Societal costs of primary progressive multiple sclerosis in Australia and the economic impact of a hypothetical disease-modifying treatment that could delay disease progression

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Original Research

ABSTRACT

Aims: Primary progressive multiple sclerosis (PPMS) has a progressive course of disability with continuous neurological worsening. We investigated societal costs of PPMS in Australia and the economic impact of increasing the independence of people with PPMS through delaying disease progression.

Methods: This prevalence-based retrospective cost-of-illness analysis used observational data from publicly available secondary data sources and literature findings. Direct and indirect costs of PPMS were considered. A replica estimated population was created using the National Centre for Social and Economic Modelling (NATSEM) microsimulation model of the Australian tax and transfer system (STINMOD+). Using a budget impact analysis approach, we modelled the effect on PPMS costs of an effective hypothetical disease-modifying treatment (DMT) that delays disease progression by a year from mild to moderate and a further year from moderate to severe PPMS.

Results: An estimated 31,650 Australians have multiple sclerosis (MS) including 4,430 with PPMS. The proportion with PPMS was estimated to increase with age and disease severity. Overall 25% of males with MS, and 10% of females, were estimated to have PPMS. Societal cost of PPMS in Australia in 2018 was estimated at AU$418.1 million. Indirect costs contributed 67.5% of total costs, attributable to reduced workforce participation and need for informal care. The modelled DMT was estimated to create savings of AU$14.9 million (3.6%). Fewer people had moderate and severe PPMS resulting in major cost savings, partially offset by increased costs of treatment, care and support for a relative increase in the number of people with mild PPMS and their increased productivity losses.

Limitations: Publicly available data may be incomplete. The potential cost of the DMT was not considered.

Conclusions: The economic burden of PPMS was estimated at AU$418 million in 2018. An effective DMT that delayed progression from disease severity states by one year could provide significant cost savings.

Introduction

Multiple sclerosis (MS) is one of the most common chronic debilitating neurological diseases. It had an estimated prevalence of 127 people per 100,000 population in Australia in 2018. This is relatively high internationally, although prevalence rates greater than 100 people per 100,000 population have also been reported for North America and Europe. There are three common clinical phenotypes of MS: relapsing remitting multiple sclerosis (RRMS), secondary progressive multiple sclerosis (SPMS) and primary progressive multiple sclerosis (PPMS). This analysis focuses on people with PPMS in Australia.

PPMS occurs in 10–15% people with MS. It is characterized by a progressive course of disability with continuous neurological worsening from the first onset of symptoms, without distinct relapses followed by complete or partial remission. PPMS is associated with older age at onset, affects men and women equally, and has considerably more rapid disease progression relative to the more prevalent RRMS. Individuals with PPMS are particularly prone to spinal cord disease, typically progressive spastic paraparesis with increasing walking difficulties due to weakness and spasticity, sphincter involvement and myelopathic pain.4

There is an emerging body of research internationally on the broader societal costs and loss of independence associated with PPMS. However, there is little evidence in the Australian context of the costs associated with PPMS and the economic burden placed on individuals, families, health...
services, Government and society at large. There is a high level of unmet need for treatments for PPMS with no effective disease modifying medicines currently subsidized through the Australian Government’s Pharmaceutical Benefits Scheme (PBS).

A key area within societal costs is the impact of lost productivity due to disease severity. Lost productivity occurs for several reasons: presenteeism when a person is at work, but their productivity is reduced because of their health condition; absenteeism from work through sickness; reduced workforce participation through changing jobs, reducing the number of hours worked or early retirement due to disability. As MS impacts people of working age, many individuals will experience presenteeism, absenteeism or are forced to reduce their working hours, change their jobs or leave the workforce prematurely. Employment rates of people with MS differ significantly by type of MS and with disease severity (as measured for example by the Expanded Disability Status Scale (EDSS)) and are substantially lower than those of age-sex matched individuals in the general population.13–19

The trends in workforce participation of people with MS reported internationally are also seen in Australia. An Australian MS Needs Analysis study reported that 66% of participants with mild MS were employed, which decreased to 39% of those with moderate MS and only 9% of those with severe MS.20 Based on data from the Australian Multiple Sclerosis Longitudinal Study (AMSLS), 48.8% of people with MS were employed either full-time or part-time compared with 63.1% of the Australian general population in 2010, rising to 57.8% in 2013 which was still significantly lower than the general population employment rate of 61.4%.21 A more recent study also using AMSLS data reported an overall labor force participation rate of 54.7% among working-aged respondents (18–64 years).22 However, less than 4% of participants in this analysis of work productivity loss had PPMS.22

The literature shows that there are no significant differences in gross earnings between people with MS and general population control subjects in the years preceding diagnosis, nor in their levels of education.23 Employment rates diverge markedly post-MS diagnosis. Disease-modifying treatments (DMTs) have the potential to slow or stop disease progression, and thus minimize the direct and indirect impacts of MS which pose a major health, social and economic challenge for any society. However, no DMT for use in patients with PPMS is currently reimbursed nationally through the Australian PBS. The objective of this study was to use publicly available data sources and economic modelling to determine 1) the societal costs of PPMS under current Australian treatment practices and 2) the economic impact of increasing the level of independence of people with PPMS through delaying disease progression from a potential DMT.

