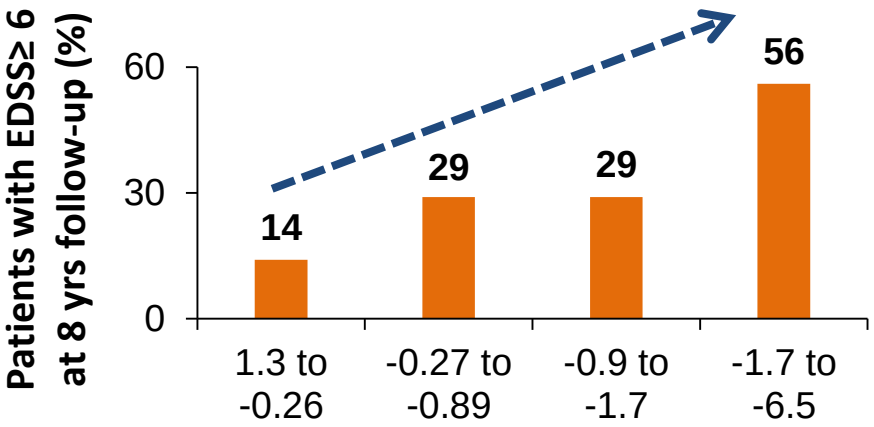
Healthy person



Person with MS



Percentage of brain volume change from baseline to year 2 (N=138)



- Whole brain atrophy is higher in MS patients than healthy controls
- Whole brain atrophy is higher in patients progressing to an EDSS ≥ 6 after 8 years of follow-up

In order to make MRI markers applicable as markers of disability progression in daily clinical practice, it is essential to develop/use a **standardised MRI protocol**. Certification of centres/neuro-radiologists implementing this standardised protocol may help acceleration.

Fisher E ,et al. Neurology 2002;59:1412-20

Call 6: Support research to find molecular biomarkers which can predict disability progression & treatment response

- There is a need for non-imaging biomarkers to:
  - Predict & monitor disease progression:
    - CIS → RRMS → SPMS
    - Disability
  - Stratification for treatment
  - Monitoring of treatment efficacy & risks
- Validation processes can best be performed by European consortia engaged in biomarker research
  - Best candidates in the cerebrospinal fluid: Immunoglobulin G index/oligoclonal bands, Chitinase-3-like-1 protein
  - Best candidates in blood: vitamin D

