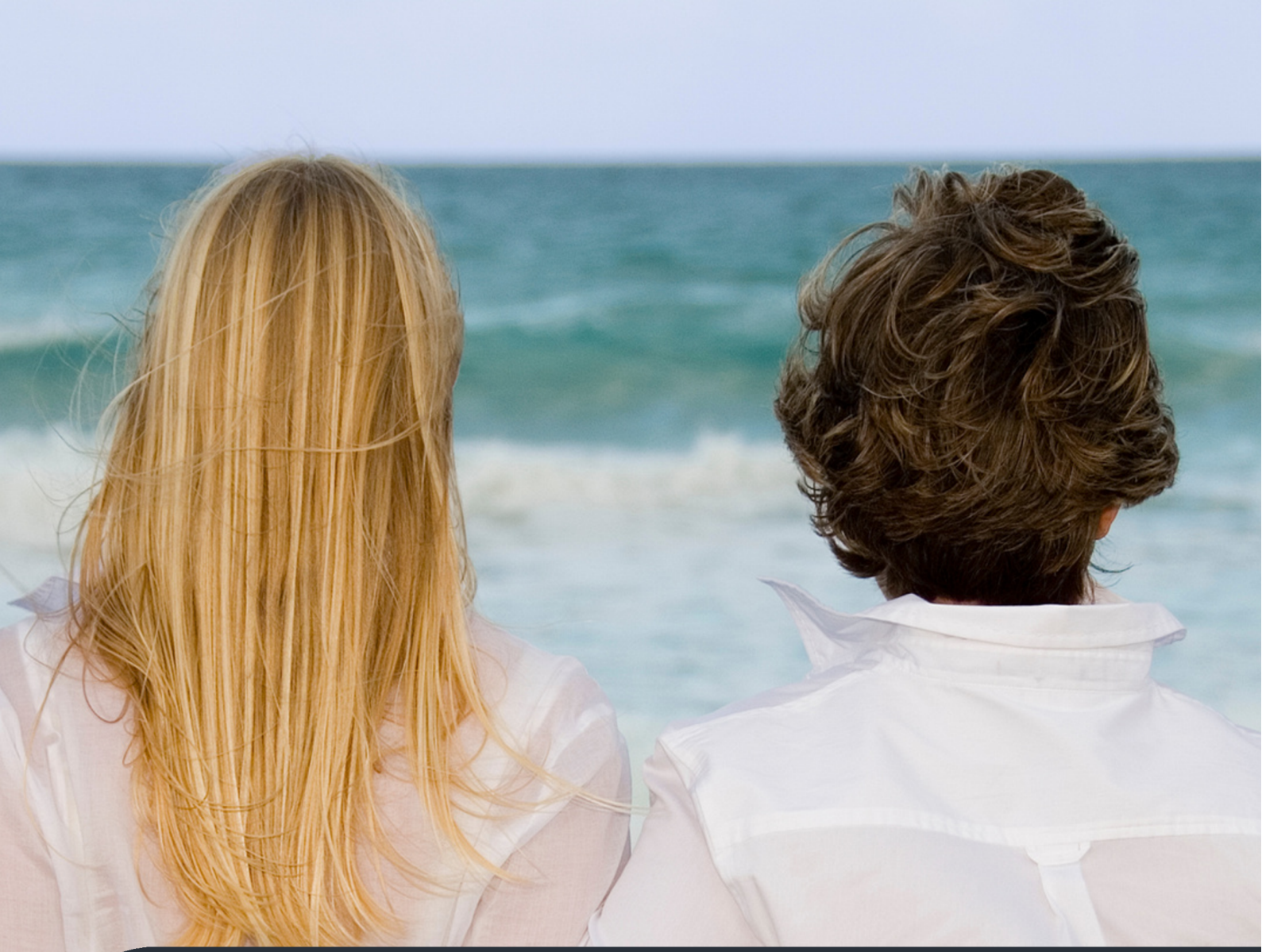

"The Cost Effectiveness of Ocrelizumab for Treatment of Primary Progressive Multiple Sclerosis (PPMS) in Aotearoa New Zealand, from Healthcare and Societal Perspectives"

A review of the "The Milne Report" and the case to support a new way of valuing Pharmac funded treatments and why they should take ALL costs into consideration

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Key Findings

"The Cost Effectiveness of Ocrelizumab for Treatment of Primary Progressive Multiple Sclerosis in Aotearoa New Zealand, from Healthcare and Societal Perspectives" (The Milne Report), used the medicine ocrelizumab (Ocrevus) for use in primary progressive multiple sclerosis (PPMS) as an example to look at the difference between funding decisions using Pharmac's current model and global best practice which takes a 'whole of society' perspective.