Methods

A bottom-up prevalence-based retrospective cost of illness approach was taken to estimate the direct and indirect costs of PPMS. The “cost of illness” has been defined as the value of the resources that are expended or foregone as a result of a health problem.24–26 A purely financial perspective has been taken for the analysis, i.e. intangible or non-financial costs have been excluded. The cost estimation used a unit cost basis to combine epidemiological data, health care resources consumption, and productivity loss. We estimated resource use and applied per capita unit costs for different groups of persons with PPMS, for example, by age and disease severity. These per capita costs were then scaled up to the estimated population with PPMS.

A budget impact analysis, taken from the perspective that the budget holder is the Australian society, was used to estimate the economic impact of the modelled hypothetical DMT intervention. This is essentially the difference between two cost of illness studies – the first based on usual care versus the introduction of the new therapy (intervention) into the treatment mix.27

Costs and benefits were estimated using 1) a cross-sectional analysis in which annual costs are presented, and 2) a life course approach in which costs are summed over the life of an individual.

Data sources and variables

Data on the prevalence, incidence and disease severity of PPMS in Australia were obtained from the international MSBase Neuro-Immunology Register, research by the Menzies Institute, data from MS Research Australia, MS Australia and review of the published literature (Table 1). The relevant data custodians ensured that at the point of primary data collection, patients had explicitly agreed to any secondary use of their data.

An estimated representative population for use in modelling was created using the base file population of the National Centre for Social and Economic Modelling (NATSEM) microsimulation model of the Australian tax and transfer system (STINMOD+). STINMOD+ was constructed from data from the Australian Bureau of Statistics (ABS) Survey of Income and House (SIH) and the Household Income and Labor Dynamics in Australia (HILDA) survey26 to replicate the general Australian population.

Primary variables included individual demographic characteristics, educational and career outcomes for people with

| Table 1. Epidemiology data sources. |
| Population characteristic | Data source |
| Prevalence of PPMS | Taylor et al.28, Jick et al.2 |
| Sex prevalence of PPMS | Giovannoni3, Stellmann et al.29 |
| Mean age of onset of PPMS | Giovannoni4, Stellmann et al.29, McKay et al.12 |
| Mean age of diagnosis of PPMS | Ahmad et al.11 |
| PPMS median progression time | Lenay et al.2, Stellmann et al.29, Raghavan et al.10 |
| PPMS life expectancy | Jick et al.5, Leray et al.2, Sandi et al.31 |
| Prevalence of MS | 2009 SDAC16, 2012 SDAC17, 2015 SDAC14 |
| Mean age at diagnosis of MS | Ahmed et al.11 |
| Age distribution of people with MS | 2015 SDAC18, Taylor et al.28, Palmer et al.35, Van Dijk et al.19, Ahmad et al.1 |
| Age-sex distribution of MS | 2015 SDAC18, Taylor et al.28 |

Abbreviations. MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis.
PPMS and carers (e.g. highest level of education, occupation, education or employment restrictions, time away from work), economic status of individuals with PPMS (e.g. employment status, hours worked, personal and household income, simulated tax rates), transfer payments and other social services costs for people with PPMS and carers, socio-psychological indicators (e.g. health-related quality of life levels of satisfaction, levels of independence, and social participation) and PPMS disease characteristics and health services utilization.

**Establishing the PPMS population in Australia**

The number of females and males with PPMS by age and disability status was projected using epidemiology data for MS and PPMS from overseas and Australia (Table 1). The 2015 ABS Survey of Disability, Ageing and Carers (SDAC) and the Australian Multiple Sclerosis Longitudinal Study (AMSLS) age distribution for people with MS was adjusted for this age difference to give an age distribution for people with PPMS (see Supplementary Table 1 for more details).

A disability distribution by age (Supplementary Table 2) was created so that the proportion of people with PPMS with mild disability (EDSS 0–3.5), moderate disability (EDSS 4–6.5) or severe disability (EDSS 7–9.5) reflected an average between the AMSLS cost of PPMS study and the US North American Research Committee on Multiple Sclerosis (NARCOMS) registry PPMS cohort and was consistent with disease onset and progression (Supplementary Tables 3–5).

PPMS has a much faster rate of disease progression than RRMS and SPMS; however, disease progression occurs at approximately the same rate for males and females, by age at onset, or type of first symptoms. Natural history data suggest that for a prevalent PPMS population where the mean duration of PPMS may be 15 years, most individuals with PPMS will have severe disability.

**Cost items**

The research focusses on the current broad economic and societal cost burden of PPMS that is placed on individuals, families, carers, health and assistive services, Government and society at large. Direct and indirect costs were included in the estimations.

Direct costs were regarded as the cost of “resources” expended on persons with PPMS. These can be either health care and support related (e.g. hospitalizations, medications, tests and formal care) or non-medical expenses and typically include out-of-pocket costs borne by individuals with PPMS, their family or carers such as cost of transport, personal care or household expenses (e.g. for home modifications). Direct costs also include Government income and welfare support payments provided through pensions and allowances to persons with PPMS.