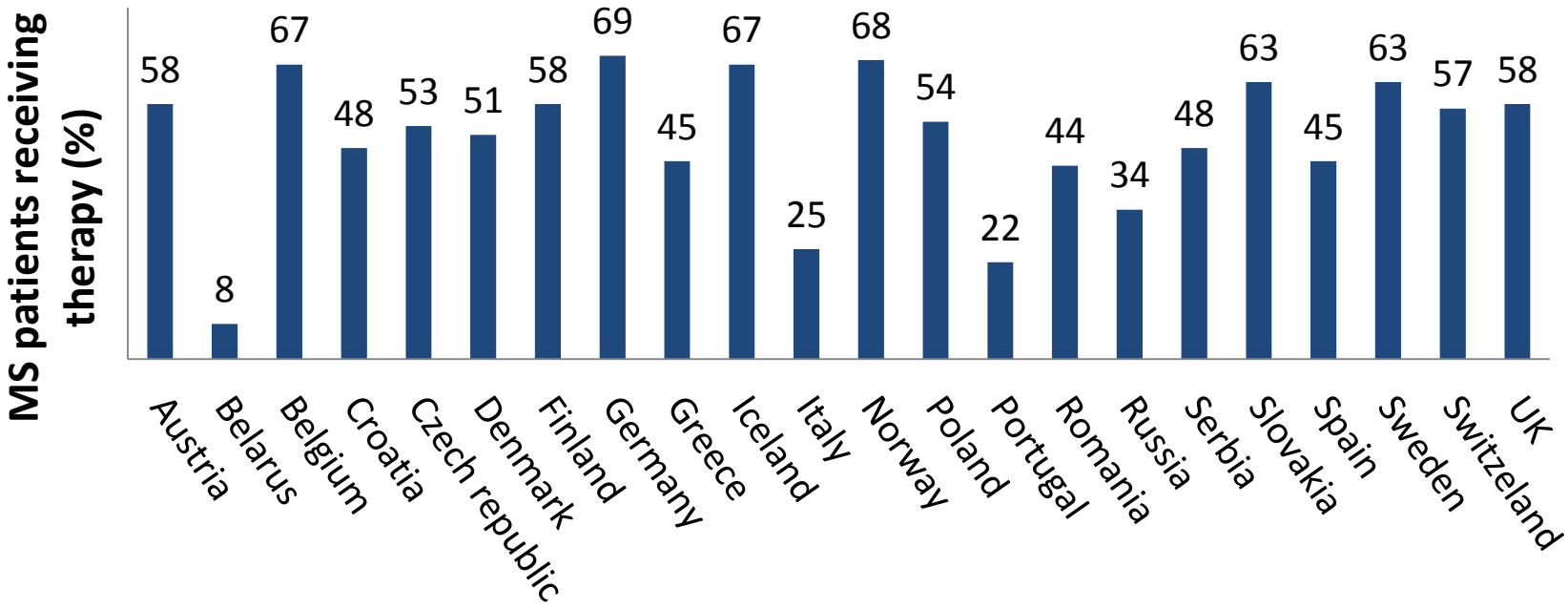
Patient's perspectives/expectations should be taken into account when evaluating "value for money" during drug approval & HTA decision making

Comabella M, et al. Lancet Neurol.2014;13:113-26

Calls addressing the need to align the market authorisation decision-making process with the health technology assessment process

Call 7: Align CHMP & health technology assessment decision making processes

- There are widespread **inequalities** in access to MS therapy across Europe



Integration of the CHMP/EMA and HTA decision processes may decrease inequality. In addition, patient perspective should also be taken into account.

European Multiple sclerosis Platform (EMSP). MS Barometer 2013; CHMP= Committee for Medicinal Products for Human Use

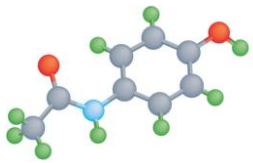
Call 8: Develop separate EMA guidelines for evaluating follow-on products of non-biological complex drugs

Simple dugs

Small molecules

e.g. paracetamol

Characterised at fine level of detail



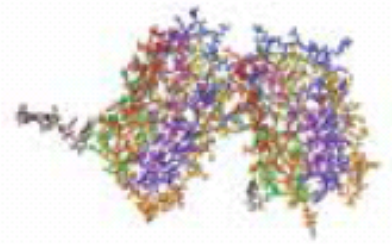
Generics guidelines

Complex drugs

Biologicals/Proteins

e.g. interferon

Characterised at reasonable level of detail

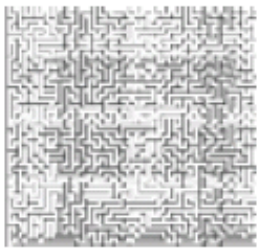


Biosimilars guidelines

Non-biologicals

e.g. glatiramer acetate

Cannot be fully characterised



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It is essential that EMA develops clearly defined guidelines for demonstrating similarity of follow-on NCBDs in order to guard the safety of MS patients.

