Healthcare expenditure and its predictors in a cohort of Australians living with sciatica

European Spine Journal (2021) 30:878–885
https://doi.org/10.1007/s00586-020-06605-2

ORIGINAL ARTICLE

Healthcare expenditure and its predictors in a cohort of Australians living with sciatica

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Received: 23 May 2020 / Revised: 3 September 2020 / Accepted: 12 September 2020 / Published online: 24 September 2020

Abstract

Purpose To estimate the healthcare resource utilisation of an Australian cohort of people with sciatica and explore individual-level factors associated with expenditure.

Methods Healthcare utilisation (services and medication) data from a randomised, double-blind, placebo-controlled trial of pregabalin in patients with sciatica ($n = 185$) were analysed to estimate healthcare expenditure of participants over 12 months. Associations between key baseline socio-economic, pain and quality of life characteristics and healthcare expenditure were examined using generalised linear imputation models.

Results On average, participants accessed AUD$1,134 of healthcare over the year, predominantly made up of $114 of medication and $914 of health services, which included $418 of physiotherapy services. Participants randomised to receive pregabalin incurred higher expenditure ($1,263 compared to $1,001 for placebo), which was largely driven by pregabalin ($158) and greater health services ($107). Healthcare expenditure was significantly higher for participants prescribed pregabalin, earning greater than $1,700 per week ($88,400 per year) and reporting poorer quality of life (physical and mental).

Conclusion Our results suggest inefficiency in the use of healthcare resources due to increased healthcare resource utilisation in people with sciatica treated with pregabalin, compared to placebo. Costs of treating sciatica varied based on individual quality of life and socio-economic characteristics.

Keywords Sciatica · Healthcare expenditure · Pregabalin · Cost predictors · Healthcare utilisation

Introduction

Sciatica (lumbosacral radicular syndrome) is characterised by radiating posterolateral leg pain that may be accompanied by back pain, sensory loss, weakness or reflex abnormalities [1]. 5–10% of the 4 million Australians who experience low-back pain (LBP) annually are estimated to have sciatica

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00586-020-06605-2) contains supplementary material, which is available to authorized users.

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[2]. Due to a lack of evidence of effective treatments for sciatica, clinical guidelines for sciatica have typically mirrored those for non-specific LBP; a stepped model of treatment: education, physiotherapy, pharmacological and surgical interventions. While acknowledging a limited evidence-base, the National Institute for Health and Care Excellence (NICE) 2017 guidelines recommend additional interventions for sciatica including epidural injections, neuropathic pain pharmacotherapy and spinal decompression [3].

Limited data exist on the type or level of care people living with sciatica receive in Australia or globally, though economic evaluations of interventions for sciatica suggest a substantial level of healthcare resources are utilised [4]. A British prospective cohort study of patients with leg pain seeking general practitioner (GP) care between 2011 and 2013 found higher National Healthcare Service (NHS) costs for patients with sciatica relative to somatic leg pain, due to more GP visits, investigations, prescriptions and specialist services [5]. Reduced societal costs were predicted by better general patient health and 3 or more physiotherapy sessions [5].

In line with NICE guidelines, neuropathic pain pharmacotherapy has been increasingly used to treat sciatica. Pregabalin, for example, has seen dramatic increases in sales in Australia (subsidised through the Australian Pharmaceutical Benefits Scheme (PBS) since 2012) and other high-income nations some of which has been used to treat sciatica (though the actual proportion is unknown) [6–8]. Recent evidence, however, has cast doubt on the clinical appropriateness of using pregabalin to treat sciatica. A double blind, randomised, placebo-controlled trial (PRECISE trial), found no benefit across numerous outcomes for people with sciatica receiving pregabalin but increased adverse events in the intervention group [9]. This aligns with other evidence finding associations between pregabalin use and an increased risk of intentional self-poisonings and ambulance attendances as well as adverse events including weight gain, peripheral oedema, visual disturbances and ataxia [6, 10, 11].