Indirect costs were defined in terms of the value of lost productivity by the persons with PPMS or their carer, such as the foregone earnings of a person with PPMS when they retire early from the paid workforce, costs of absenteeism and presenteeism attributable to PPMS, or lost productivity of a carer who reduces the number of hours worked in order to care for the person with PPMS. This potentially impacts on retirement savings accumulation, the running down of savings and sale of personal or family assets as well as a reduction in income tax revenue for Government.

Intangible costs are non-material costs such as the costs of pain and suffering, emotional toll, stress, sadness, fear, social exclusion and impact on personal relationships and family including activities and use of time. Such qualitative attributes could be quantified as for example in disability-adjusted life years (DALYs). However, monetization of intangible costs is difficult. Since a purely financial perspective was applied for the analysis, quantification of intangible costs were out of scope for this analysis.

Cost items included in the cost analyses and source of data are given in Table 2.

A per capita cost was estimated for people with PPMS by age, gender and disease severity and scaled up to the estimated population with PPMS. Where necessary, the cost estimation used econometric modelling of the latest available cost data and costing procedures and strategies found in the literature and publicly available data sources.

Productivity losses, derived from reductions in working hours, absenteeism or sick leave, presenteeism and permanent retirement from the work force due to MS, were calculated using a human capital approach. Costs were calculated using national gender-stratified average gross hourly and annual earnings, similar to the approach used by Fogarty. The replacement cost method of valuing informal care was adopted, similar to the approach used by Access Economics and more recently by Ruutuainen in estimating the costs and quality of life of Finnish patients with MS. Average monthly hours of help needed from non-paid carers by persons with mild, moderate and severe PPMS were estimated, scaled up to annual hours of assistance provided and multiplied by the hourly wage of a respective professional caregiver.

All costs were uprated to 2018 Australian dollars using appropriate inflators.

**Modelling the impact of increased independence on costs of PPMS**

We modelled the effect on costs of PPMS resulting from the introduction of a hypothetical effective DMT. It was assumed that the treatment could delay disease progression by an additional year from mild disability to moderate disability and a further year from moderate disability to severe disability. While the overall age-sex profile of people with PPMS remains the same, the distribution by disability state is changed with the change in transition of people through each disability state over time due to the impact of the intervention. Disease progression is rapid for PPMS. Under this scenario, the assumed average time for a person with PPMS to move from mild to moderate severity increased from three to four years and from moderate to severe disability from five to six years. A 30-year simulation period was used to capture the long-term societal impact and highlight...
the enduring opportunity cost in the absence of an effective disease modifying therapy. This in essence created a new PPMS population to which the 2018 resource utilization rates and unit costs could be applied to estimate societal costs under the DMT scenario.

**Results**

**PPMS population in Australia**

It was estimated that 31,650 Australians had MS in 2018 based on the increase in number of people with MS from the 2009 to 2015 SDAC.²⁻³ The prevalence of MS in Australia in 2009 was 108.3 per 100,000 increasing to 121.9 per 100,000 in 2015. This is higher than the prevalence of MS identified in the 2016 Economic Impact Survey (EIS) of MS in Australia, which was estimated to be 25,607 in 2017.¹ However, they also reported that the number of people with MS had increased by 20.3% since 2010.

MS Australia reports that 15% of people with MS are diagnosed with PPMS. Of the MS patients enrolled in the AMSLS, 14.1% of participants had PPMS.²⁸ A similar prevalence rate (13.9%) was reported in the New Zealand MS prevalence study but a lower rate (10.2%) was recorded in the Tasmanian MS Prevalence & Genetics Study.²⁸ We assumed that 14% of the estimated 31,650 people with MS had PPMS in 2018 (4,430 people)⁶ and that there was an equal number (2,215) of males and females with PPMS.⁶,¹²,⁶,⁹,⁻¹⁰

The age-sex distribution of Australians with MS was estimated by averaging the percentage distributions reported in the 2015 SDAC and the AMSLS population described in Taylor et al.,²⁸ for males and females (Table 3). The estimated age-sex distribution is very similar to that reported for the UK⁶ as well as with persons registered with MS Australia.³⁹

People with PPMS were assumed to be 12 years older than those with RRMS, reflecting the difference in age of onset.⁶,³⁰ The mean age of onset of PPMS is about 40 years; the mean age of people with PPMS was estimated to be 62 years. The percentage of people with MS who have PPMS was estimated to increase with age to 36.8% of those aged 65 years or older, and with disease severity to 65% of people

