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The health and productivity burden of migraines in Australia

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Abstract

Objective

The present study aimed to quantify the health and productivity burden of migraines in Australia, measured by quality-adjusted life years (QALYs), productivity-adjusted life years (PALYs, a novel measure of productivity) and associated healthcare and broader economic costs.

Methods

A Markov state-transition model was constructed to simulate follow up of Australians aged 20-64 years over the next ten years. The model was first run using current prevalence estimates of migraine. It was then re-run assuming that people with migraine hypothetically did not have the condition. Differences in outcomes between the two model simulations represented the health and productivity burden attributable to migraine. All data inputs were obtained from published sources. Gross domestic product (GDP) per equivalent full-time worker in Australia was used to reflect the cost of each PALY (AU\$177,092). Future costs and outcomes were discounted by 5% annually.

Results

Currently, 1,274,319 million (8.5%) Australians aged 20-64 years have migraine. Over the next ten years, migraine was predicted to lead to a loss of 2,577,783 (95% confidence interval (CI) 2,054,980 to 3,000,784) QALYs among this cohort (2.02 per person and 2.43% of total QALYs), and AU\$1.67 (95% CI \$1.16 to \$2.37) billion in healthcare costs (AU\$1,313 per person, 95% CI \$914 to \$1,862). There would also be 384,740 (95% CI 299,102 to 479,803) PALYs lost (0.30 per person and 0.53% of total PALYs), resulting in AU\$68.13 (95% CI \$44.42 to \$98.25) billion of lost GDP (AU\$53,467 per person, 95% CI \$34,855 to \$77,102).

Conclusion

Migraines impose a substantial health and economic burden on Australians of working age. Funding interventions that reduce the prevalence of migraines and/or its effects are likely to provide sound return on investment.

Introduction

The World Health Organisation specifically acknowledges that migraines impose a substantial health burden around the world. Around 11% of the global population is affected, with three times as many women than men.¹

Migraines typically present with a unilateral throbbing headache. Other symptoms include aura, nausea and vomiting, photophobia and phonophobia. The pathophysiology of migraine remains uncertain, with multiple theories purported.

Migraines are typically classified into chronic and episodic categories. Chronic migraines are defined by the occurrence of 15 or more headaches a month for more than three months, with at least 8 episodes a month exhibiting the features of migraine headache, while episodic migraines are defined by less than 15 headaches a month.²

Although there is no significant mortality associated with migraines,³⁻⁶ it is associated with a significant morbidity burden, which includes impairment to work or schooling.⁷ Furthermore, direct and indirect costs are high. Direct costs are attributed to use of healthcare services, including inpatient and outpatient services, imaging and pharmaceutical services, while indirect costs include those lost to reduced productivity, including via absenteeism (time spent away from work) and presenteeism (lost productive time at work).⁸

Compared to most other chronic diseases, which affect older populations, the relative burden of migraine on work productivity is large given its high prevalence among people of working age.⁹ A recent report prepared by Deloitte Access Economics for Novartis Australia estimated a loss of AU\$16.3 billion due to reduced productivity in people with migraine in 2018. In that year, the estimated productivity cost per person was AU\$11,132 (US\$7,562)¹⁰ for chronic migraine sufferers and AU\$2,707 (US\$1,839) for episodic migraine sufferers.¹¹ In Brazil, researchers have estimated a loss of R\$37.5 billion (US\$9.6 billion) annually from indirect (productivity) costs and 45.1 million years lived with disability.¹² In Sweden, the productivity burden was estimated to be €10,790 (US\$12,083) per person per year, and almost three times higher among people with chronic than episodic migraine.¹³

However, no study has thus far estimated lost productivity due to migraine in a longitudinal manner; that is, over an extended period of time.

In the present study, we sought to quantify the productivity burden of migraine in Australia over the next ten years, measured in terms of productivity-adjusted life years (PALYs),¹⁴⁻¹⁹ and the associated impact on the broader economy.

