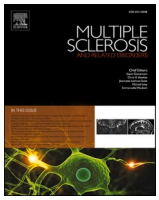
Multiple Sclerosis and Related Disorders 68 (2022) 104219

Contents lists available at ScienceDirect

Multiple Sclerosis and Related Disorders

journal homepage: www.elsevier.com/locate/msard



Correspondence

Life expectancy in multiple sclerosis by EDSS score

ARTICLE INFO

Keywords
Multiple sclerosis
Expanded disability status scale
Life expectancy
Mortality

SUMMARY

The median survival time of newly-diagnosed MS patients without severe disabilities is approximately 30-35 years. The prognosis after the onset of severe disability has not been reported. Based on Harding et al.'s 2018 study of the Southeast Wales MS registry, we calculated life expectancies according to the Expanded Disability Status Scale (EDSS). Upon loss of independent ambulation (EDSS 6-6.5; mean age 51.2) life expectancy was 13.3 additional years. At EDSS 9-9.5 (mean age 70.8) life expectancy was 1.1 additional years. These figures provide an empirical basis for discussions of advanced MS care planning.

1. Introduction

Many studies document increased mortality of persons with MS (PwMS), with a median survival time of approximately 30-35 years from diagnosis (Burkill et al., 2017; Harding et al., 2018; Koch-Henriksen et al., 2017; Lunde et al., 2017; Manouchehrinia et al., 2016). Risk factors for reduced survival in newly diagnosed PwMS include: older age (Harding et al., 2018; Koch-Henriksen et al., 2017), male sex (Harding et al., 2018; Koch-Henriksen et al., 2017; Lunde et al., 2017), and primary progressive disease type (Harding et al., 2018; Lunde et al., 2017).

However, the prognosis for an MS patient who has already lived with the disease for 5, 10, or 20 years remains unclear. The answer undoubtedly depends on how quickly their MS has advanced and the severity of their current neurological disabilities. This is reflected in a recent study by Harding et al. (2018), demonstrating that mortality increases significantly according to disability severity as assessed by the Expanded Disability Status Scale (EDSS).

As MS progresses and leads to increasing levels of dependence, evidence-based discussions of life expectancy (i.e., average survival times) are critical for patient counselling, care planning and advanced decision making. But to our knowledge no study published to date has examined life expectancy of patients according to level of disability. This study expands upon the work of Harding et al. (2018) by providing life expectancies for PwMS according to EDSS score.

2. Materials and methods (207)

We utilized previously published results derived from the Southeast Wales MS registry (Harding et al., 2018). Since 1999, this registry has collected data on demographics and disability (measured using EDSS) for MS patients treated at University Hospital of Wales and Royal Gwent Hospital. The registry has enrolled more than 97% of the region's MS patients (Hirst et al., 2009). As of 2018, it included 2,604 patients (mean age at onset; 32.9) who contributed 45,379 person-years of follow-up time. A total of 579 (22.2%) had died.

Harding's Table 4 gave SMRs according to EDSS band (<4.0, 4.0–5.5, 6.0–6.5, 7.0–7.5, 8.0–8.5, and 9.0–9.5) together with median time until progression to a higher EDSS score. The SMR is the ratio of the observed number of deaths to that expected among persons of the same age and sex in the general population (GP). To calculate MS mortality rates, we applied the EDSS-specific SMRs to the appropriate age-specific mortality rates from the 2012-2014 interim Welsh GP life table (Office of National Statistics, 2015). For EDSS <4.0, we used an SMR of 1 (i.e., no excess mortality risk). Life expectancies were calculated from life tables in the standard way.

This study did not require Institutional Review Board approval as the analysis consisted solely of the use of previously published, aggregated data.

3. Results (127)

Life expectancies according to age and EDSS band are presented in Table 1.

Prior to the onset of severe disability (EDSS 0-3.5) life expectancy of newly diagnosed MS patients (mean age 32.9) was 30.9 additional years, to age 63.8. Equivalently this was 63% of the Welsh GP figure. Remaining life expectancy decreased markedly with disease progression and increasingly severe disability. Among patients who were essentially wheelchair-bound (EDSS 7.0-7.5, mean age 57.9), life expectancy was 7.6 additional years, or to age 65.5 (30% of GP). Once they became bedridden (EDSS 8.0-8.5, mean age 61.6) it declined to 4.6 additional years (20% of GP). Those in the most advanced stages who are completely immobile and unable to communicate effectively or to safely feed orally live roughly one additional year.