| Table 2. Cost items and data sources. |
| --- |
| **Cost item** | **Main data source(s)** |
| Direct costs | AIHW National Hospital Morbidity Database; Australian hospital statistics 2016–17; Admitted Patient Care Ch 7: Costs and funding |
| Hospitalization | Bettering the Evaluation and Care of Health (BEACH) survey; MBS statistics; ABS Patient Experiences in Australia, 2016–17 Survey ³⁸ |
| Medical and health professional services (e.g. visits to a general practitioner, specialist, allied health professional or other health care practitioner) | 2017 AMSLS cost of PPMS study¹¹; 2010 AMSLS EIS³⁹,⁴⁵ |
| Medical tests (e.g. diagnostic tests, pathology) | PBS statistics; 2017 AMSLS cost of PPMS study¹¹ |
| PBS medicines | 2017 AMSLS cost of PPMS study¹¹ |
| Other medications | Aged Care Financing Authority data; Report on Government Services 2018, Ch 14 Aged Care Services⁴⁰ |
| Residential care | Aged Care Financing Authority data; Report on Government Services 2018, Ch 14 Aged Care Services⁴⁰ |
| Home care packages program (HCPP) | Aged Care Financing Authority data; Report on Government Services 2018, Ch 14 Aged Care Services⁴⁰ |
| Commonwealth home support program (CHSP) | ABS 2015 SDAC³⁴; Aged Care Financing Authority data; Report on Government Services 2018, Ch 14 Aged Care Services⁴⁰ |
| National disability insurance scheme (NDIS) | NDIS national dashboard data |
| **Indirect costs** | |
| **Disability support pension (DSP) – transfer payments** | Australian Government Department of Human Services (DSR extract blue book); ABS 2015 SDAC³⁴ |
| **Lost productivity for people with PPMS through early retirement or reduced hours of work** | 2016 HILDA survey³⁶; STINMOD Book; ABS 2015 SDAC³⁴ |
| **Absenteeism and presenteeism** | 2016 HILDA survey³⁶; STINMOD Book; ABS 2015 SDAC³⁴ |
| **Informal care** | 2016 HILDA survey³⁶; STINMOD Book; ABS 2015 SDAC³⁴ |
| **Carer payments and benefits** | Australian Government Department of Human Services |

**Table 3. Australians with PPMS as a proportion of all Australians with MS by age, gender and disease severity.**

| Age (years) | Females (%) | Males (%) | All persons (%) |
| --- | --- | --- | --- |
| <35 | No. PPMS | No. MS | % | No. PPMS | No. MS | % | No. PPMS | No. MS | % |
| 35–44 | 156 | 4,414 | 3.5 | 157 | 1,734 | 9.1 | 313 | 6,148 | 5.1 |
| 45–54 | 399 | 6,931 | 5.8 | 400 | 2,239 | 17.9 | 799 | 9,170 | 8.7 |
| 55–64 | 564 | 5,203 | 10.8 | 563 | 2,415 | 23.3 | 1,127 | 7,618 | 14.8 |
| 65+ | 1,049 | 3,566 | 29.4 | 1,048 | 2,126 | 49.3 | 2,097 | 5,692 | 36.8 |
| Mild (EDSS 0–3.5) | – | – | – | – | – | – | 753 | 13,610 | 5.5 |
| Moderate (EDSS 4–6.5) | – | – | – | – | – | – | 1,194 | 14,242 | 8.4 |
| Severe (EDSS 7–9.5) | – | – | – | – | – | – | 2,483 | 3,798 | 65.4 |
| All | 2,215 | 22,575 | 9.4 | 2,215 | 9,075 | 23.3 | 4,430 | 31,650 | 14.0 |

**Abbreviations.** EDSS, Expanded Disability Status Scale; MS, multiple sclerosis; PPMS, primary progressive multiple sclerosis.
with severe MS. Nearly 25% of males with MS were estimated to have PPMS and almost 50% of males aged 65 years or older, compared to 10% of females with MS and almost 30% of females aged 65 years or older (Table 3).

**Direct and indirect costs of PPMS in 2018**

The societal cost of PPMS in Australia in 2018 was estimated to be AU$418.1 million (Table 4). Indirect costs contributed 67.5% of the cost (AU$282.2 million), attributable to reduction in workforce participation and the need for informal care. People with severe PPMS accounted for 74.4% of total costs, those with moderate symptoms 20.0% and those with mild PPMS only 5.5% of the societal economic burden of PPMS. The major contributors to overall costs were the direct costs of residential care (12.8%) and the National Disability Insurance Scheme (NDIS) (9.5%), and indirect costs of informal care (27.1%), lost productivity (21.4%) and the disability support pension (9.3%).

**Costs of hospitalization**

Age-sex patterns of hospitalizations for MS for 2017–2018 were estimated and then apportioned to people with PPMS based on their share of the MS population. A total of 2,505 separations and 5,806 patient days (average length of stay 2.3 days) were estimated. Hospitalization costs by PPMS severity were estimated by apportioning the total costs by the number of people with mild, moderate or severe PPMS and the ratio of the per capita costs of hospital stay by EDSS reported in Ahmad et al.11 and Palmer et al.35 This indicated that only 5% of hospital costs would be incurred by patients with mild PPMS, 15% by patients with moderate PPMS and 80% of hospital costs by those with severe PPMS.