Methods

Model structure

A Markov state-transition model was developed to simulate the progress of Australians currently aged 20 to 64 years with migraine, with simulated follow-up over ten years. Separate sex and five-year age cohorts were constructed based on 2019 Australian population data, with the cohort starting at the midpoint of the age-group (that is, 22 years for age-group 20-24 years, 27 years for age-group 25-29 years, etc). The model comprised four health states: 'No migraine', 'Episodic migraine', 'Chronic migraine' and 'Dead' (Figure 1). The numbers of people occupying the three living health states at baseline were determined using migraine prevalence data (discussed below). With each annual cycle, individuals in the 'No migraine' health state were at risk of dying, individuals in the 'Episodic migraine' health state were at risk of developing chronic migraine or dying, and individuals in the 'Chronic migraine' health state were at risk of remitting to episodic migraine or dying. The risk of each of these transitions is described further below. Individuals continued to cycle through the model for up to ten years, or until death. The model estimated total years of life, quality-adjusted life years (QALYs) and PALYs lived by the cohort, as well as related direct healthcare costs and broader economic costs. Total deaths were estimated to allow calculation of years of life, assuming that deaths occurred halfway through the cycle. Utility and productivity indices (described below) were applied to years of life to determine QALYs and PALYs, respectively.

To estimate the health and economic burden lost to migraine, the model was first simulated for the Australian population over ten years, assuming the currently-observed prevalence of migraine. The model was then re-simulated assuming that people with migraine hypothetically did not have the condition. That is, the prevalence of migraine was set to zero, and all subjects occupied the 'No migraine' health state in the model.

Differences in outcomes between the two model simulations in terms of years lived, QALYs lived, PALYs lived and costs represented the health and productivity burden attributable to migraine.

Data sources

All data inputs are included in Table 1.

Population

The demographic profile of the cohort was drawn from Australian Bureau of Statistics (ABS) data for 2019, the most recent year of available data.²⁰

Age and sex-specific prevalence of migraine was drawn from the 2017-18 National Health Survey.²¹ The mid-point of each age-group was used to develop polynomial functions (see Supplementary Appendix 1) to estimate the prevalence of migraine for each single year of age. We estimated the specific prevalence of chronic and episodic migraine within each sex-and-age stratum by applying the proportional distributions of each type of migraine noted in the American Migraine Prevalence and Prevention Study.²² Age and sex-specific population estimates for the total Australian population, as well as those with chronic and episodic migraine are included in Supplementary Appendix 2. As per the International Burden of Migraine Study, we assumed that those with episodic migraine experienced mean headache days of 10.4 days in a three-month period, and 64.4 days for those with chronic migraine.²³ Therefore, with each annual cycle, those with episodic and chronic migraine experienced mean headache days of 41.6 and 257.6, respectively.

Transitions between episodic and chronic migraine

An annual rate of developing chronic migraine of 2.5% was applied to individuals in the 'Episodic migraine' health state as per Bigal et al.²⁴ Manack et al demonstrated that over two years, 26.1% of chronic migraineurs had remitted.²⁵ Therefore, we assumed 13.1% of those in the 'Chronic migraine' health state remitted to episodic migraine over one year. This is consistent with findings from Bigal et al, who found that 14.7% of those with chronic migraine remitted or were assigned a different diagnosis.²⁴

Mortality risk

Australian age and sex-specific mortality rates were applied to determine total deaths in each cycle.²⁶ Mortality in those with and without migraine was assumed to be the same; that is, we assumed no increased risk in all-cause mortality associated with migraine.³⁻⁶

Utilities

Australian quality of life norms by age and gender were applied to all subjects in the model (Supplementary Appendix 3).²⁷ To reflect the impaired quality of life associated with migraine, the utilities for those with episodic and chronic migraine were reduced. The utilities for chronic and episodic migraines were sourced from Gillard et al. (2012),²⁸ who used an algorithm to convert migraine-specific questionnaire (MSQ) utility values to EuroQoL-5D (EQ-5D) from the International Burden of Migraine Study. The utilities for episodic and chronic migraines were 0.670 and 0.450, respectively.

Productivity impacts

Productivity indices represent relative impairment in productivity, and range from 0 (completely unproductive) to 1 (completely productive). The productivity index for those without migraine were based on the mean absent days (8.8 days) per year (due to any reason) in the general Australian population,²⁹ and the average number of working days lost per employee per year in Australia due to presenteeism (6.5 days).³⁰ Productivity indices for episodic and chronic migraines were based on the mean lost days due to any reason for those with low (<10 headache days in past three months), moderate (10-29 days), high (30-44 days), and chronic migraine (≥ 45 days), as reported by Stewart et al.³¹ The mean absenteeism (time spent away from work) and presenteeism (lost productive time while at work) in terms of hours per week were used to determine the mean days lost per year. Episodic migraine included all those experiencing <45 mean headache days in the past three months (low, moderate and high categories). The weighted average days lost per year to absenteeism and presenteeism due to any reason in those with episodic migraine were 9.0 and 19.3, respectively, equating to 28.3 lost productive days in total. The equivalent values for those with chronic migraine were 11.4, 34.2 and 45.6 days. Assuming full-time workers work 48 weeks a year (52 weeks minus four weeks annual leave) and five days a week (a total of 240 days), the productivity indices for those without migraine, and with episodic and chronic migraine were 0.94, 0.88 and 0.81, respectively. Details regarding the estimation of lost work days and productivity indices are included in Supplementary Appendix 4.