Given the lack of evidence for effective treatments and the substantial patient population with sciatica, it is important to understand their care patterns to inform service design and resource allocation decisions. This paper seeks to fill this knowledge gap through an analysis of individual-level data collected in the PRECISE trial. Our aim is to identify the level of healthcare resources devoted to treating a patient cohort with current sciatica in Australia and analyse how costs vary across key baseline socio-economic, pain and quality of life characteristics.

We hypothesise that people with sciatica taking pregabalin incur greater costs than those who do not and their healthcare costs vary according to individual clinical and socio-economic characteristics.

Methods

Participants

Data were collected during the PRECISE trial, a double-blinded randomised placebo-controlled trial that investigated the effectiveness of pregabalin in addition to usual care relative to placebo over a one-year follow-up [9, 12, 13]. Participants were patients presenting with current moderate to severe sciatica present for at least one week and at most one year, to outpatient services (e.g. GPs) in New South Wales, Australia. Sciatica was defined as pain radiating into one leg below the knee, accompanied by nerve-root or spinal-nerve involvement as indicated by the presence of at least one of the following clinical features: dermatomal leg pain, myotomal weakness, sensory deficits or diminished reflexes. Participants were excluded if: known or suspected serious spine pathology, considering spine interventions, was unable to cease medication for neuropathic pain, epilepsy, depression or sedation, severe depression or suicidal thoughts, pregnant or planning conception. More details on selection of participants, consent and trial methodology, have been published elsewhere [12, 13]. One hundred eighty-five participants were included in this analysis (89% of the original trial population), excluding individuals who had taken excluded medications post-randomisation (to remove potential confounders), had withdrawn and with completely missing expenditure data (to reduce imprecision from lack of data to impute on).

The Australian health system

The Australian health system is financed by a combination of government (State and Federal), private health insurance and out-of-pocket patient contributions. Primary GP care services are heavily subsidised for Australians by the Federal government through its Medicare programme, while hospital services are predominantly public, free at the point of delivery and run and funded by state governments. Pharmaceuticals are largely funded by the federal government's universal medicines access scheme (PBS) with most patients (aside from targeted groups, e.g. Aboriginal and Torres Strait Islander Australians) required to pay a co-payment for each medicine.

Outcomes

The annual health expenditure of each patient was the dependent outcome variable, calculated by summing health services and medication expenditure over one year. This included costs borne by patients and the public health

system. An intention to treat approach analysed placebo patients who took pregabalin prescribed by external health providers (e.g. GP) in the non-intervention group. The Australian Bureau of Statistics health consumer price index [14] was used to inflate service costs incurred in earlier years to 2016 Australian dollars ($1 AUD = $0.74 USD = €0.67 Euro = £0.56 lb [15]).

Service and medication use

Health service use data related to sciatica over a one-year period included GP consultations, hospitalisations, physiotherapy, imaging, surgical or interventional procedures, medical specialist consultations and other services (e.g. meal delivery). Medications prescribed over the year were categorised into non-steroidal anti-inflammatory (NSAID) drugs (e.g. ibuprofen), simple analgesics (e.g. paracetamol), opioid combinations (e.g. paracetamol and codeine), strong opioid analgesics (e.g. oxycodone) and other (e.g. amitriptyline). Health services were costed based on Australian government estimates where possible. Specifically, Medicare Benefits Schedule (MBS) items were used to cost applicable health services, Comcare estimates for allied health services and medications using PBS data (sources and costs described in Online Resource 1). Participants were randomly assigned to receive either pregabalin (75 mg capsules) at a starting dose of 150 mg per day, adjusted to a maximum dose of 600 mg per day or matching placebo prescribed for up to 8 weeks. Placebo drugs were assigned a zero cost to reflect the counterfactual where patients with sciatica are treated without pregabalin. The data were collected at weeks 4, 12, 26 and 52 with patients self-reporting their service and medication use over the preceding period in interviews.