**National disability insurance scheme**

As of March 2018, there were 3,124 active participants with MS as their primary disability with an approved NDIS plan. In absence of more detailed data on the characteristics of NDIS participants with MS, it is assumed that no person with mild MS will receive support. Assuming 55% of those with moderate MS and all patients with severe MS aged less than 65 years are eligible for an NDIS package, then about 16% of these eligible individuals are likely to have PPMS, that is 496 individuals. The total cost of NDIS funded support packages to people with PPMS with approved plans is estimated to be AU$39.7 million in 2018, including AU$11.7 million for those with moderate PPMS, and AU$27.9 million for those with severe PPMS.

**Residential care**

As with the NDIS, it is assumed that those in residential care will have moderate or severe disease. PPMS contributes to about 15% of people with MS aged less than 65 years and who have moderate or severe disease, and about 58% of those aged 65 years and above. Thus, it is estimated that PPMS is contributing to an additional 484 permanent aged care residents (48 aged less than 65 years and 436 aged 65 years and above).

In 2017, the annual average cost of accommodation support was estimated to be AU$108,516 per person.11 This includes both Government subsidies and consumer fees and payments, excluding accommodation deposits. Inflating this cost using the CPI of 1.9% to 2018, gives a total cost of AU$110,578 per capita. Applying this unit cost to the number of additional residents in care because of their PPMS gives a total cost of AU$53.5 million in 2018.

**Lost productivity from changes in employment of persons with PPMS**

As MS impacts people of working age, many individuals experience presenteeism, absenteeism or are forced to reduce their working hours, change their jobs or leave the workforce prematurely. Disease severity and type of MS strongly influences the proportion of participants below

### Table 4. Direct and indirect costs by symptom severity (AU$million 2018).  

|                      | Mild (EDSS 0–3.5) | Moderate (EDSS 4–6.5) | Severe (EDSS 7–9.5) | All | % of costs (All) |
|----------------------|-------------------|-----------------------|---------------------|-----|------------------|
| **Direct costs**     |                   |                       |                     |     |                  |
| Hospitalization      | 0.791             | 2.311                 | 12.197              | 15.299 | 3.7             |
| Medical and health professional services | 0.946 | 1.385 | 2.832 | 5.163 | 1.2 |
| Medical tests        | 0.175             | 0.393                 | 0.441               | 1.009 | 0.2             |
| Medications          | 3.834             | 3.396                 | 9.891               | 17.122 | 4.1            |
| Residential care     | –                 | 12.938                | 40.582              | 53.520 | 12.8 |
| Home care and support (HCPP and CHSP) | – | 1.023 | 3.018 | 4.041 | 1.0 |
| NDIS                 | –                 | 11.735                | 27.945              | 39.680 | 9.5             |
| **Total direct costs** | 5.746             | 33.181                | 96.906              | 135.834 | 32.5 |
| **Indirect costs**   |                   |                       |                     |     |                  |
| Disability support pension | – | 12.645 | 26.049 | 38.693 | 9.3 |
| Lost productivity*   | 14.888            | 25.450                | 49.315              | 89.653 | 21.4 |
| Absenteeism and presenteeism | 1.725 | 2.797 | 1.789 | 6.311 | 1.5 |
| Informal care costs* | 0.819             | 9.657                 | 102.665             | 113.140 | 27.1 |
| Carer payments*      | –                 | –                     | 34.425              | 34.425 | 8.2             |
| **Total indirect costs** | 17.432            | 50.549                | 214.243             | 282.222 | 67.5 |
| **Total costs**      | 23.178            | 83.730                | 311.149             | 418.056 | 100.0 |

**Abbreviations.** CHSP, Commonwealth Home Support Program; EDSS, Expanded Disability Status Scale; HCPP, Home Care Packages Program; NDIS, National Disability Insurance Scheme; PPMS, primary progressive multiple sclerosis.

*For persons with PPMS retired from the workforce or shifting to part-time work due to PPMS.

*Cost due to lost productivity of carers.

*Includes carer payments and carer supplement payment.
retirement age who are in employment. Employment rates of people with PPMS are especially low, and absenteeism and presenteeism are experienced by a large proportion of the population.

The number of persons who are out of the workforce or have changed from full-time to part-time work because of PPMS can be calculated as the difference between the “observed” number in employment (Table 5) and the number that would be “expected” to be in employment if PPMS had no impact on employment. The findings suggest that 579 females and 783 males with PPMS are no longer in the paid workforce because of PPMS (Table 6). As expected, employment decreases with increasing disease severity for both males and females. The greatest reduction occurs in the full-time employment of males aged 45–64 years. The findings suggest the shift to part-time work is most pronounced for males with PPMS, and particularly younger males. There are higher numbers of males with PPMS aged 20–44 years in part-time work compared to that expected from the part-time employment rate in the general male population aged 20–44 years.