Direct healthcare costs

Direct healthcare costs were drawn from the Australian Institute of Health and Welfare's report entitled 'Disease expenditure in Australia, 2015-16'.³² This tabled the total (Australia-wide) costs of allied health services, general practitioner services, medical imaging, pathology, drugs and specialised services (outpatient, inpatient emergency department and community-based) for all people with migraine, stratified by sex and five-year age-groups. To estimate the per person cost for those with chronic and episodic migraine, the following formulae were employed:

Per person cost of episodic migraine =

$$\frac{\text{Total cost of migraine}}{\text{Prevalence of episodic migraine}}$$

Pricing ratio x prevalence of chronic migraine + (1 – prevalence of chronic migraine)

Per person cost of chronic migraine = per person cost of episodic migraine x pricing ratio

The total annual costs of healthcare for patients with chronic and episodic migraine in the UK reported by Bloudek et al (€3718.44 and €866.56, respectively) were used to determine the ratio of costs for chronic to episodic migraine.³³ A pricing ratio of 4.29 was applied to estimate the weighted costs for those with chronic and episodic migraine in Australia, as described above.

Healthcare costs were inflated to 2018-19 values using the Australian health price index.³⁴

Productivity costs

In 2018-19, the total gross domestic product (GDP) in Australia was AU\$1,886,576 million.³⁵ The estimated number of equivalent full-time (EFT) Australian workers, determined from Australian employment statistics, was 10,516,116 (Supplementary Appendix 5).³⁶ To estimate the cost of lost productivity, we ascribed a financial value to the PALY in terms of cost per EFT worker. Therefore, the estimated cost of each PALY was AU\$177,092. This value was maintained across the model time horizon.

Discounting

All outcomes and costs were discounted by 5% per annum, in line with Australian recommendations.³⁷

Sensitivity and scenario analyses

Deterministic sensitivity analyses were undertaken to determine the impact of uncertainty surrounding productivity impacts, costs and utilities. Specific variation of other parameters is included in Table 1. In addition, a number of scenario analyses were undertaken to explore model assumptions: applying only absenteeism impacts, reducing the time horizon to five years, reducing the annual discount rate 3.5% and 0%, altering the value of the PALY with each year according to trends in GDP,³⁸ and employing migraine prevalence rates from the Global Burden of Disease (GBD) study as per the Deloitte Access Economics whitepaper.¹¹ Finally, we explored the impact of reducing the prevalence of migraine by 10% and 50%, and the possibility of treating those with chronic migraine so that they become episodic migraineurs. We also investigated a 15% increased risk of all-cause mortality associated with migraine.³⁹ Estimation of death rates in people with and without migraine are included in Supplementary Appendix 6.

A probabilistic sensitivity analysis (PSA) was performed to assess uncertainty surrounding key input parameters simultaneously. The PSA consisted of a second order Monte Carlo simulation with 10,000 iterations. The key input parameters, variation and distributions are included in Table 1.

The model was developed in Microsoft Excel, with the PSA performed using the Microsoft Excel add-in, @Risk (Palisade, 2020).

Results

In 2019, there were an estimated 1,175,941 people with episodic migraine and 98,378 with chronic migraine in Australia. Of those with episodic migraine, 62.4% were female, while for those with chronic migraine, 69.2% were female. In that year, our model estimated that migraine led to 317,819 QALYs lost (0.25 per person affected), 47,963 PALYs lost (0.03 per person) and AU\$8.49 billion (AU\$6,665 per person) in GDP lost.

