

**Table S1** Cost-effectiveness of PC intervention in patients with MS

References, title, country	Objetives	Population	Intervention	Results
<b>A: prospective randomized clinical trials</b>				
Rosato <i>et al.</i> 2021, Living with severe multiple sclerosis: Cost-effectiveness of a palliative care intervention and cost of illness study, Italy	-Assess the cost-effectiveness of HPA for people with MS -Assess the direct costs of healthcare in this population	Adults with advanced MS (n=76): group 1 =50, group 2 =26	Evaluation of the cost-benefit ratio of a household palliative approach; group 1: HPA, group 2: standard-of-care; duration: 6 months; cost-effectiveness evaluation at the beginning of the second, after 3 and 6 months, through national evaluation of the health system and scales: (I) POS-S-MS, (II) EQ-5D-3L QALYs)	<ul style="list-style-type: none"> <li>• The mean QALYs were close to zero, and the mean difference of the groups was -0.006</li> <li>• The average cost difference was -394€</li> <li>• The cost-benefit ratio POS-S-MS showed a slight reduction in symptoms, with unchanged costs</li> <li>• Average costs due to MS were €23,195/year, almost equally distributed by the national health system (€13,108) and house DCs (€10,087)</li> <li>• Personal care, medications, and home rehabilitation accounted for 80% of the total expenses</li> </ul>
Solari <i>et al.</i> 2018, Randomized controlled trial of a home-based palliative approach for people with severe multiple sclerosis, Italy	Assess the effectiveness of a palliative approach at home for adults with advanced MS and their caregivers	Adults with MS and caregivers (n=78): group 1 =50 HPA, group 2 =26 standard care	Application of HPA or standard care (ratio 2:1); duration: 6 months; evaluation at 3 and 6 months: POS-S-MS and SEIQoL-DW	<ul style="list-style-type: none"> <li>• Reduced symptom load in the HPA group (P=0.047)</li> <li>• SEIQoL-DW did not differ in either group: quality of life and secondary outcomes (patient and caregiver)</li> <li>• There was no effect of HPA on ZBI score (P=0.83), or interaction between intervention and center (P=0.20)</li> </ul>
Higginson <i>et al.</i> 2011, Evaluation of a new model of short-term palliative care for people severely affected with multiple sclerosis: a randomized fast-track trial to test timing of referral and how long the effect is maintained, United Kingdom	-Evaluate whether the timing of referral to the PC affects the results -Evaluate the potential for modification due to PC intervention -Assess whether the effect of PC intervention is maintained over time	Adults with advanced MS and caregivers (n=52)	Referral to the PC (multiprofessional team)/intervention group (short term) + control group (after 12 weeks); duration: 6 weeks (follow-up six months); evaluation: (I) whether the timing of referral to the PC in the short term affects the results and (II) potential effect of the PC team's intervention in the short-term (sustained long-term results after withdrawal of PC intervention) POS-S-MS (pain, nausea, vomiting, mouth problems and sleep disorders) and ZBI	<ul style="list-style-type: none"> <li>• After the PC intervention, an improvement in PC was found</li> <li>• Higher ZBI score in the intervention group (short term)</li> <li>• After withdrawal of the PC intervention, the effects were maintained for 12 weeks with no recurrence at 24 weeks</li> </ul>
<b>B: retrospective study</b>				
Lee <i>et al.</i> 2018, Ten-year trends of palliative care utilization associated with multiple sclerosis patients in the United States from 2005 to 2014, USA	Examine the trends of 10 years of PC in hospitalized users	Hospitalized users diagnosed with MS (n=228,444)	Evaluation of PC time trends in patients admitted to the 2005–2014 National Health System (PC association and costs)	<ul style="list-style-type: none"> <li>• National trends in PC use increased 120 times (2005–2014)</li> <li>• PC proportion in in-hospital deaths gradually increased by 7.7% in 2005 to 58.8% in 2014</li> <li>• PC in MS patients may affect hospital use and charges</li> <li>• Hospital PC was associated with increased length of hospital stay and hospital death, but reduced hospital expenses</li> </ul>
<b>C: PC telephone line</b>				
Strupp <i>et al.</i> 2020, Follow-Ups with callers of a palliative and hospice care hotline for severely affected multiple sclerosis patients: Evaluation of its impact, Germany	Assess the impact of the hotline and analyze challenges and possible barriers to the integration of PHC services	Patients with MS and caregivers (n=303)	Implementation of advice/access to PC through a direct national telephone line (MS German Society); duration: 3 years	<ul style="list-style-type: none"> <li>• 303 phone calls (54.5% women, mean age =51 years, 87.7% progressive chronic MS, mean disease duration =17 years)</li> <li>• 27.7% of PC or hospice care were indicated</li> </ul>
Strupp <i>et al.</i> 2017, Evaluation of a palliative and hospice care telephone hotline for patients severely affected by multiple sclerosis and their caregivers, Germany	Set up a national helpline to facilitate access to PHC	-Patients with MS and caregivers (n=222)	Implementation of advice/access to PC through a direct national telephone line (MS German Society); duration: 27 months	<ul style="list-style-type: none"> <li>• 222 phone calls (114 users, 61 careers, 8 healthcare professionals, 8 users of the German MS Society, 31 not specified)</li> <li>• Average age of users 51.12 years, and the mean duration of the disease was 18 years</li> <li>• A total of 31.1% of those who called reported "typical" palliative symptoms (such as pain =88.4%), 50.5% reported symptoms of MS progression, and 35.6% reported psychosocial problems</li> <li>• Consultations included information on PC and hospice care (28.8%), access to PC and hospice care (by previous refusal 5.4%), general care of MS (36.1%), adequacy of housing (9.0%), and emotional support in crisis situations (4.5%)</li> </ul>
Knies <i>et al.</i> 2015, A palliative care hotline for multiple sclerosis: A pilot feasibility study, Germany	-Implement pilot PC advice through direct telephone line for users with MS and their caregivers -Assess its preliminary feasibility through a pilot study	-Implement pilot PC advice through direct telephone line for users with advanced MS and their caregivers -Assess its preliminary feasibility through a pilot study	Pilot study of implementation of advice/access to PC through a direct national telephone line (MS German Society); links driven by a structured script quantitative (number of calls) and qualitative evaluation (PC eligibility criteria); duration: 1 year	<ul style="list-style-type: none"> <li>• 18 phone calls, 15 users (10 eligible for PC—medical features, nursing care, care overload, and death/dying concerns)</li> </ul>