Table 5. Employment status of people with PPMS by age, gender and symptom group (2018).

|                | Female | Male | All Persons |
|----------------|--------|------|-------------|
|                | Mild |
| 20–44 years    | 62   | 10  | 74  | 36.3 |
| 45–64 years    | 43   | 113 | 156 | 22.3 |
| 65+ years      | 0    | 0   | 0   | 0    |
| All            | 105  | 123 | 228 | 13.0 |
| Employed < 65 years, % | 38.6 | 31.7 | 12.1 | 24.8 |
| Employed total PPMS population, % | 27.7 | 20.6 | 4.9 | 13.0 |
| Employed full-time |       |      |     |      |
| 20–44 years    | 36   | 5   | 41  | 20.8 |
| 45–64 years    | 25   | 61  | 86  | 11.9 |
| 65+ years      | 0    | 0   | 0   | 0    |
| All            | 61   | 66  | 127 | 7.1  |
| Employed < 65 years, % | 22.4 | 17.0 | 6.0 | 13.5 |
| Employed total PPMS population, % | 16.1 | 11.1 | 2.5 | 7.1 |
| Employed part-time |       |      |     |      |
| 20–44 years    | 26   | 5   | 31  | 15.6 |
| 45–64 years    | 18   | 52  | 70  | 10.4 |
| 65+ years      | 0    | 0   | 0   | 0    |
| All            | 44   | 57  | 101 | 5.9  |
| Employed < 65 years, % | 16.2 | 14.7 | 6.1 | 11.3 |
| Employed total PPMS population, % | 11.7 | 10.6 | 2.2 | 5.9 |

Abbreviations. Empl, employed; PPMS, primary progressive multiple sclerosis.

aMild: Expanded Disability Status Scale (EDSS) 0–3.5.
bModerate: EDSS 4–6.5.
cSevere: EDSS 7–9.5.

Table 6. Cost of lost productivity of people with PPMS through reduced employment (2018).

|                | Female | Male | All PPMS |
|----------------|--------|------|----------|
|                | FT     | PT   | FT and PT | FT     | PT   | FT and PT |
| “Expected” number employed |       |      |           |        |      |           |
| 20–44 years    | 84     | 64   | 148      | 146    | 30   | 176       |
| 45–64 years    | 347    | 287  | 634      | 638    | 103  | 741       |
| 65+ years      | 26     | 60   | 86       | 77     | 95   | 172       |
| Total          | 457    | 411  | 868      | 861    | 228  | 1,089     |
| “Observed” number employed |       |      |           |        |      |           |
| 20–44 years    | 42     | 32   | 74       | 49     | 37   | 86        |
| 45–64 years    | 115    | 100  | 215      | 118    | 102  | 220       |
| 65+ years      | 0      | 0    | 0        | 0      | 0    | 0         |
| Total          | 157    | 132  | 289      | 167    | 139  | 306       |
| People with PPMS out of the paid workforce due to PPMS |       |      |           |        |      |           |
| 20–44 years    | 42     | 32   | 74       | 97     | 97   | 97        |
| 45–64 years    | 232    | 187  | 419      | 520    | 520  | 520       |
| 65+ years      | 26     | 60   | 86       | 77     | 95   | 172       |
| Total          | 300    | 279  | 579      | 394    | 89   | 783       |
| Average gross wages and salary (from all jobs, AU$2018)$a |       |      |           |        |      |           |
| 20–44 years    | 66,984 | 32,328 | 99,312 | 82,862 | 92,715 | 175,577 |
| 45–64 years    | 72,981 | 33,836 | 106,817 | 86,841 | 87,682 | 174,523 |
| 65+ years      | 62,351 | 22,686 | 85,037 | 61,302 | 63,984 | 125,286 |
| Total          | 213,516 | 188,840 | 402,356 | 231,005 | 243,381 | 474,387 |
| Annual cost of lost wages and salaries due to PPMS, 2018 (AU$ million) |       |      |           |        |      |           |
| 20–44 years    | 2.813  | 1.034 | 3.848 | 8.038 | –0.189 | 7.849 |
| 45–64 years    | 16.932 | 6.327 | 23.259 | 45.212 | 0.032 | 45.244 |
| 65+ years      | 1.621  | 1.361 | 2.982 | 4.720 | 1.751 | 6.471 |
| Total          | 21.366 | 8.723 | 30.089 | 57.970 | 1.594 | 59.564 |

Abbreviations. FT, full-time; PPMS, primary progressive multiple sclerosis; PT, part-time.

$2016$ HILDA data was inflated using growth in average weekly earnings.

Abbreviations. Empl, employed; PPMS, primary progressive multiple sclerosis.
Table 7. Cost of lost productivity through reduced employment by severity of PPMS symptoms (2018).

