ECONOMIC EVALUATION OF THE NPS MEDICINEWISE PROGRAM: CHRONIC PAIN: OPIOIDS AND BEYOND (2015)

Cost-Benefit and Cost-Effectiveness Analysis Report

Independent, not-for-profit and evidence based, NPS MedicineWise enables better decisions about medicines and medical tests. NPS MedicineWise receives funding from the Australian Government Department of Health.

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Suggested citation

Economic evaluation of the NPS MedicineWise Program: Chronic Pain: Opioids and Beyond (2015). NPS MedicineWise. Sydney, September 2019.

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HIGHLIGHTS OF THE REPORT

The problem

- Chronic pain is a major health problem which is associated with significant consequences to patients, families and society. These include emotional, physical, social and financial impacts
- Approximately 20% of Australian adults report experiencing chronic pain
- There are significant safety and quality use of medicines (QUM) issues evident in the complex area of chronic non-cancer pain.

The intervention

- In 2015 NPS MedicineWise launched the '*Chronic pain: opioids and beyond visiting program'*
- This Program aimed to improve the management and well-being of patients with chronic non-cancer pain who are managed in general practice
- The Program was a national program with 7,346 general practitioners (GPs) participating in interactive interventions including 1-1 educational visits, small group case-based meetings, a clinical e-audit, and an interactive case study. A personalised Pharmaceutical Benefits Scheme (PBS) feedback report was sent to all practising GPs and online learning modules were available.

This report

- This report focuses on the impact and economic evaluation of the whole Program on opioids dispensed on the PBS and the management of patients with chronic non-cancer pain who attend general practice.
- The objective of this economic evaluation was to identify, in monetary terms, the costs and benefits of the national and interactive components of the Chronic Pain Program from the perspective of the payer, the Australian Government Department of Health.
- Two independent studies were conducted:
  - a cost-benefit and cost-effectiveness analysis at the population level using PBS data
  - a cost-benefit analysis of the interactive components of the Program at the GP practice level using data from the MedicineInsight program.

The results

- For the national Chronic Pain program:
  - The net benefit of program was $8,771,975
  - For every $1 spent on the program $3.67 was gained in monetary benefit to the payer, the Australian Government Department of Health.
  - The dispensing of one opioid prescription was averted per every $7.48 spent on the program
- For GPs who participated in interactive components of the program:
  - The net benefit of the program was $1,881.63 per intervention GP
  - For every $1 spent on the program $5.32 was gained in monetary benefit to the payer, the Australian Government Department of Health.

EXECUTIVE SUMMARY

Chronic pain is a major health problem which is associated with significant consequences to patients and families, increased costs of health care utilisation as well as societal costs related to lost work productivity. Approximately 20% of Australian adults report experiencing chronic pain. Living with chronic pain can have substantial emotional, physical, social and financial impacts on consumers and their carers or family members, and left untreated, can lead to significant human suffering.

In 2015 NPS MedicineWise launched the *Chronic pain: opioids and beyond visiting program*. NPS MedicineWise selected to run this program due to the safety and quality use of medicines (QUM) issues evident in the complex area of chronic non-cancer pain. The key QUM issues which informed the design of the program were: the increased prescribing of opioids in Australia despite limited evidence of benefit for chronic non-cancer pain; the potential for misuse and harm; and evidence of inadequate assessment, management, and monitoring of pain in general practice. The overarching goal of the Chronic Pain Program was to improve well-being in patients with chronic non-cancer pain who are managed in general practice. This economic evaluation focused on the program's impact on opioid use at a national level and on general practitioners (GPs) who actively participated in the interactive components of the Program, referred to as participating GPs.

The Chronic Pain Program was a national program with 7,346 GPs participating in interactive interventions including 1-1 educational visits, small group case-based meetings, a clinical e-audit, and an interactive case study. A personalised Pharmaceutical Benefits Scheme (PBS) feedback report was sent to all practising GPs and online learning modules were available.

The objective of this economic evaluation was to identify, in monetary terms, the costs and benefits of the national and interactive components of the Chronic Pain Program from the perspective of the payer, the Australian Government Department of Health (DoH).

Two independent studies were conducted: the first was a cost-benefit analysis of the program as a whole, at the population level using PBS data and the second was a cost-benefit analysis of the interactive components of the Program at the GP practice level using data from the MedicineInsight program.

Study one: population level cost-benefit analysis

This study involved an impact evaluation of the changes in medicine utilisation on the PBS. It measured the benefit of the national Chronic Pain Program in terms of reductions in unnecessary costs to the DoH. Time series analysis was used to measure the impact of the program on provider level reimbursement data for opioid medicines listed on the PBS. The analysis used data for 1 January 2006 to 30 June 2017 obtained from Services Australia.