4. Discussion (487 → 626)

To our knowledge this is the first study to estimate life expectancies for MS patients according to disease severity as measured by EDSS. As expected, the average remaining years declined as patients became older

Abbreviations: MS, Multiple sclerosis; EDSS, Expanded disability status scale; SMR, Standardized mortality ratio; GP, General population.

https://doi.org/10.1016/j.msard.2022.104219
Received 6 July 2022; Received in revised form 24 September 2022; Accepted 4 October 2022
Available online 5 October 2022

Table 1
Life Expectancy (additional years) by EDSS Score.

EDSS Score	Median Time at EDSS (yrs)	SMR	Mean Age	Life Expectancy (Standard Error)	% of GP*
0-3.5	14.4	1.00	32.9	30.9 (0.3)	63%
4-5.5	3.9	2.02	47.3	16.9 (0.3)	48%
6-6.5	6.7	3.86	51.2	13.3 (0.3)	42%
7-7.5	3.7	4.76	57.9	7.6 (0.3)	30%
8-8.5	9.2	22.17	61.6	4.6 (0.3)	20%
9-9.5	3.3	60.74	70.8	1.1 (0.1)	7%

* Welsh Interim General Population Life Expectancy (2012-2014); the figures represent the 69:31 female:male and 85:15 relapsing remitting:primary progressive type ratios in the MS registry.

and more disabled. By comparison with age- and sex-matched persons in the Welsh GP, newly diagnosed MS patients without severe disabilities can expect to lose about one third of their normally remaining years. The relative disparity increases as the disease progresses to more advanced EDSS: for those who are completely immobile and unable to effectively communicate or safely swallow (EDSS 9-9.5), the life expectancy is just over 1 year and less than 10% of the GP figure.

The above estimates are subject to the following technical assumptions:

- The assumption of no excess mortality in EDSS 0-3.5 (before the onset of severe disability) may overestimate life expectancy by neglecting the increased risk of suicide recognized in young MS patients (Cutter et al., 2015).
- The rate of progression observed in our study may be somewhat pessimistic for persons with early stage disease who are treated with novel disease-modifying treatments. Because only 5.4% of deceased patients in the registry had been treated with them (Harding et al., 2018), we were not able to analyze their effects on life expectancy.
- Our analysis also excluded the possibility of EDSS score improvement or simultaneous progression through multiple EDSS bands. The former has been shown to occur somewhat more frequently at lower EDSS scores (Freilich et al., 2018), and our estimates may therefore be too low for newly diagnosed patients. We note, for example, that our life expectancy estimate for newly diagnosed PwMS is 4.6 years lower than the median survival time in the Southeast Wales MS registry (Harding et al., 2018). Conversely, the life expectancies for persons with advanced MS may be too high.
- Data collection in the register began in 1985 before adoption of the McDonald diagnostic criteria and widespread use of MRI scanning. These have resulted in earlier diagnosis and, therefore, have increased patients' time living with the MS diagnosis without necessarily improving survival with the disease. Future studies attempting to examine trends in survival over time – particularly those interested in the effects of novel treatments – must take this into account.

Given the composition of the registry, the life expectancies presented here are most applicable to patients with relapsing-remitting MS whose age is similar to the mean age in the corresponding EDSS band.

Our estimates are likely too high for persons with early-stage primary progressive disease, who progress to severe disability earlier and die younger than the mostly relapsing-remitting patients studied here. Median survival times from onset of primary progressive disease, for instance, have been shown to be 25-40% lower than that of cohorts with relapsing-remitting MS (Harding et al., 2018; Lunde et al., 2017). Further research is necessary to determine whether life expectancy differs by disease type among persons who already have severe disabilities.

The estimates are also likely to be too high for persons diagnosed at older ages. This is only partially explained by normal increases in mortality rates with age. Research by Tremlett et al. (2006) has shown that severe disability is accumulated faster by patients diagnosed at older ages – this will in turn lead to higher mortality and reduced life expectancy. We hope to carry out similar analyses stratified by age of MS diagnosis in a follow-up study.

Finally, they may be slight underestimates for women and slight overestimates for men.

Despite these caveats, we believe that the life expectancies presented here are the best available prognostic survival data on long-term MS survival according to EDSS score. We hope that they prove useful for guiding discussions regarding long-term care planning among PwMS, their family members, and their physicians.

Funding/Support

None.

Role of funder/sponsor

None.