Statistical analysis

Healthcare utilisation was analysed through a descriptive comparison of healthcare expenditure between intervention and placebo groups including a components analysis of health services and medication (pregabalin considered separately) expenditure. Two-sample *t* tests were conducted for selected demographic variables regardless of intervention group. A relatively large proportion of participants (64%) failed to record at least one input of service and medication use data (weeks 4, 12, 26, 52). While each expenditure input had only 16–21% missing observations, complete case analysis (CCA) would significantly reduce sample size (by 40%), precision, power and would bias estimates [16]. Hence, a multiple imputation (MI) approach was undertaken in line with published guidelines [16, 17]. Forty imputations were made to match the percentage of incomplete cases [17], using a predictive mean matching algorithm to impute missing expenditure data at the same frequency as the original data collected (weeks 4, 12, 26, 52), as the types of resource use had similar patterns of missing data at that level [18]. All baseline variables and outcomes were included in the imputation model. Sensitivity analysis regressing missingness on all variables suggested data was missing at random once controlling for age.

Associations between key baseline variables (socioeconomic, pain and quality of life) and annual healthcare expenditure were analysed using regression techniques. Specifically, variables examined: age, sex, income, employment, insurance status, occupation, whether the leg pain was compensable, history of leg pain (days), leg and back pain measured by the Numeric Pain-Rating Scale (NPRS), level of disability measured by the Roland Disability Questionnaire (RDQ) for Sciatica, likelihood of neuropathic pain measured by the pain detect score (PDQ), current pain relative to onset measured by the global perceived effect score (GPE) and quality of life measured by the SF-12-v2 absolute scores (physical and mental). These variables were chosen to cover multidimensional aspects of functionality in disease states. A generalised linear model (GLM) model with gamma distribution and log link was used for right-skewed expenditure data; an approach also established in the only previous analysis of patient costs related to sciatica [5, 19]. Results were reported using coefficients and confidence intervals. All analyses were performed using Stata 16.1 (StataCorp).

Trial registration

The PRECISE study was registered with the Australian and New Zealand Clinical Trials Registry (ACTRN12613000530729) and ethics approval was obtained from the University of Sydney Human Research Ethics Committee (15,333).

Results

Table 1 summarises baseline characteristics of this cohort by trial arm. There were slight differences across the groups with a statistically significant higher proportion of females receiving the pregabalin intervention. These potential confounders were controlled for in regression analyses.

Healthcare expenditure of participants is summarised in Fig. 1 and Table 2. Figure 1 shows average expenditure by segment (total, health services and medication) and Table 2 summarises average total expenditure according to baseline demographic characteristics. On average patients accessed $1,134 of healthcare over the year, predominantly health services ($941, including $418 of physiotherapy services) and medication expenditure ($114). Average expenditure was higher for patients receiving pregabalin with an average cost of $1263 (versus $1001 for control), with the difference

Table 1 Baseline characteristics excluding individuals who took excluded medications at baseline, with completely missing expenditure data and withdrawn participants ($n = 185$)

Factor	Pregabalin treatment ($n = 94$)	Placebo treatment ($n = 91$)	p value[g]
Female, no. (%)	60 (64%)	45 (49%)	0.05
Age, mean (SD)	53.3 (17.3)	55.0 (16.1)	0.50
Paid employment no. (%)	46 (49%)	45 (49%)	0.94
Income groups $[a]/wk ($/yr)			0.37
No income	3 (3%)	7 (8%)	
$1–$649 ($1–$33,799)	38 (40%)	34 (37%)	
$650–$1,699 ($33,800–$88,399)	28 (30%)	25 (27%)	
$1,700 or more ($88,400 or more)	8 (9%)	14 (15%)	
Chose not to answer	17 (18%)	11 (12%)	
Insurance status no. (%)			0.15
No insurance	41 (44%)	53 (58%)	
Department of Veteran's Affairs (DVA) insurance	1 (1%)	1 (1%)	
Private hospital only	6 (6%)	8 (9%)	
Private ancillary (extras) only	4 (4%)	6 (7%)	
Private hospital and ancillary (extras)	40 (43%)	21 (23%)	
Chose not to answer	2 (2%)	2 (2%)	
Compensable sciatica no. (%)	1 (1%)	4 (4%)	0.16
Duration of leg pain (days), mean (SD)	62.1 (71.7)	60.0 (74.7)	0.84
Leg-pain intensity score[b], mean (SD)	6.3 (1.8)	6.1 (1.8)	0.45
Back-pain intensity score[b], mean (SD)	5.8 (2.7)	5.2 (2.9)	0.16
Extent of disability score[c], mean (SD)	14.7 (4.9)	15.3 (4.5)	0.40
Global perceived effect score[d] (score), mean (SD)	-0.7 (2.2)	-1.0 (2.4)	0.32
Physical quality of life absolute score[e], mean (SD)	36.4 (9.6)	36.4 (9.7)	1.00
Mental quality of life absolute score[e], mean (SD)	47.8 (11.6)	46.6 (12.3)	0.48
PainDETECT score[f], mean (SD)	14.7 (6.9)	13.8 (6.2)	0.39