Following the launch of the program, and with increasing GP participation, there was a statistically significant decline in the national rate of opioid dispensing. The program was associated with a reduction in the dispensed volume of opioids prescribed by GPs by a relative 2.56% between July 2015 and June 2017 (two years following launch of program). There was an estimated 501,989 fewer prescriptions dispensed, which corresponded to an estimated saving to the PBS of $13,787,177.

The results from the time series analysis and program cost data collected from NPS MedicineWise finance and project management systems were used to conduct the cost-benefit and cost-effectiveness analysis. A discounting rate of 5% p.a. was applied to all costs, benefits and effect that occurred after the first year, and all program costs were adjusted to 2016-17 currency. The net benefit of the program was $8,771,975, calculated by the difference in the estimated savings from changing opioid dispensing patterns for the PBS and the estimated costs of the program. The benefit to cost ratio was 3.67, indicating that for every dollar spent on the program, $3.67 was gained in monetary benefit.

For the outcome of averted opioid prescriptions dispensed, an incremental cost effectiveness ratio (ICER) was calculated for the program with the alternative of no program. For every $7.48 spent on the program, the dispensing of one opioid prescription was averted.

Based on the findings of this economic evaluation, the NPS MedicineWise 2015 Chronic Pain Program was successful at reducing the dispensing of opioid prescriptions in Australia and the net effect of the program resulted in a monetary benefit to the payer, the Australian Government Department of Health.

Study two: GP behaviour level cost-benefit analysis

This study involved an evaluation of the Chronic Pain Program's impact on GP prescribing practice and management of patients with chronic pain using MedicineInsight data. MedicineInsight is a general practice longitudinal data program that includes over 700 practices from across Australia. Three outcomes were considered in this analysis: prescribing of opioid medicines for chronic pain; encounters with chronic pain patients and initiation of medicines for patients with chronic pain.

Time series analysis was conducted between June 2010 and May 2018 to measure the impact of the interactive component of the Chronic Pain Program on MedicineInsight GPs who chose to participate in these interventions. The analyses included the GP control group who did not participate and who did not work in general practices where intervention GPs practised. Based on the results of this impact evaluation at the GP level, a cost-benefit analysis was conducted estimating the net benefit and benefit to cost ratio prescriptions and GP encounters averted. Each significant outcome was considered in relation to the total cost of the program calculated at a unit level, the individual GP. A sensitivity analysis was conducted where appropriate given uncertainty and variance around the parameters in the cost-benefit ratio.

Among MedicineInsight GPs who participated in the interactive interventions, the Chronic Pain Program was associated with a significant relative 7.5% reduction (95% CI: 2.8%, 12%) in the prescription of opioid medicines in patients with chronic non-cancer pain for the period June 2015 to June 2018. Participation in the interactive interventions was also associated with a significant relative 6.3% reduction (95% CI: 3%, 9.5%) in encounters with those patients.

The total program cost per GP was $435.67 as at June 2017, inclusive of visiting costs per GP of $256.75. The net benefit per GP can be conservatively estimated as $1,881.63, calculated by the difference in savings from changing opioid prescribing and encounter behaviour and the estimated benefit attributable. The benefit to cost ratio was calculated as 5.32, indicating that for every dollar spent on the program, $5.32 was gained in monetary benefit to the payer, the Australian Government Department of Health.

The strengths of this evaluation centre around the data sources used, the analysis methods applied, and the results verified by the different studies. The studies conducted used two different data sources, PBS and MedicineInsight, to investigate the impact of the national and interactive components of the Chronic Pain Program on opioid prescribing and dispensing patterns for general practice patients. The MedicineInsight analysis allowed the evaluation to explore benefits not available in the PBS dataset and explore the impact of the interactive interventions of the program.

The time series methods used in both studies allowed for the estimation of the attributable benefits and costs of the national and interactive components of the NPS MedicineWise Chronic Pain Program. The positive impact of the program on reducing opioid prescriptions was supported by the findings from Study 1, Study 2 and previous evaluations of the program.

Conclusion

This economic evaluation found that the national 2015 NPS MedicineWise Chronic Pain Program had economic benefits in terms of reducing costs to the PBS and a positive impact on the behaviour of GPs who participated in the interactive components of the program. The MedicineInsight analysis revealed the additional benefit of the interactive components of the Chronic Pain program on the outcomes investigated. This evaluation highlights the value of multimodal programs to improve clinical practice when the quality use of medicine issues are complex and multifaceted.

INTRODUCTION

In 2015, NPS MedicineWise launched the *Chronic pain: opioids and beyond visiting program* (hereafter referred to as the Chronic Pain Program). The overarching goal of this program was to improve well-being in patients with chronic non-cancer pain who are managed in primary care.