With simulated ten-year follow-up of Australians currently aged 20 to 64 years, and assuming currently-observed prevalence of migraine, the cohort was estimated to live 121,046,340 (discounted) years of life (9,038,644 among people with episodic migraine and 1,204,702 among people with chronic migraine), 106,291,968 (discounted) QALYs (6,055,891 among people with

episodic migraine and 542,116 among people with chronic migraine) and 72,306,559 (discounted) PALYs (4,778,707 among people with episodic migraine and 582,029 among people with episodic migraine). Sex-specific results for people with and without migraine are included in Table 2.

Assuming that migraine did not exist, the same cohort would live 121,046,340 years, 108,869,751 QALYs and 72,691,299 PALYs (all discounted), equating to zero years of life gained, 2,577,783 QALYs gained (2.02 per person with migraine) and 384,740 PALYs gained (0.30 per person with migraine) over ten years. Sex-specific results are included in Table 2.

In terms of economic gains, there would be savings of \$68.13 billion (discounted) in terms of GDP (due to increased productivity), and \$1.67 billion (discounted) in direct healthcare costs. Thus, the net societal benefits over ten years would amount to \$69.81 billion (discounted), equivalent to \$54,780 per person with migraine. Results by for those with and without migraine, and by type of migraine, are presented in the Supplementary Appendix 7.

Sensitivity and scenario analyses are included in Table 3. Results were most sensitive to utility and cost inputs, but not in terms of PALYs. Compared to the base case, applying the lower and upper bounds of utility inputs resulted in a 42.0% decrease and 36.4% increase in QALYs, respectively. In scenario analyses, reducing the discount rate to 3.5% and 0% resulted in a 6.1% and 22.9% increase in PALYs, respectively. Applying only absenteeism estimates, resulted in a 96.8% reduction in PALYs and associated costs. Adjusting the risk of death by the increased risk of mortality associated with migraine, resulted in a 1.4% increase in PALYs. Reducing the prevalence of migraines by 10% and 50% resulted in GDP gains of AU\$6.81 billion and AU\$34.06 billion, respectively. Finally, if all those with chronic migraine were managed so that they became episodic migraineurs, there would be a 12.9% reduction in PALYs, resulting in estimated savings in GDP of AU\$8.76 billion over the ten years.

The PSA demonstrated that savings would range between \$44.42 and \$98.25 billion (discounted) in terms of GDP (due to increased productivity), and \$1.16 and \$2.37 billion (discounted) in direct healthcare costs. Thus, the net societal benefits over ten years would range between \$46.02 and \$99.93 billion (discounted), or \$36,116 and \$78,421 per person with migraine, respectively. More detailed results on the relative gains from the PSA are included in Supplementary Appendix 8.

Discussion

Our study highlights the substantial health and economic burden of migraines in Australia, notable for its higher relative impact on people of working age. While migraines affect more females at a population level, the individual impact is greater on affected males (1.99 QALYs lost per woman and 2.10 QALYs lost per man; 0.26 PALYs lost per woman and 0.40 PALYs lost per man). These differences reflect sex differentials in background utility and employment.

Our model estimated that in 2019, migraine led to over AU\$8.4 billion lost in GDP. This estimate is in keeping with a recent report by Deloitte Access Economics, which estimated that the productivity cost of migraines in Australia was AU\$16.3 billion in 2018.¹¹ Our estimates were lower because we limited our analysis to Australians aged 20-64 years and we used lower prevalence estimates for migraine (17.7% versus 8.5%). However, in a scenario analysis that employed prevalence of migraine from the 2016 GBD study, as per Deloitte Access Economics, our estimate increased to \$25.2 billion in lost GDP. These differences are likely attributable to the costing approach, whereby the Deloitte Access Economics analysis adopted a human capital approach to quantify costs, based on average weekly earnings, while our study estimated costs in terms of GDP per EFT.

Studies from other countries have also pointed to the considerable burden of migraines. A retrospective questionnaire of 630 people in Sweden showed that 76.2% and 17.9% of participants undertook short- and long-term leave during the year due to migraine, respectively, while 89% reported working an average of 30 days while sick in a year.¹³ This resulted in a loss of €21,782 and 0.25 QALYs per person per year among those with chronic migraine, and €7598 and 0.06 QALYs among those with episodic migraine. Of costs, 80% were due to productivity losses and 20% were due to healthcare costs.¹³ A Brazilian study found there was a total toll of R\$37.5 billion annually to the workforce due to migraine, R\$22.4 billion due to absenteeism and R\$15.1 due to presenteeism.¹² A prospective web-based survey involving 509 full-time US workers with episodic migraines (mean three attacks per person) demonstrated that 68% of migraine attacks impacted on work productivity.⁴⁰ It is estimated that 28% of these migraines caused absenteeism (with 1169 hours lost in total), and 62% of these migraines caused presenteeism (1470 hours lost or 1% of total lost productivity).