Calls addressing the need to keep MS patients active and working, as long as possible

Call 9: Stimulate the implementation of specialised care centres and support MS patients in being active & working

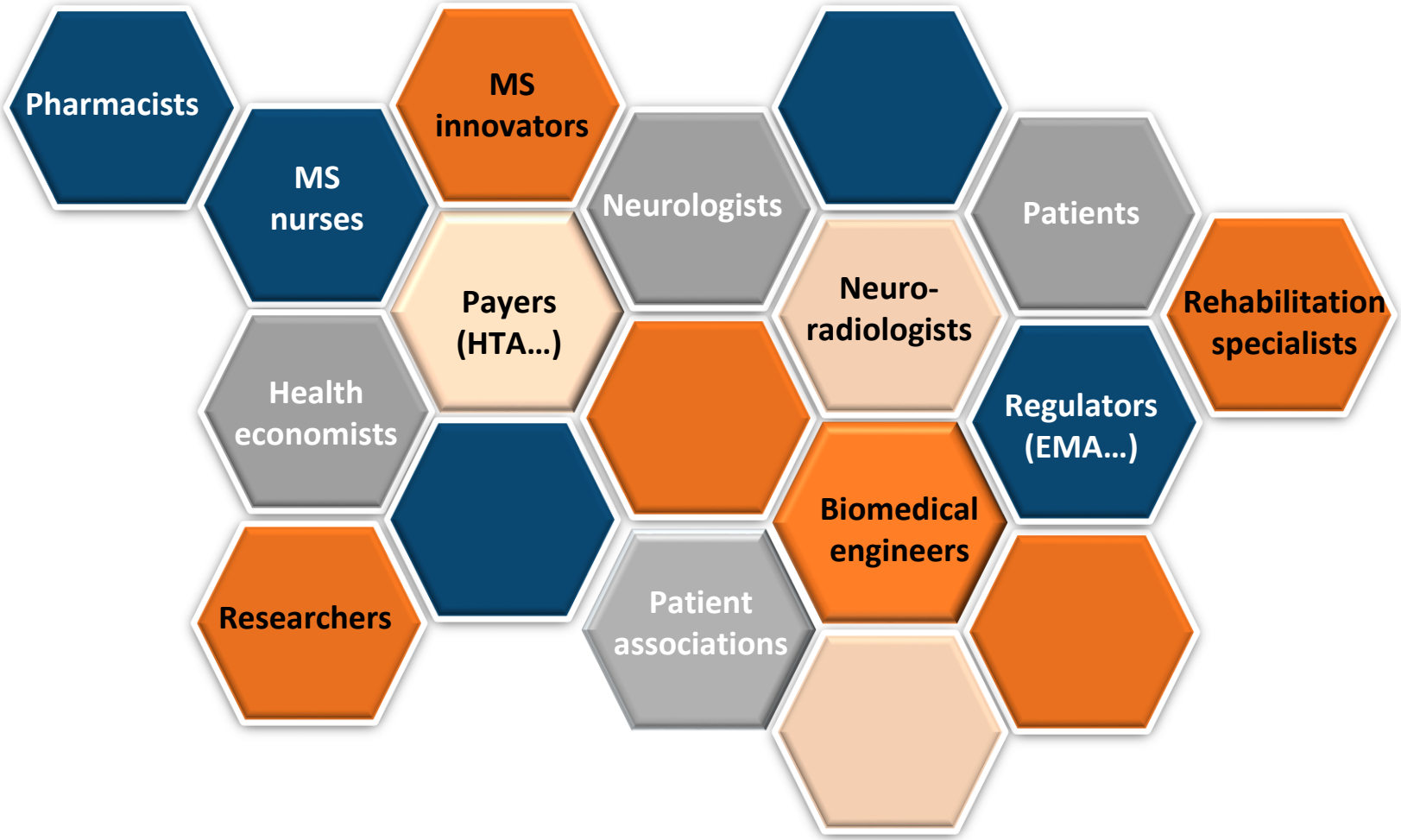
Activity stimulates muscle function

- Keeps them mobile & out of a wheelchair
- They can continue to work & socialise
  - Positive impact on their mental quality of life
  - Their family members can continue to live their own life & perform their own job

Reduces indirect costs and improves the quality of life (intangible costs)

Exercise-related activities for MS patients should be supported and incentive for employers to retain/employ MS patients should be provided.

Call 10: Support the continuation of the multi-stakeholder colloquia to stimulate innovation



EMA=European Medicines Agency; HTA=health technology assessment