Objectives of this report

The objective of this report is to present an economic evaluation of the 2015 Chronic Pain Program, which identifies, in monetary terms, the costs and benefits and the cost-effectiveness of the program at achieving the anticipated outcomes.

Due to the availability of different levels of data, this evaluation is presented as two studies:

- Study one provides an economic evaluation at the population level. The program effectiveness is evaluated using a time series analysis of national administrative data from the PBS. Total program costs are used to conduct a cost-benefit analysis.
- Study two provides an economic evaluation at the GP behaviour level. The program effectiveness is evaluated using time series analysis of GP clinical software data from the MedicineInsight dataset. Both prescribing and patient management outcomes are evaluated in a cost-benefit analysis.

The NPS MedicineWise Program

Rationale for the program

Chronic pain is a major health problem which is associated with significant consequences to patients and families, increased costs of health care utilisation as well as societal costs related to lost work productivity.(1) Chronic (non-cancer) pain is defined as constant daily pain lasting more than three months.(2) Approximately 20% of Australian adults report experiencing chronic pain, which is most commonly attributed to an injury or diseases of the musculoskeletal system and connective tissue.(3) Living with chronic pain can have substantial emotional, physical, social and financial impacts on consumers and their carers or family members, and left untreated, can lead to significant human suffering.(3) There is a need for the implementation of effective pharmacotherapeutic as well as non-pharmacological regimens to improve quality of life and productivity for these people.

Health professionals report that management of chronic pain in general practice is complex and challenging.(3) This is attributed to a number of factors including: difficulty in identifying the underlying causes of pain, the close correlation of chronic pain with mental illness disorders, the number of pharmacotherapy options, variability in the use of non-pharmacological strategies as well as concerns surrounding the potential for opioid addiction and misuse.(3) Despite the availability of prescribing guidelines, a number of potential safety and quality use of medicines issues are evident in this complex area. The following were identified in the NPS MedicineWise Formative Research report on chronic pain and informed the design of the 2015 NPS MedicineWise Chronic Pain Program.(3)

- Increased prescribing of opioids despite limited evidence of long-term benefit for chronic non-cancer pain and high rates of adverse effects
    - Opioids are a highly relied upon pharmacotherapy in both the hospital and community health environment and play a critical role in pain management. However, recent statistics in Australia highlight considerable increases in the use of opioids, reflecting international trends associated with the overuse of opioids. The Australian Institute of Health and Welfare (AIHW) report that opioid prescriptions rose by 24% between 2010-11 and 2014-2015, from 369 to 456 prescriptions per 1,000 population.(4) According to

the Therapeutic Goods Administration (TGA) in 2014, almost 3 million people in Australia were prescribed at least one opioid under the PBS or Repatriation PBS (RPBS).(5) Whilst opioids have an established role in acute-pain conditions, such as following trauma or major surgery and in the treatment of cancer pain, their application in chronic pain management is complex and controversial.(1)

- Overall, it is suggested that opioids are less effective for persistent pain than acute pain, and there are limited amounts of quality evidence that demonstrate the efficacy of opioids beyond 12 weeks of use.(6)
- It is reported that in patients taking opioids for non-cancer pain, approximately 80% will experience at least one adverse effect.(7) The most commonly reported side effects of opioids including constipation, nausea, headache, dry mouth, respiratory depression and sedation.(3, 8) Most of these side-effects require additional pharmacotherapy to alleviate symptoms, such as laxatives, and may also require additional hospitalisation or medical care. Long-term effects have been reported as including opioid-induced hyperalgesia as well as immune suppression.(3)
- The POINT study reported that participants with higher opioid consumption had multiple risk factors for adverse outcomes including dependence and overdose, and had higher levels of indicators of poorer wellbeing.(9-11) This study indicated that there is a need for multifaceted, multidisciplinary and differential approaches to treatment of chronic pain that address the numerous co-morbidities that are seen in this group of patients rather than the use of strong opioids singularly as primary therapy.(9, 11)

▷ Inadequate assessment, management, and monitoring of pain

- A range of GP-related barriers to optimal prescribing in chronic pain management have been identified in the literature including: poor assessment of pain; inadequate knowledge and concerns about dependence; addiction; side effects; and misuse and diversion of prescribed opioids.(3)

▷ Variability in use and choice of non-pharmacological therapy

▷ Consumers expressed a reluctance to seek or use pain medicines (particularly opioids) due to concerns about potential side effects and stigma along with fears of addiction, dependence or tolerance.(3)

▷ Difficulties identifying patients at risk of misuse, or misusing opioids (including OTC codeine)