[a]2016 AUD, ($1 AUD = $0.74 USD = €0.67 Euro = £0.56 lb) [22]

[b]Leg-pain intensity and back-pain intensity were measured by means of the Numeric Pain-Rating Scale (NPRS), whereby patients were asked to rate their average pain over the previous 24 h on a scale from 0 to 10, with 0 indicating no pain, and 10 indicating the worst possible pain

[c]Disability was measured by means of the Roland Disability Questionnaire (RDQ) for Sciatica (scores range from 0 to 23, with higher scores indicating greater disability)

[d]For the assessment of global perceived effect (GPE), patients were asked to compare their current leg pain to the pain they had when this episode first started, as measured on a Likert scale; scores range from − 5 (vastly worse) to 0 (unchanged) to + 5 (completely recovered)

[e]Quality of life was measured by means of the Short Form Health Survey 12, version 2, questionnaire (scores on the physical and mental components of the questionnaire range from 0 to 100, with higher scores indicating a better quality of life)

[f]Pain DETECT questionnaire scores range from − 1 to 38: a score of 12 or less indicated a neurologic component was unlikely, a score of 13–18 that the status of a neurologic component was unclear, and a score of 19 or more that a neurologic component was likely

[g]Two tailed T test for difference of means for numerical variables and Chi-squared test for categorical variables

largely due to the cost of pregabalin (difference of $158) and higher health services costs (difference of $107). Patients in the highest income category ($88,400 or more per year) had higher average expenditure ($2,203 as opposed to $1,020; t test for difference of means less than 0.05).

Table 3 summarises the results of multivariate regression modelling after multiple imputation. A coefficient greater than zero indicates that a variable has a positive association with increased expenditure; a negative coefficient indicates decreased expenditure (controlling for all variables included). Total healthcare expenditure was significantly associated with patient income, randomisation group and quality of life scores (mental and physical). Patients earning $1,700 or more per week ($88,400 or more per year) and in the pregabalin intervention group were predicted to incur significantly greater expenditure. Higher SF-12 physical and