Data sharing statement

Not applicable - all utilized data has been previously published in Harding et al. (2018).

CRediT authorship contribution statement

Lucas Walz: Conceptualization, Formal analysis, Investigation, Methodology, Validation. **Jordan C. Brooks:** Conceptualization, Formal analysis, Investigation, Methodology, Validation. **Robert M. Shavelle:** Conceptualization, Validation. **Neil Robertson:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation. **Katharine E. Harding:** Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation.

Declarations of Competing Interest

Lucas Walz has no conflicts of interest. Jordan Brooks and Robert Shavelle have served as expert witnesses on life expectancy for persons with neurological disabilities including some with multiple sclerosis. Neil Robertson has received honoraria and/or support to attend educational meetings from Biogen, Novartis, Genzyme, Teva, Roche. His research group has also received research support from Biogen, Novartis and Genzyme. Katharine Harding has received honoraria and/or support to attend educational meetings from Biogen, Novartis, Merck Serono, and Roche.

Acknowledgements

None.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2022.104219.

References

Burkill, S., Montgomery, S., Hajiebrahimi, M.H., Hillert, J., Olsson, T., Bahmanyar, S., 2017. Mortality trends for multiple sclerosis patients in Sweden from 1968-2012. Neurology 89 (6), 555–562.
Cutter, G.R., Zimmerman, J., Salter, A.R., Knappertz, V., Suarez, G., Waterbor, J., et al., 2015. Causes of death among persons with multiple sclerosis. Mult. Scler. Relat. Disord. 4 (5), 484–490.
Freilich, J., Manouchehrinia, A., Trusheim, M., Baird, L.G., Desbiens, S., Berndt, E., et al., 2018. Characterization of annual disease progression of multiple sclerosis patients: a population-based study. Mult. Scler. J. 24 (6), 786–794.

Harding, K., Anderson, V., Williams, O., Willis, M., Butterworth, S., Tallantyre, E., et al., 2018. A contemporary study of mortality in the multiple sclerosis population of south east Wales. Mult. Scler. Relat. Disord. 25, 186–191.
Hirst, C., Ingram, G., Pickersgill, T., Swingler, R., Compston, D.A.S., Robertson, N.P., 2009. Increasing prevalence and incidence of multiple sclerosis in South East Wales. J. Neurol. Neurosurg. Psychiatry 80 (4), 386–391.
Koch-Henriksen, N., Laurden, B., Stenager, E., Magyari, M., 2017. Excess mortality among patients with multiple sclerosis in Denmark has dropped significantly over the past six decades: a population based study. J. Neurol. Neurosurg. Psychiatry 88 (8), 626–631.
Lunde, H.B., Assmus, J., Kjell-Morten, M., Grytten, N., 2017. Survival and cause of death in multiple sclerosis: a 60-year longitudinal population study. J. Neurol. Neurosurg. Psychiatry 88 (8), 621–625.
Manouchehrinia, A., Tanasescu, R., Tench, C.R., Constantinescu, C.S., 2016. Mortality in multiple sclerosis: meta-analysis of standardised mortality ratios. J. Neurol. Neurosurg. Psychiatry 87 (3), 324–331.
Tremlett, H., Paty, D., Devonshire, V., 2006. Disability progression in multiple sclerosis is slower than previously reported. Neurology 66 (2), 172–177.
Office of National Statistics. 2015. National Life Tables, Wales, period expectation of life, based on data for the years 2012-2014. [Online: Accessed 14th April 2022]. https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetableswalesreferencetables.

Lucas Walz[a], Jordan C. Brooks[a], Robert M. Shavelle[a], Neil Robertson[b,c], Katharine E. Harding[b,d,*]

[a] *Life Expectancy Project, 1439 17th Avenue San Francisco, CA 94122, USA*

[b] *Institute of Psychological Medicine and Clinical Neuroscience, Cardiff University, University Hospital of Wales, Heath Park, Cardiff, United Kingdom*

[c] *Helen Durham Centre for Neuroinflammatory Disease, Department of Neurology, University Hospital of Wales, Heath Park, Cardiff, United Kingdom*

[d] *Aneurin Bevan University Health Board, Department of Neurology, Royal Gwent Hospital, Cardiff Road, Newport NP20 2UB, United Kingdom*

[*] Corresponding author at: Department of Neurology, Royal Gwent Hospital, Cardiff Road, Newport NP20 2UB, UK.
E-mail address: katharineharding@doctors.org.uk (K.E. Harding).