|                                      | Female |                |                | All Persons |                |                |
|--------------------------------------|--------|----------------|----------------|-------------|----------------|----------------|
|                                      | FT     | PT             | FT and PT      | FT          | PT             | FT and PT      |
| Persons with mild PPMS out of the paid workforce due to PPMS |        |                |                |             |                |                |
| 20–44 years                          | 28     | 22             | 50             | 9           | 6              | 12             |
| 45–64 years                          | 17     | 17             | 34             | 48          | 8              | 9              |
| 65+ years                            | 3      | 6              | 9              | 8           | 9              | 17             |
| Total                                | 48     | 45             | 93             | 126         | 7              | 119            |
| Persons with moderate PPMS out of the paid workforce due to PPMS |        |                |                |             |                |                |
| 20–44 years                          | 7      | 5              | 12             | 17          | 1              | 15             |
| 45–64 years                          | 68     | 54             | 122            | 175         | 14             | 161            |
| 65+ years                            | 5      | 12             | 17             | 15          | 19             | 34             |
| Total                                | 80     | 71             | 151            | 207         | 5              | 212            |
| Persons with severe PPMS out of the paid workforce due to PPMS |        |                |                |             |                |                |
| 20–44 years                          | 7      | 5              | 12             | 11          | 1              | 12             |
| 45–64 years                          | 147    | 116            | 263            | 296         | 23             | 319            |
| 65+ years                            | 18     | 42             | 60             | 54          | 67             | 121            |
| Total                                | 172    | 163            | 335            | 361         | 91             | 452            |
| Annual cost of lost wages and salaries due to mild PPMS, 2018 (AUs$ million) |        |                |                |             |                |                |
| 20–44 years                          | 1.876  | 0.711          | 2.587          | 5.718       | 0.216          | 5.501          |
| 45–64 years                          | 1.241  | 0.575          | 1.816          | 4.260       | 0.256          | 4.004          |
| 65+ years                            | 0.187  | 0.136          | 0.323          | 0.490       | 0.166          | 0.656          |
| Total                                | 3.303  | 1.423          | 4.726          | 10.468      | 0.306          | 10.162         |
| Annual cost of lost wages and salaries due to moderate PPMS, 2018 (AUs$ million) |        |                |                |             |                |                |
| 20–44 years                          | 0.469  | 0.162          | 0.631          | 1.409       | 0.000          | 1.409          |
| 45–64 years                          | 4.963  | 1.827          | 6.790          | 15.216      | 0.448          | 14.767         |
| 65+ years                            | 0.312  | 0.272          | 0.584          | 0.920       | 0.350          | 1.270          |
| Total                                | 5.743  | 2.251          | 8.004          | 17.544      | 0.098          | 17.446         |
| Annual cost of lost wages and salaries due to severe PPMS, 2018 (AUs$ million) |        |                |                |             |                |                |
| 20–44 years                          | 0.469  | 0.162          | 0.631          | 0.911       | 0.027          | 0.939          |
| 45–64 years                          | 10.728 | 3.925          | 14.653         | 25.736      | 0.736          | 26.473         |
| 65+ years                            | 1.122  | 0.953          | 2.075          | 3.310       | 1.235          | 4.545          |
| Total                                | 12.319 | 5.039          | 17.359         | 29.958      | 1.998          | 31.956         |

Abbreviations. FT, full-time; PPMS, primary progressive multiple sclerosis; PT, part-time.

20–44 years (14.5% vs. 18.0%). The rate of part-time work for males aged 45–64 years with PPMS is the same as that for all Australian males aged 45–64 years. In all of the other age-sex employment status groups, the proportion of people with PPMS who are employed is significantly lower than those of the general population.

The cost of the lost productivity is the sum of the lost annual wages and salaries for those out of the paid workforce or who shifted to part-time work due to PPMS. Multiplying the wages and salaries for full-time and part-time workers in the general population by the numbers of people with PPMS “missing” from the labor force gives the cost of lost earnings due to PPMS.

As shown in Table 6, these indirect costs are calculated to be AUs$89.7 million in 2018. A third of these costs are attributable to females who changed their employment status due to PPMS and two-thirds to males. Nearly 90% of the costs are from the reduction in full-time work by people with PPMS. Table 7 provides estimates of the lost wages and salaries by severity of PPMS.

Informal care

Of all people with MS, 38% received assistance from informal carers. This overall rate is dominated by those with severe disability, of whom 81% had an informal carer. The assumed distribution of people with MS using informal care – mild (12%), moderate (52%) and severe (81%) – was obtained by comparison with data from Australia and countries in Europe with similar rates of informal care.

The number of hours of care provided by informal carers was estimated through comparison with similar European countries due to limited data available in Australia. It was estimated that 31 h of care per month were provided to people with MS with mild symptoms, 53 h to those with moderate symptoms and 174 h to those with severe MS. These average numbers of hours were applied to the estimated number of Australians receiving informal care per month, summed across the disability categories and expressed as the average weekly number of hours of care per person with MS receiving care. This calculation yields an average of 20.2 h of care per week provided by Australian informal carers to the 38% of people with MS receiving informal care. The result is very similar to the number of hours extrapolated from the 2015 SDAC data on the average weekly hours of care provided by primary carers to people with MS.

The use of informal care by disability severity is assumed to be independent of the type of MS. However, because many more people with PPMS have moderate and severe disability, overall 61% of people with PPMS are expected to receive care from family members and friends, with informal carers providing over 4.6 million hours of care per year.