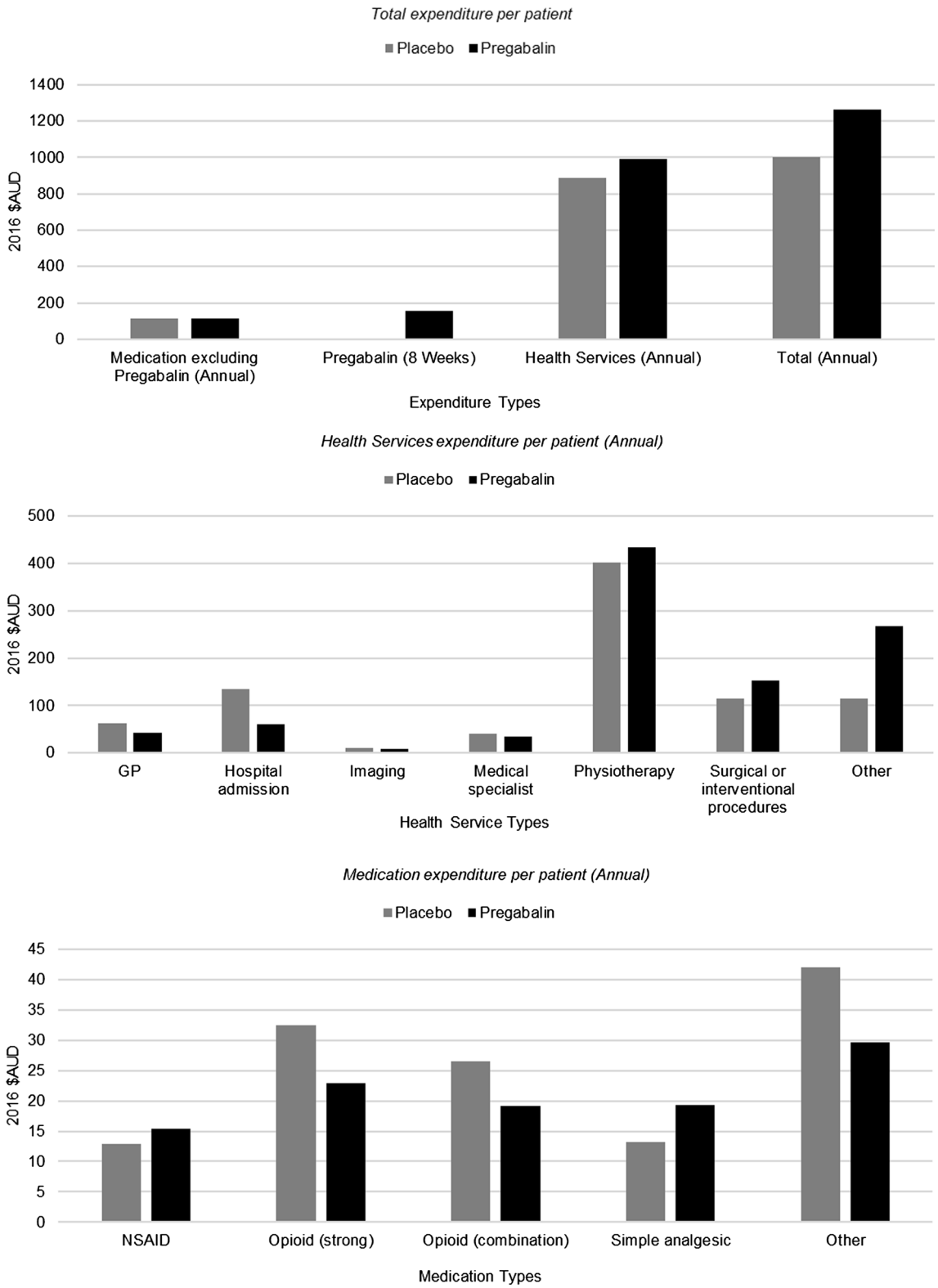

Fig. 1 Breakdown of participant expenditure

Table 2 Average total healthcare expenditure (per patient) for different demographic variables ($n = 185$)

Demographic variable	Breakdown	Average annual total healthcare expenditure (2016 AUD)	Standard deviation	2 tailed *T* test (*p* value)
N/A	Cohort	1,134	2,051	N/A
Gender	Male	1,169	2,121	0.84
	Female	1,107	2,006	
Paid employment	Employed	1,096	1,981	0.80
	Unemployed	1,173	2,132	
Age	Age < 65 years	1,211	2,191	0.45
	Age ≥ 65 years	965	1,711	
Insurance status	Not insured	1,006	1,970	0.35
	Insured	1,295	2,139	
Income level	Income < $1,700 per week ($88,400 per year)	1,020	1,711	0.02
	Income ≥ $1,700 per week ($88,400 per year)	2,203	3,594	
Compensable	Not compensable	1106	2,044	0.27
	Compensable	2134	2,303	
Intervention		1,001	2,289	0.39
	Pregabalin	1,263	1,795	

mental scores (i.e. better physical and mental quality of life) were associated with significantly lower expenditure.