- Cheaper medicines are not necessarily cost saving when societal costs are considered.
- The costs of a chronic illness such as PPMS go well beyond the cost of medicine alone.
- The current Pharmac cost utility model only looks at direct medical costs.
- Loss of income, loss of tax and superannuation contributions, costs of hospitalisations, cost of equipment, cost of associated disorders or comorbidities and the cost of caring for those with a disability are amongst the many significant societal costs that could also be considered using cost utility analysis.
- The model illustrated by Milne, and widely used overseas, provides sound rationale for funding a high value medicine and funding the medicine earlier to reduce long-term disability and long-term societal costs.
- For example, the model shows that based on Treasury's guidelines, ocrelizumab would be cost effective up to NZ$22,057 per person per annum, when societal costs are taken into account. However, considering only healthcare costs, it would be cost effective up to NZ$4,673 per person per annum.
- Waiting for cheaper prices and/or generic entry delays medicine funding. For people with PPMS, this delay increases the likelihood of unnecessary premature disability, disease progression, loss of brain tissue and reduced quality of life.
- As disability and poor health advances, not only are individuals and their families impacted, but also the cost to society escalates.
- If Pharmac made funding decisions based on the total cost to society it would change the ranking of pharmaceuticals listed for funding, reflecting the true value of the medicine, enabling quicker and smarter funding choices for medicines to treat chronic conditions.
- The model demonstrates that the early and appropriate funding of medicines enables those with PPMS and their whānau to lead fuller and more productive lives.
- Adopting these recommendations would assist Pharmac to meet the Associate Minister of Health's Expectations as detailed in the 16th July 2024 letter that it: *Updates its decision-making and evaluation models to include the wider fiscal impact of funding or not funding a medicine or medical device to the whole of government and has tools to consider the wider societal impact.*
- The approach taken by Richard Milne and colleagues could be redeveloped for treatments of other chronic conditions.

Introduction

In January 2023 Multiple Sclerosis NZ (MSNZ) contracted Health Economist Richard Milne PhD, to conduct an economic evaluation of ocrelizumab for Primary Progressive MS (PPMS) from healthcare and societal perspectives. The project included researching how PHARMAC should, or could, assess a medicine to be in accordance with societal expectations and best global practice. This report is a summary of the key findings of The Milne Report finalised in 2024, "The Cost Effectiveness of Ocrelizumab for Treatment of Primary Progressive Multiple Sclerosis in Aotearoa New Zealand, from Healthcare and Societal Perspectives."

Pharmac's current model is a cost utility analysis (CUA) which is a subset of cost effectiveness analysis. Pharmac weighs up the direct heathcare costs and makes decisions relative to its own ringfenced and capped budget. It analyses the cost of buying the medicine and administering it to the patient, the cost savings that the medicine could provide to the New Zealand healthcare system, and the potential improvement in the patient's quality of life. In a CUA, the medicine cost is compared to incremental health improvements, or quality adjusted life years (QALYs).

Both a cost utility analysis and a cost benefit analysis are described in the Milne Report. These analyses both appreciate that healthcare interventions have a societal impact as well as a healthcare one. Treasury recommends that cost benefit analysis models with a societal perspective be utilised by government departments in budgetary decisions, similar to many OECD countries.

In chronic progressive conditions like MS, it is sensible to take into account all costs to society since as disease and disability progresses, so do non-medical and indirect costs. These costs include specialised equipment, home modifications, and informal care. Increased levels are also reported in un- and under-employment and absenteeism of both those diagnosed and their family carers providing support. The Milne Report strongly makes the case that earlier access to treatment both in age and disability make a treatment more cost effective.

The report demonstrates that indirect costs account for over half of the total cost to society annually and therefore are not currently accounted for in funding decisions.

The model in the Milne Report justifies Pharmac spending 4.7-fold more per annum per person on the case study treatment Ocrelizumab for Primary Progressive MS than justified by the current economic model focussed solely on healthcare costs.

Overall, the case presented in The Milne Report, clearly highlights that the current Pharmac model which only includes direct medical costs severely underestimates the savings to society that can be made by investing in life-improving treatments. MSNZ supports Pharmac taking a societal perspective in cost benefit and/or cost utility analysis to account for non-health and indirect costs absorbed by the wider economy, society, patients and their whānau.