The total value of family and other informal care provided to Australians with PPMS was estimated at AUs$113.1 million.
indirect costs (AU$millions)

Direct costs (AU$millions)

The impact of an effective DMT on costs of PPMS in 2018 was estimated to be a saving of AU$14.9 million (Table 9). The largest contributors to savings in direct costs are reduced need for residential care and support from the NDIS for people with moderate and severe PPMS (Table 9). Major savings in indirect costs include the reduced need for informal care, particularly for people with severe disease, reduced productivity losses for people with moderate and severe PPMS and reduced Government carer payments and dependence on the disability support pension for people with severe PPMS. Savings are offset in part by the increased costs associated with treatment, including the hypothetical effective DMT introduced, as well as the care and support of the increased number of people with mild PPMS and their increased productivity losses.

Discussion

This cost of illness analysis shows that the economic burden of PPMS in Australia is high, at an estimated AU$418 million in 2018. These results are generally consistent with findings from the international literature and other economic impact

Table 8. Scenario PPMS population by age, gender and disability status (2018).

Table 9. Impact of delayed disease progression on costs of PPMS.

Abbreviations. NDIS, National Disability Insurance Scheme; PPMS, primary progressive multiple sclerosis.

in 2018, the majority of costs (91%) being associated with the care provided to people with severe PPMS symptoms.

The impact of increased independence on costs of PPMS

To identify how many people would have mild, moderate or severe PPMS in 2018 under the DMT intervention scenario, aggregate progression rates from one disability state to another were changed, and cases summed over a 30-year simulation period. The DMT scenario population and change in numbers are given in Table 8. The intervention results in 176 more individuals having mild PPMS, 60 fewer people having moderate symptoms and 116 fewer having severe disability. Just over half of those with improved disability status are under 65 years of age and around 48% are aged 65 years and above.

The impact of an effective DMT on costs of PPMS in 2018 was estimated to be a saving of AU$14.9 million (Table 9). There are major cost savings from reducing the number of people with moderate and severe PPMS symptoms. The
studies in Australia.\textsuperscript{1,16,44} An almost identical cost of PPMS is obtained when the per person costs by disease severity from the 2016 EIS\textsuperscript{1} are applied to the number of individuals in this study with mild, moderate and severe PPMS, allowing for inflation.

Costs increase significantly with disease severity from AU$23.2 million for individuals with mild PPMS to AU$311.1 million for those with severe disability, a 13-fold increase in annual costs. Indirect costs were found to contribute 67.5\% of the total cost of PPMS, reflecting both the age of patients and the level of disease severity. This was similar to the breakdown of costs reported for people with PPMS in the 2016 Australian EIS. Informal care costs were the largest component of total costs at 27.1\%, followed by lost productivity from people with PPMS retiring from the workforce, reducing their hours of work or changing jobs (21.4\%). In the 2016 EIS, informal care costs were 21.6\% and lost productivity was 24.2\%.

Support provided by the Government is significant with the NDIS estimated to be contributing to nearly 10\% of the annual costs of PPMS, the Disability Support Pension (DSP) to over 9\% and carer payments a further 8\%. Given the level of disability of people with PPMS, the need for residential care and formal home care and support is considerably higher than that within the general population, with PPMS contributing to an expected additional AU$57.6 million in expenditure in 2018.

The introduction of an effective DMT that could delay disease progression by a year from mild disability to moderate disability and a further year from moderate disability to severe disability could reduce the societal cost of PPMS in Australia by AU$15 million per year, an overall saving of 3.6\%. While major savings are made for people with moderate and severe disability, these are partly offset by increased costs with increasing numbers of people having mild PPMS.

The findings in this study add to the evidence base demonstrating that PPMS is associated with a high economic burden. People with PPMS are on average older and have greater disease severity than individuals with RRMS. This is reflected in higher needs for care and support, and lower rates of workforce participation and productivity. However, the introduction of an effective DMT that delays disease progression would not only improve patients’ subjective wellbeing and quality of life but also lead to major cost savings.

Limitations

Limitations of the study include the need to estimate direct and indirect costs based on publicly available data, which may be incomplete. Also, the potential cost of the modelled effective DMT has not been included in the analysis.

Conclusions

The economic burden of PPMS was estimated to be AU$418 million in 2018. An effective DMT would provide significant cost savings through delaying disease progression, potentially improving the quality of life of people with PPMS, their families and carers.

Transparency

Declaration of funding

This study was funded by Roche Products Pty Ltd.

Declaration of financial/other relationships

LJB is an employee of the NATSEM Institute for Governance and Policy Analysis, University of Canberra and has received funding from Roche to perform the research.

JL is an employee of the NATSEM Institute for Governance and Policy Analysis, University of Canberra and has received funding from Roche to perform the research.

MB is an employee of Roche Products Pty Ltd, the research sponsor.

MS is an employee of Roche Products Pty Ltd, the research sponsor.

HAL is an employee of the NATSEM Institute for Governance and Policy Analysis, University of Canberra and has received funding from Roche to perform the research.

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Author contributions

LJB, MB and MS were involved in the study design, formulation of the research question and data interpretation. LJB, JL and HAL were involved in data collection and data interpretation. All authors critically revised the draft manuscript for intellectual content and approved the final version for submission. All authors agree to be accountable for all aspects of the work and fulfil the ICMJE guidelines for authorship.

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