MS, multiple sclerosis; HPA, home-based palliative approach; PC, palliative care; POS-S-MS, The Palliative Outcome Scale-Symptoms-MS; EQ-5D-3L-QALYs, The EuroQol five-dimension descriptive system quality-adjusted life years; SEIQoL-DW, Schedule for the Evaluation of Individual Quality of Life-Direct Weighting; ZBI, Zarit Burden Interview; PHC, palliative and hospice care.

**Table S2** Perception of the unmet needs of patients with MS by patients, caregivers and health professionals

References, title, country	Objetives	Population	Intervention	Results
Koffman <i>et al.</i> 2022, "I wanna live and not think about the future" what place for advance care planning for people living with severe multiple sclerosis and their families? A qualitative study, United Kingdom	Explore under what situations, with whom, how, and why do people with MS their families engage in advance care planning	Users with MS and family members (n=49): 5 healthcare professionals; 27 users with MS; 17 family members	Interviews and ethical discussion group	Participants' narratives focused on three major themes: (I) planning for an uncertain future; (II) perceived obstacles to engaging in ACP that included uncertainty concerning MS disease progression, negative previous experiences of ACP discussions and prioritizing symptom management over future planning; (III) preferences for engagement in ACP included a trusting relationship with a health professional and that information then be shared across services. All groups have difficulty in indicating the ideal time to start this discussion of care
Bužgová <i>et al.</i> 2021, Satisfaction of Patients with Severe Multiple Sclerosis and Their Family Members With Palliative Care: Interventional Study, Czech Republic	Determine the factors that affect satisfaction with care in patients with MS and their caregivers	Adults with advanced MS and caregivers n=200 (103 patients + 97 caregivers); group 1: PC intervention, group 2: control group	Patients in the intervention group had access to neuropalliative care in the form of consultations with a multidisciplinary team. The control group provided standard care with routine neurology consultation; duration: 3 months; evaluation through modified questionnaire, CANHELP Lite (patients and family)	Group 1 presented > satisfaction in all areas analyzed (relationship with the doctor, disease management and decision/communication) + functional status of the user
Dadsetan <i>et al.</i> 2021, Palliative care needs of patients with multiple sclerosis in southeast Iran, Iran	Compare PC needs from the point of view of nurses and patients	154 neurology nurses + 132 MS patients	Application of questionnaire to assess palliative care needs; duration: 4 months	The results showed a significant difference between the two groups in terms of all dimensions (physical, social, spiritual, psychological, and economic dimension) for palliative needs
Cheong <i>et al.</i> 2019, Accessing palliative care for multiple sclerosis: A qualitative study of a neglected neurological disease, Malaysia	Examine and contrast the perceptions of MS users, neurologists and palliative care physicians in relation to PC provision	Adults with advanced MS and healthcare professionals (n=22): 12 patients with MS; 5 neurologists; 5 PC doctors	Semi-structured interview	Patients and neurologists associated PC at the end of life and struggled to understand the need for PC in MS. Another barrier was the lack of understanding about the PC needs of patients with MS. PC physicians also identified the scarcity of resources and their lack of experience with MS as barriers to adequate care provision. The current reference-based care route was considered a barrier to the provision of PC
Noormohammadi <i>et al.</i> 2019, Identification of Concepts of Spiritual Care in Iranian Peoples with Multiple Sclerosis: A Qualitative Study, Iran	Explore and explain dimensions of spiritual care for patients with MS	Adults with advanced MS and caregivers (n=25)	Interviews (4–100 min); duration: 13 months	For the explanation of the concept of spiritual care was an important the concept of restoration of identity essence and nature, disease as a factor of proximity to God, giving meaning to life and disease as a facilitator for the game of self-purification
Leclerc-Loiselle and Legault, 2018, Introduction of a palliative approach in the care trajectory among people living with advanced MS: perceptions of home-based health professionals, Canada	Describe the perceptions of health professionals about the introduction of a PC approach in the trajectory of care of people living with MS	Health professionals of patients with advanced MS (n=13)	Focus groups; individual interviews with nurses, occupational therapists, and social workers	The professionals reported difficulties in introducing a PC approach. Healthcare professionals reported that they feel that a PC approach for people living with advanced MS is mandatory; however, they do not feel comfortable integrating it systematically into their care