Discussion

Australian patients with sciatica received services and medications worth an average of $1,134 over the year, though this varied according to socio-economic and quality of life characteristics. Specifically, a patient's income (earning $88,400 or more per year), quality of life (physical and mental) and receiving pregabalin significantly influenced overall healthcare expenditure. While no absolute pain indicators significantly explained variation in cost, improved quality of life measures (physical and mental) at baseline reduced healthcare expenditure, indicating an economic rationale of managing patient expectations of pain; and supporting patients to live with chronic pain.

Patients prescribed pregabalin had higher health costs than placebo patients. In the PRECISE trial, there was no benefit found for prescribing pregabalin but an increased risk of harms [9]; our analysis builds on this by demonstrating increased healthcare costs above pregabalin itself. Taken together, these results indicate inefficient use of healthcare resources that could be more effectively directed to other care options.

In our cohort there was no significant relationship between healthcare expenditure and age, gender, insurance, worker's compensation eligibility or pain intensity scoring. The significance of higher incomes ($88,400 or more per year) increasing healthcare expenditure is in line with other health economic studies demonstrating a general positive income elasticity effect [20]. The only previous study examining predictors of healthcare expenditure in patients with sciatica found none of their selected variables (SF-1 general health, RDQ and Hospital Anxiety and Depression Scale (HADS-D)) were predictive of healthcare costs [5]. The only common predictor with our study, the RDQ, was also not significant in our analysis. Notably however, they found that factors associated with quality of life outcomes included disability, pain intensity and depression, which may align with the significant SF-12 quality of life scores in our study. More generally, in LBP cohorts, cost predictors have included poor physical health, high functional disability, poor quality of life, high intensity of pain, comorbidities, opiates, NSAIDs and depression [21, 22]. While some of these factors were relevant to our study, further research is required to conclusively determine the differences in healthcare utilisation patterns and cost predictors in sciatica populations compared to LBP populations.

The health services expenditure of our cohort was largely driven by physiotherapy (44% of health services expenditure). While our costing methodology may have underestimated medication costs in particular (and thus overstated the relative portion of care attributed to physiotherapy), our findings reflect European studies of sciatica care patterns,

Table 3 Multivariable model: predictors of total healthcare expenditure ($n = 185$)

	Coef	95% Confidence interval (lower, upper)	p value
Age	−0.01	−0.03, 0.00	0.15
Female sex	−0.14	−0.64, 0.35	0.57
Income $/wk ($/yr)			
Chose not to answer	Reference group		
No income	1.12	−0.12, 2.35	0.08
$1–$649 ($1–$33,799)	0.41	−0.31, 1.14	0.26
$650–$1,699 ($33,800–$88,399)	0.41	−0.31, 1.13	0.26
$1,700 or more ($88,400 or more)	1.45**	0.55, 2.35	0
Pregabalin intervention	0.56*	0.09, 1.04	0.02
Employed	−0.33	−0.88, 0.21	0.23
Insurance			
Chose not to answer	Reference group		
No insurance	−0.3	−2.00, 1.40	0.73
DVA insurance	0.74	−1.99, 3.46	0.6
Private hospital only	0.17	−1.77, 2.10	0.87
Private ancillary (extras) only	0.35	−1.36, 2.05	0.69
Private hospital and ancillary (extras)	0.00	−1.94, 1.95	1
Compensable sciatica	1.18	−0.35, 2.71	0.13
Duration of leg pain (days)	0.00	−0.01, 0.00	0.32
NPRS leg pain score	0.09	−0.05, 0.24	0.21
NPRS back pain score	−0.07	−0.16, 0.01	0.09
Extent of disability score	0.05	−0.02, 0.11	0.18
Pain DETECT score	−0.03	−0.07, 0.01	0.13
Global perceived effect score	−0.11	−0.23, 0.01	0.07
SF-12 physical absolute score	−0.03*	−0.06, 0.00	0.03
SF-12 mental absolute score	−0.03*	−0.05, 0.00	0.02

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

where ~ 40–60% of primary care patients with sciatica were referred to physiotherapy in the Netherlands [23, 24] and 43% of NHS costs to treat patients with sciatica was related to physiotherapy [5]. Our findings also broadly align with the Paracetamol for Low-Back Pain Study (PACE) study, which evaluated the costs of taking paracetamol as part of first line care for acute LBP, finding no improvement in a range of outcomes, but increased healthcare costs by 30–50% over a 12-week period [25].