While the findings of the above studies are not comparable to those of our study, the conclusions are shared - that migraines impose a substantial productivity burden on people affected, and on society at large. Hence investments to reduce the prevalence of migraine and/or its impact on people with migraine offer good potential return. This is further strengthened by our PSA that demonstrated that despite the variability in key model input parameters, the benefits are considerable.

Acute treatments for migraines comprise 'simple' analgesics (such as paracetamol and non-steroidal anti-inflammatory drugs), triptans and anti-emetics. Prophylactic agents include antihypertensives (beta-blockers), antidepressants (amitriptyline), anti-epileptics (sodium valproate, topiramate), ergots (methysergide) and botulinum toxin, but less than 50% of patients report that currently-available prophylactic agents reduce the frequency of migraine attacks by more than 50%.⁴¹

However, novel therapies are emerging. There are two main classes of calcitonin gene-related peptides (CGRP) antagonists: gepants and monoclonal antibodies. Gepants are small molecule CGRP receptor antagonists, of which telcagepant has been the most studied.⁴² Although a study that found there was relief from acute pain with telcagepant compared to placebo, there are concerns regarding hepatotoxicity when the drug is used prophylactically at 140mg or 280mg twice daily.⁴³

CGRP monoclonal antibodies are large molecule antagonists that bind to the CGRP ligands or receptors. A double-blinded randomised controlled trial demonstrated decreased frequency of migraines and increased work productivity in those who used erenumab compared to placebo.⁴⁴ In Australia, three CGRP monoclonal antibodies, erenumab, galcanezumab and fremanezumab, have been approved by the Therapeutic Goods Administration, but none are yet available on the Pharmaceutical Benefits Scheme, which subsidises the costs of drugs for Australians. As such, these expensive drugs (AU\$750 to \$850 per month for private prescriptions of erenumab)⁴⁵ are not accessible to many Australians with migraine. A recent cost-effectiveness analysis of erenumab in the US demonstrated that, at an annual acquisition cost of US\$6900, erenumab is likely to be cost-effective from a payers perspective in those with chronic migraine (with incremental cost-effectiveness ratios of US\$23,079 compared to no preventive treatment and US\$65,720 compared

to onabotulinumtoxinA). It is, however, less likely to be cost-effective in those with episodic migraine.⁴⁶

There are several limitations to our study that warrant mention. First, we did not include new (incident) cases of migraine, and only considered prevalent cases. Prevalence of migraine was determined from Australian self-report data from the National Health Survey. These estimates are lower than those reported in the recent migraine report by Deloitte (whose prevalence data were drawn from the 2016 GBD study). A scenario analysis employing prevalence of migraine from the 2016 GBD study demonstrated that the estimated number of QALYs and PALYs saved were 200% greater than the base case, and therefore the number of people affected by migraine may be conservative in our analysis. In addition, the age- and sex-specific ratios of chronic to episodic migraine were drawn from a US study, which may not reflect the ratios among the Australian population.

Second, while we did consider movement between episodic and chronic migraine, we assumed that individuals remained in their migraine classification for the duration of the cycle. However, the Chronic Migraine Epidemiology and Outcomes (CaMEO) Study demonstrated a high degree of short-term variability in headache days per month. That is, over the course of fifteen months, there were frequent transitions between episodic and chronic migraine at three-month intervals, with substantial in-person variation.⁴⁷ This has implications for diagnosis and classification of migraine, however in clinical practice, migraine diagnosis is often assumed to remain stable.

Third, chronic and episodic migraine specific costs were not available in Australia. As such, we used the ratio of chronic to episodic costs from the UK to determine specific costs, which may not be applicable to the Australian setting.

Fourth, utilities associated with chronic and episodic migraine were sourced from the International Burden of Migraine Study (IBMS), a cross-sectional web-based observational study. The IBMS included participants from Australia, the US, Canada, Germany, the UK, France, Spain, Italy, Taiwan and Brazil.