Golla <i>et al.</i> 2015, Unmet needs of caregivers of severely affected multiple sclerosis patients: A qualitative study, Germany	Gain insight into the subjectively dissatisfied needs of caregivers of patients with MS	Caregivers of patients with advanced MS (n=12)	Interviews	The unmet needs were classified into the following categories: "relationship with the doctor", "individual support of the health system", "relationship with the individual severely affected by MS", "end-of-life issues", "self-care" and "greater awareness of MS". Caregivers tend to refer to the unmet needs of their recipients and not exactly their own
Borreani <i>et al.</i> 2014, Unmet Needs of People with Severe Multiple Sclerosis and Their Carers: Qualitative Findings for a Home-Based Intervention, Italy	Identify unmet needs of patients with advanced MS living at home	Adults with advanced MS (n=10)	Interviews; three focus group meetings with caregivers and users with advanced MS+. Two focus groups with health professionals	Unmet needs transcended medical issues and embraced organizational and psychosocial issues, as well as health policies. Dealing with disability rather than end-of-life was a major concern of patients and caregivers
Galushko <i>et al.</i> 2014, Unmet Needs of Patients Feeling Severely Affected by Multiple Sclerosis in Germany: A Qualitative Study, Germany	Explore the subjectively unmet needs of users with MS	Adults with MS (n=15)	Interviews	Unmet needs were identified in the main categories of "support to family and friends", "health services", "manage the day-to-day" and "maintain biographical continuity". The patients expressed the desire for greater support from their families and to be seen as distinct individuals. They see a substantial deficit in the doctor-patient relationship and in the coordination of services. A decrease in the unmet needs expressed was found for more severely affected and less socially integrated patients
Strupp <i>et al.</i> 2013, Self-rating makes the difference: identifying palliative care needs of patients feeling severely affected by multiple sclerosis, Germany	Identify the specific PC needs of patients who felt severely affected by MS	Adults with MS (n=573)	Questionnaire	358 (62.48%) felt more advanced stages of the disease. Compared to patients who feel less affected, they found that stress on their next of kin was greater. They needed a greater number of home visits and neurology consultations. They also needed more emotional support from the nursing services
Golla <i>et al.</i> 2014, Multiple sclerosis and palliative care – perceptions of severely affected multiple sclerosis patients and their health professionals: a qualitative study, Germany	Investigate how health professionals understand PC for patients with advanced MS	Adults with advanced MS and healthcare professionals (n=38): 15 users with MS and 23 health professionals (3 social workers, 7 nurses, and 13 physicians in outpatient settings)	Semi-structured interviews (patients and health professionals). Focus groups (health professionals)	Patients with MS were not, for the most part, familiar with the term "PC" or were only aware of this concept related to cancer and death. They did not take this concept as relevant to themselves. Health professionals assumed PC for diagnosis of terminal cancer. Most physicians doubted its relevance to patients in the area of neurology and did not consider MS as a possible cause of death. However, most felt that they already offered their patients sufficient PC support or thought they could not meet the more complex needs of MS patients. Most nurses and social workers recognize deficits in existing care structures and consider PC as a care opportunity for patients with MS
Golla <i>et al.</i> 2012, Unmet needs of severely affected multiple sclerosis patients: The health professionals' view, Germany	Assess perception of the unmet needs of MS patients by healthcare professionals	Health professionals of users with advanced MS (n=23): 13 doctors; 7 nurses; 3 social workers	Interviews. Focus groups	Unmet needs were identified in four main categories ("family/friends support"; "health services"; "managing everyday life"; "maintaining biographical continuity"). While physicians assessed the most dissatisfied needs in the "health services" category, nurses and social workers focused on unmet needs in the categories "support from family/friends" and "maintain biographical continuity"

CANHELP, the Canadian health care evaluation project questionnaire; PC, palliative care; MS, multiple sclerosis; ACP, advance care plan.