Multiple Sclerosis

Multiple sclerosis (MS) is a disease in which the body's immune system attacks its nervous system. The immune cells of the body attack the brain, spinal cord and nerves which can cause a range of different symptoms. New Zealand is a high-risk country for MS, with a prevalence of 73.1 per 100,000 population.

The way that MS presents can be different in different people, but MS can be largely grouped into three different sub-groups; relapsing-remitting (RRMS), primary progressive (PPMS) and secondary progressive (SPMS). Milne's research focuses on PPMS which accounts for approximately 15% of people with MS, and a newly available treatment for this type of MS, called ocrelizumab.

Unlike other types of MS, in PPMS there are no periods of remission, where symptoms are relieved. From the very first symptoms, there is a progressive decline in symptoms and therefore worsening disability. Typically, people with PPMS will experience worsening in their ability to walk, worsening fatigue and cognitive impairment. Another common symptom is muscle spasticity where muscles seize or cramp up, causing pain, stiffness, and impaired mobility.

PPMS is most likely to be diagnosed in New Zealanders 25 to 50 years of age meaning that most people are diagnosed in their prime working years. Due to the disability that PPMS causes, many who are working are likely to reduce how much or how strenuously they work or have to stop work completely, which causes a significant loss of income to them and their family. This also results in a reduction in income tax contributions and retirement savings.

MS not only affects the individual, their daily life and ability to work, but it also impacts the individual's whānau and carers. As the disease progresses, so does the need for help with daily activities, transport, financial assistance and help navigating the healthcare system. In some cases, this care is covered by formal arrangements with paid carers, but often this care is provided by whānau, friends, or charities such as MS organisations. Although this is not often paid for, it does come at a significant cost.

Ocrelizumab (Ocrevus®)

Ocrelizumab, or Ocrevus, is a newly available treatment for PPMS. It is the first and only treatment available globally that has been shown to slow down the progression of PPMS. It is administered much like other MS treatments, as a six-monthly intravenous infusion into the blood stream. Ocrelizumab was approved for use in New Zealand by MedSafe in December 2017 and only funded by Pharmac for PPMS, in October 2023, 6 years later. Delays in funding valuable interventions, in this case, the first and only medicine available for those with PPMS, has led to unnecessary disability, and cost.

The Benefits of Ocrelizumab

The cost effectiveness of ocrelizumab depends largely on its cost to Pharmac and how much it can slow disease progression. Delaying disease progression delays disability and the associated costs of disability. In a large overseas clinical trial of ocrelizumab in people with PPMS, it was shown that those treated with ocrelizumab were 24% less likely to show the same disease progression as those untreated*. The Milne model confirms that treatment with ocrelizumab delays wheelchair dependence by between 4-6 years on average**. This delay in progression of the disease means that patients spend more time with less disability and therefore require fewer health system and other resources. Importantly, it also means that quality-of-life is preserved for longer. Early diagnosis and treatment provide a longer delay in disability than late diagnosis and treatment.

* Montalban X, Hauser SL, Kappos L, Arnold DL, Bar-Or A, Comi G, et al. Ocrelizumab versus placebo in primary progressive multiple sclerosis. N Engl J Med. 2017;376(3):209-20; https://www.nejm.org/doi/full/10.1056/NEJMoa1606468

**See also: Butzkueven H, Spelman T, Horakova D, Hughes S, Solaro C, Izquierdo G, et al. Risk of requiring a wheelchair in primary progressive multiple sclerosis: Data from the ORATORIO trial and the MSBase registry. European Journal of Neurology. 2022;29(4):1082-90.

Funding Decisions

When Pharmac evaluates a treatment to decide whether it should be funded by the government, it assesses how well the drug works, how many patients will be affected, how accessible the treatment is, and other factors. One important consideration is the annual cost to Aotearoa New Zealand, because Pharmac operates under a capped budget and must fund medicines for all New Zealanders. Another is the cost effectiveness of the new treatment compared with standard practice. In the case of ocrelizumab, comparing the cost effectiveness of a new drug and the impact this would have on clinic/staff time against the cost effectiveness of no treatment requiring no clinic/staff time. Pharmac uses a cost utility model to weigh up the cost of buying the drug and administering it to the patient, the cost savings that the drug could provide to the New Zealand healthcare system, and the potential improvement in the patient's quality of life.

In contrast, the research proposes including all costs to society in a cost benefit or cost utility model, to give a wider view of the financial impact of a disease, in addition to medical costs.

A cost benefit analysis model was recommended by the NZ Treasury in 2015 for all budget initiatives. It has never been made clear why PHARMAC has used a cost utility analysis instead of cost benefit model.