Limitations

There were a number of limitations to our work. First, while, to the best of our knowledge, this is the largest study examining the healthcare utilisation patterns of people living with sciatica in the Australian context, the relatively small sample size and subpopulations (e.g. only 5 individuals eligible for worker's compensation) restricted our inferences. Our study also analysed people with clinically diagnosed sciatica, meaning our study reflects the cost implications of treating sciatica in Australian clinical practice rather than sciatica confirmed by imaging. Second, incomplete cost data meant dependent outcome variables were imputed for 40% of included patients. Nonetheless, this was offset somewhat by the large number of cost observations (each cost input had only 16–21% missing observations). Further, the only variable associated with missing data was age, which was insignificant in regression analysis. Our analysis also focused on direct quantifiable costs and did not measure indirect costs due to sick leave or disability. Finally, health service data was self-reported. While patients were provided diaries to keep track of service use between interviews, this is subject to potential recall bias.

Conclusion

We have presented a detailed breakdown of the healthcare services accessed by a cohort of Australians with sciatica in normal clinical practice. People prescribed pregabalin, on higher incomes and with worse physical and mental quality

of life, were found to utilise a greater amount of healthcare services. In combination with recent findings demonstrating pregabalin to be no more effective than placebo in treating sciatica, our results highlight the inefficient use of healthcare resources associated with the use of pregabalin in the management of sciatica.

Funding This research was completed without funding. The original trial Pregabalin in Addition to Usual Care for Sciatica (PRECISE) was supported by a Grant (ID APP1042073) from the National Health and Medical Research Council of Australia with in-kind support from Pfizer Australia. Investigators of the PRECISE trial retained full autonomy over the design, conduct, analysis and reporting of the trial.

Compliance with ethical standards

Conflicts of interest AC, CL, SJ, JL, BK, RD, LB and BA declare no conflict of interest. CM received support from PHP International Pty Ltd for supply of heat wraps to a clinical trial; AM received support from GlaxoSmithKline Australia for a Ph.D. scholarship under his supervision. The authors confirm full control of all primary data and are happy for the journal to review if requested.

Availability of data and material The data sets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