Fifth, we assumed no increased risk of all-cause mortality associated with migraine, as per a recent systematic review and several other studies.³⁻⁶ However, Gudmundsson et al demonstrated that compared to those with no headache, people with any migraine were at a significantly increased risk of all-cause mortality (hazard ratio (HR) 1.15, 95% confidence interval (CI) 1.08 to 1.23).³⁹ People with migraine with aura have been reported to have a further increased risk of all-cause mortality (HR 1.21, 95% CI 1.12 to 1.30) as well as an increased risk of cardiovascular outcomes, predominantly due to stroke. Because the evidence is inconclusive, to err on the side of conservatism, excess mortality due to migraine was not assumed. Nonetheless, a scenario analysis was undertaken which applied an increased risk of mortality associated with any migraine, and the results were only minimally altered.

Last, we were unable to assess labour force drop-out/unemployment due to migraine due to a paucity of available data, which may increase the productivity loss attributable to migraine and associated economic costs. In addition, those unemployed due to migraine may be on disability support payments, which were not captured in our model. All of the above would have led to our under-estimation of the financial burden of migraine.

Conclusion

Migraines affect almost 10% of the Australians of working age and impose a substantial health and economic burden on Australian society. Funding of interventions that reduce the prevalence of migraines and/or its effects are likely to provide sound return on investment.

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Table 1: Input parameters used in the model.

Parameter	Input	Variation	Distribution	Source
Transition probabilities				
Episodic: chronic	2.5%	$\pm 15\%$	Beta ($\alpha = 209, \beta = 8,219$)	Bigal et al
Chronic: episodic	13.1%	$\pm 15\%$	Beta ($\alpha = 100, \beta = 383$)	Manack et al
Utilities				
No migraine	See Supplementary Appendix 3		Uniform ^a	Hawthorne et al
Episodic migraine	0.670	95% CI (0.662 to 0.678)	Beta ($\alpha = 8,857, \beta = 4,362$)	Gillard et al
Chronic migraine	0.450	95% CI (0.405 to 0.495)	Beta ($\alpha = 209, \beta = 255$)	Gillard et al
Lost days due to migraine				
No migraine	15.3	$\pm 30\%$ (10.7 to 19.9)	Normal ^b	Australian Human Resources Institute; Medibank
Episodic migraine	28.3	95% CI (25.5 to 31.1)	Normal ^b	Stewart et al
Chronic migraine	45.6	95% CI (36.5 to 54.7)	Normal ^b	Stewart et al
Costs				

Annual direct healthcare ^{c, d}				
Episodic migraine	\$79 - 393	±30%	Gamma	ABS
Chronic migraine	\$384 - 1685	±30%	Gamma	ABS
Per PALY	\$177,092	±30%	Uniform	ABS

- a. A uniform distribution was applied to the utilities for no migraine using the median and interquartile range.
- b. A normal distribution was applied using the mean and standard error. For no migraine, the standard error was not provided. Standard error was estimated using the upper and lower bounds (±30% variation).
- c. The annual direct healthcare costs for episodic and chronic migraine are age-group and sex-specific and fall within the ranges specified.
- d. A gamma distribution was applied to healthcare costs assuming that the variance (standard error) is equal to the mean.

Table 2: QALYs, PALYs and costs for the current Australian working-age population (with and without migraine), over the next ten years, and assuming migraine does not exist, and the relative gains.

	Cohort including migraine	Cohort assuming migraine does not exist	Total gains if migraine did not exist	Gains per person with migraine
QALYS				
Men	53,519,645	54,265,009	745,364	2.10
Women	52,772,323	54,604,742	1,832,419	1.99
Total	106,291,968	108,869,751	2,577,783	2.02
PALYs				
Men	43,024,222	43,165,545	141,323	0.40
Women	29,282,337	29,525,753	243,416	0.26
Total	72,306,559	72,691,299	384,740	0.30
Direct healthcare costs				
Men	-\$522,081,746	\$0	-\$522,081,746	-\$1,472
Women	-\$1,151,158,514	\$0	-\$1,151,158,514	-\$1,252
Total	-\$1,673,240,260	\$0	-\$1,673,240,260	-\$1,313
Productivity costs				
Men	\$7,619,265,534,123	\$7,644,292,848,501	\$25,027,314,378	\$70,554
Women	\$5,185,681,279,454	\$5,228,788,450,916	\$43,107,171,462	\$46,876
Total	\$12,804,946,813,577	\$12,873,081,299,417	\$68,134,485,840	\$53,467
Net societal costs				
Men			\$25,549,396,125	\$72,026
Women			\$44,258,329,975	\$48,128
Total			\$69,807,726,100	\$54,780

PALYs: productivity-adjusted life years; QALYs: quality-adjusted life years.