The Research

A economic model was constructed to consider all the costs and benefits to society and the potential improvement in quality of life over the lifetime of a typical person with PPMS. The model considers all the costs of treatment, the financial benefits to the whole of society, and the improvement in quality of life of the person with PPMS. Because the cost of ocrelizumab to Pharmac is confidential, the analysis considered a wide range of acquisition costs. It also included Treasury's value of a year of life adjusted for quality of life.

The Costs

The current Pharmac economic model does not account for loss of income due to disability. The 2006 MS Incidence Study referred to in The Milne Report, showed that 69% of people in NZ with MS, who are of working age, reported that their employment status had changed due to their MS. The median income for people in NZ with MS is substantially lower than the general population, even at low levels of disability. The most frequent self-reported reasons for this were fatigue (37%), lower body motor dysfunction (30%) and impaired cognition (12%). Loss of income by individuals with PPMS is included in the Milne model but not in Pharmac's.

Informal care is mostly unpaid and provided by whānau and friends, but it still is a cost of having MS. Underemployment has been reported in carers of those with MS, as carers often have a reduced capacity for employed work. In Australia the costs of absenteeism alone, for those who provide this care, ranges from days to weeks of paid work. This cost disproportionately affects women. In New Zealand in 2018, over 80% of unpaid carers were women*.

To assess cost savings, an accurate assessment of the true cost of MS must be made. The loss of income and the cost of informal care are some of the wider costs included in the Milne model. To create the new model, costs were calculated using data from Australia, which show direct medical, direct non-medical, indirect and total costs at varying degrees of disease severity. Australian data were used due to the lack of availability of NZ data. These costs were translated into 2022 NZ dollars and divided into healthcare and societal (total) costs. Annual costs per person range from approximately $30,000 at the lowest level of disability, to over $140,000 at the most extreme level of disability.

Across all degrees of disease severity, the indirect costs of MS represented over half of the total cost to society annually. For example, at a level of disability where a walking aid is required, approximately $80,000 of the total approximately $110,000 of costs are indirect and therefore not currently accounted for in funding decisions. These indirect costs include loss of productivity for those who work and the cost of informal care (i.e., provided by friends or family members) and these costs increase with disease severity. The current Pharmac model which only includes direct medical costs severely underestimates the savings to society that are made by treatment with ocrelizumab.

*Synergia. The state of caring in Aotearoa. A report for Carers NZ and the Carers Alliance. 2022 [Available from: https://carers.net.nz/state-caring-report/.]

Evaluating Cost-Effectiveness

In order to get a true picture of the cost effectiveness of treatment of PPMS with ocrelizumab, the Milne Report, included all costs and delays in progression of disability. These include the use of the hospital, staff, equipment, ocrelizumab, and other medicine costs.

Also considered is ocrelizumab's patent expiry in 5 years. This means that any manufacturer will be able to produce the medicine which will drive down the cost significantly in the future.

The price paid for a drug by Pharmac is confidential. This protects Pharmac's ability to negotiate considerably lower prices than those publicly listed. The current list price for ocrelizumab in NZ is $37,384 + GST per patient per annum. Using the current Pharmac model of only including health care costs, Pharmac would need a significant reduction in the price and would only be able to justify purchasing ocrelizumab at $4,673 per person per annum, based on Pharmac's criteria.

However, based on this research, including the wider costs to New Zealand, Pharmac would be justified in paying up to $22,057 per annum per person for the drug to be cost effective.

Closing Remarks

If New Zealand made funding decisions based on the total cost to society, it would change the ranking of new pharmaceuticals listed for funding whilst reflecting the true value of the medicine. Treatments that reduce long term disability and improve quality of life would be meaningfully valued, meaning that patients can have a better quality of life for longer, enabling them to either return to work, or work more productively.

MS Brain Health

People with multiple sclerosis (MS) need access to effective medicines, known as disease modifying therapies/treatments (DMTs), as soon after diagnosis as possible. This ensures the best chance of preserving brain and spinal cord tissue, optimising long-term brain health outcomes.

*"Even in the early stages of MS, cognition, emotional well-being, quality of life, day-to-day activities and ability to work can be markedly affected by the damage occurring in the brain and spinal cord. As the disease progresses, increasing disability – such as difficulties in walking – imposes a heavy burden on people with MS and on their families. It also leads to substantial economic losses for society, owing to diminished working capacity."**

MS Brain Health
Time Matters

*Giovannoni, G. et al. Brain Health: Time matters in multiple sclerosis (2017) www.msbrainhealth.org

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