References

1. Ropper AH, Zafonte RD (2015) Sciatica. New Engl J Med 372:1240–1248. https://doi.org/10.1056/NEJMra1410151
2. Australian institute of health and welfare (2019) Back pain and problems. In: Australian institute of health and welfare. https://www.aihw.gov.au/reports/chronic-musculoskeletal-conditions/back-problems/contents/what-are-back-problems. Accessed 30 January 2020
3. Bernstein IA, Malik Q, Carville S, Ward S (2017) Low back pain and sciatica: summary of NICE guidance. BMJ 356:6748–6761. https://doi.org/10.1136/bmj.i6748
4. Lewis R, Williams N, Matar HE et al (2011) The clinical effectiveness and cost effectiveness of management strategies for sciatica: systematic review and economic model. Health Technol Assess. https://doi.org/10.3310/hta15390
5. Kigozi J, Konstantinou K, Ogollah R et al (2019) Factors associated with costs and health outcomes in patients with back and leg pain in primary care: a prospective cohort analysis. BMC Health Serv Res 19:1–9. https://doi.org/10.1186/s12913-019-4257-0
6. Cairns R, Schaffer AL, Ryan N, Pearson SA, Buckley NA (2019) Rising pregabalin use and misuse in Australia: trends in utilization and intentional poisonings. Addiction 114:1026–1034. https://doi.org/10.1111/add.14412
7. Goodman CW, Brett AS (2017) Gabapentin and pregabalin for pain: is increased prescribing a cause for concern? New Engl J Med 377:411–414. https://doi.org/10.1056/NEJMp1704633
8. Urquhart L (2018) Top drugs and companies by sales in 2017. Nat Rev Drug Discov 17:232. https://doi.org/10.1038/nrd.2018.42
9. Mathieson S, Maher CG, McLachlan AJ et al (2017) Trial of pregabalin for acute and chronic sciatica. New Engl J Med 376:1111–1120. https://doi.org/10.1056/NEJMoa1614292
10. Crossin R, Scott D, Arunogiri S et al (2019) Pregabalin misuse-related ambulance attendances in Victoria, 2012–2017: characteristics of patients and attendances. Med J Aust 210:75–79. https://doi.org/10.5694/mja2.12036
11. Onakpoya IJ, Thomas ET, Lee JJ, Goldacre B, Heneghan CJ (2019) Benefits and harms of pregabalin in the management of neuropathic pain: a rapid review and meta-analysis of randomised clinical trials. BMJ Open 9:1–19. https://doi.org/10.1136/bmjopen-2018-023600
12. Mathieson S, Maher CG, McLachlan AJ et al (2013) PRECISE-pregabalin in addition to usual care for sciatica: study protocol for a randomised controlled trial. Trials 14:213. https://doi.org/10.1186/1745-6215-14-213
13. Mathieson S, Billot L, Maher CG et al (2016) PRECISE-pregabalin in addition to usual care: statistical analysis plan. Trials 17:53. https://doi.org/10.1186/s13063-016-1174-y
14. Australian Bureau of Statistics (2020) CPI: Group, Sub-group and expenditure class, Weighted Average of Eight Capital Cities. In: Australian Bureau of Statistics https://www.abs.gov.au/ausstats/meisubs.nsf/log?openagent&640105.xls&6401.0&Time%2520Series%2520Spreadsheet&FE59025F60645238CA25855800153F5B&0&March%25202020&29.04.2020&Latest. Accessed 30 January 2020
15. XE (2017) Current and historical rate tables. XE https://www.xe.com/currencytables/?from=AUD&date=2016-06-30. Accessed 30 January 2020
16. Pigott T (2001) A review of methods for missing data. Educ Res Eval 7:353–383. https://doi.org/10.1076/edre.7.4.353.8937
17. White IR, Royston P, Wood AM (2011) Multiple imputation using chained equations: issues and guidance for practice. Stat Med 30:377–399. https://doi.org/10.1002/sim.4067
18. Faria R, Gomes M, Epstein D, White IR (2014) A Guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials. PharmacoEconomics 32:1157–1170. https://doi.org/10.1007/s40273-014-0193-3
19. Mihaylova B, Briigs A, O'Hagan A, Thompson SG (2011) Review of statistical methods for analysing healthcare resources and costs. Health Econ 20:897–916. https://doi.org/10.1002/hec.1653
20. Ang J (2010) The determinants of health care expenditure in Australia. Appl Econ Lett 17:639–644. https://doi.org/10.1080/00036840802297868
21. Mutubuki E, Luitjens MA, Maas ET et al (2019) Predictive factors of high societal costs among chronic low back pain patients. Eur J Pain 24:325–337. https://doi.org/10.1002/ejp.1488
22. Becker A, Held H, Redaelli M et al (2010) Low back pain in primary care: costs of care and prediction of future health care utilization. Spine 35:1714–1720. https://doi.org/10.1097/brs.0b013e3181cd656f
23. Luijsterburg P, Verhagen AP, Braak S, Oemraw A, Avezaat CJ, Koes BW (2005) General practitioners' management of lumbosacral radicular syndrome compared with a clinical guideline. Eur J Gen Pract 11:113–118. https://doi.org/10.3109/13814780509178250
24. Spijker-Huiges A, Groenhof F, Winters JC et al (2015) Radiating low back pain in general practice: Incidence, prevalence, diagnosis, and long-term clinical course of illness. Scand J Prim Health Care 33:27–32. https://doi.org/10.3109/02813432.2015.1006462
25. Lin CC, Li Q, Williams CM et al (2018) The economic burden of guideline-recommended first line care for acute low back pain. Eur Spine J 27:109–116. https://doi.org/10.1007/s00586-016-4781-0