All costs are reported in 2018-19 Australian dollars (AU\$). All outcomes were subject to an annual discount rate of 5%.

Table 3: Sensitivity and scenario analyses

	QALYs				PALYs			
	Gains if migraine did not exist	% change in compared to base case	Direct healthcare costs (\$, billion)	Healthcare cost savings per person with migraine	Gains if migraine did not exist	% change in compared to base case	Productivity costs in terms of GDP (\$, billion)	GDP savings per person with migraine
Base case	2,577,783		\$1.67	\$1,313	384,740		\$68.13	\$53,467
Transition probabilities lower bound*	2,568,412	-0.36	\$1.67	\$1,300	382,919	-0.47	\$67.81	\$53,214
Transition probabilities lower bound*	2,586,091	+0.32	\$1.69	\$1,324	386,357	+4.2	\$68.42	\$53,692
Productivity indices lower bound**	2,577,783	-	\$1.67	\$1,313	411,476	+7.0	\$72.87	\$57,183
Productivity indices upper bound**	2,577,783	-	\$1.67	\$1,313	358,003	-7.0	\$63.40	\$49,752
Utilities lower bound†	1,494,921	- 42.0	\$1.67	\$1,313	384,740	-	\$68.13	\$53,467
Utilities upper bound†	3,515,858	+36.4	\$1.67	\$1,313	384,740	-	\$68.13	\$53,467

Healthcare costs lower bound‡	2,577,783	-	\$1.17	\$919	384,740	-	\$68.13	\$53,467
Healthcare costs upper bound‡	2,577,783	-	\$2.17	\$1,707	384,740	-	\$68.13	\$53,467
GDP per PALY lower bound‡	2,577,783	-	\$1.67	\$1,313	384,740	-	\$47.69	\$37,427
GDP per PALY upper bound‡	2,577,783	-	\$1.67	\$1,313	384,740	-	\$88.57	\$69,508
Absenteeism only	2,577,783	-	\$1.67	\$1,313	12,520	-96.8	\$2.22	\$1,740
5 year time horizon	1,451,524	-43.7	\$0.87	\$680	218,901	-43.1	\$38.77	\$30,421
Discounting of 3.5%	2,735,888	+6.1	\$1.78	\$1,400	408,058	+6.1	\$72.26	\$56,708
Discounting of 0%	3,176,007	+23.2	\$2.09	\$1,644	472,891	+22.9	\$83.75	\$65,718
Temporal trend in GDP	2,577,783	-	\$1.67	\$1,313	384,740	-	\$71.24	\$55,905
Prevalence of migraine reduced by 10%	2,320,005	-10.0	\$1.51	\$1182	346,266	-10.0	\$61.32	\$48,121
Prevalence of migraine reduced by 50%	1,288,892	-50.0	\$0.84	\$657	192,370	-50.0	\$34.07	\$26,734
Only episodic migraineurs	2,323,536	-10.0	\$1.22	\$955	335,242	-12.9	\$59.37	\$46,589
GBD prevalence of	7,747,501	+200.0	\$1.71	\$450	1,155,555	+200.0	\$204.64	\$53,929

migraine								
Mortality associated with migraine	2,586,366	+0.3	\$1.67	\$1,311	390,058	+1.4	\$69.08	\$54,206

GBD: global burden of disease; GDP: gross domestic product; PALYs: productivity-adjusted life years; QALYs: quality-adjusted life years.

All costs are reported in 2019-20 Australian dollars (AU\$). All outcomes were subject to an annual discount rate of 5%.

*Transition probabilities for the transition from episodic to chronic migraine, and chronic migraine to episodic migraine, were varied by 15%.

**Productivity indices were varied by altering the absent days lost. For episodic and chronic migraines, 95% confidence intervals were employed. For no migraines, a 30% variation was applied. Lower bound productivity indices for no migraines, episodic migraines and chronic migraines were 0.952, 0.870 and 0.772, respectively. The upper bound values were 0.974, 0.894 and 0.848, respectively.

†Utilities were varied using the interquartile range for the Australian general population norms, and 95% confidence intervals for those with episodic and chronic migraines.

‡Both healthcare costs and productivity costs (GDP per PALY) were varied by 30%.

Figure 1: Markov model demonstrating the possible health states and transitions in the model.

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