- An increase in the misuse of pharmaceutical opioids has been reported.(3) Opioid use and misuse can result in dependence, overdose, physical harm or, in the worst case, death.(4) Self-reported data from the National Drug Strategy Household Survey conducted in 2016 highlighted that 3.6% of people aged 14 and over had recently used pharmaceutical opioids for non-medical purposes.(4) Opioid deaths increased by 60% in 2011-2015 compared with 2001-2005.(5) Accidental death from oxycodone, morphine or codeine is responsible for most opioid-related deaths.(5) The TGA identified six main outcomes and/or drivers of opioid overuse (5).
    - Overdose resulting in morbidity or mortality
    - Tolerance, requiring higher doses of the product being required to achieve the same level of analgesia, but with accompanying increases in adverse effects
    - Addiction
    - Deliberate abuse, encompassing use of high doses of immediate release opioids and manipulation of ‘abuse deterrent’ dose forms
    - Overuse or inappropriate use
    - Diversion of legally-prescribed product to others for abuse purposes

Key program objectives and messages

The primary objectives of the NPS MedicineWise 2015 Chronic Pain Program aimed to improve the awareness, knowledge and skills of health professionals and consumers in line with key messages.

The key messages for **Health professionals** were:

1. For assessment and management of chronic non-cancer pain, take a planned approach, consider co-morbidities and address physical and psychological factors
2. Opioids have limited value in chronic non-cancer pain: assess for discontinuation at each review.

The key messages for **Consumers** were:

1. By working together with your doctor and health care team, you can achieve your pain management goals
2. Opioids may have short term benefits but often have side effects and are usually not effective for long term pain management
3. There are many strategies available to help you manage your pain. Using a combination of these is more likely to help than using a single strategy.

Overview of the program's interventions and reach

The Chronic Pain Program was a national visiting program targeted primarily at health professionals that was in the field being delivered by NPS MedicineWise Educational Visitors from June 2015 to November 2016. The main activities and interventions for the Chronic Pain Program are shown in Table 1 including the number of pharmacists, nurses and GPs reached. The Chronic Pain Program reached 7,346 GPs through involvement in educational activities as well as other health professionals such as pharmacists, nurses and medical specialists.

Table 1: INTERVENTION AND ACTIVITIES SUITE FOR THE NATIONAL 2015 NPS MEDICINEWISE CHRONIC PAIN PROGRAM

Health professionals (interactive)	Health professionals (other)	Consumer
1-1 educational visit (3,165 GPs, 65 pharmacists, 157 nurses)	Health professional hub (website)	Consumer hub (website)
Small group case-based meeting (3,759 GPs, 116 pharmacists, 546 nurses)	MedicineWise News	Chronic pain communication tool
Clinical e-audit (514 GPs)	PBS feedback with Prescribing Practice Review.	Chronic pain videos
Case study (285 GPs), 1,061 pharmacists, 993 nurses)	NPS Direct	My pain diary
Pharmacy practice review (938 pharmacists)	NPS for Nurses	Chronic pain fact sheet
Online learning module (232 GPs, 390 pharmacists, 467 nurses)	GP & Pharmacist Update (471 pharmacists)	Social media posts

Interactive components of the program included:

- Educational visiting involves an NPS MedicineWise Educational Visitor meeting with the GP individually in their practice to discuss evidence-based therapy on a particular topic. A discussion aid (educational visiting card) is used to guide the conversation and left for the GP as a reference. This type of intervention is also known as academic detailing and is one of the most effective and proven intervention to bring about prescribing behaviour change.
- Small group case-based discussions between GPs and other health professionals are another intervention facilitated by an NPS MedicineWise Educational Visitor, previously known as Clinical Service Specialists. These groups may also include members of the practice's multidisciplinary team such as pharmacists and practice nurses. In this intervention a case scenario depicting real clinical dilemmas is used as the basis of discussion in a group of up to 10 participants.
- Clinical audits are quality improvement activities that allow GPs to self-reflect on their management of patients with a condition or using a particular class of medicines. GPs review their practice, receive individual and peer feedback and implement changes to practice on a specific therapeutic topic.
- Interactive case studies are a reflective learning activity for GPs, pharmacists and nurses. They take the form of a case scenario accompanied by a set of questions. Participants receive feedback on their own and the aggregated responses, evidence-based practice points and expert commentary on the case. Distributed in print via NPS News until 2012, case studies are now provided online via NPS MedicineWise's learning site and are developed for most therapeutic topics.

Other interventions included a Prescribing (PBS) feedback, known as a prescribing practice review. It is a paper-based intervention sent via mail to the majority of practising Australian GPs (approximately 26,000). The Prescribing (PBS) feedback presents GPs with their prescribing patterns for the selected therapeutic topic in comparison with their peers. It also contains relevant messages for reflection and information on the quality use of medicines. This personalised prescribing feedback data is drawn from PBS data and coordinated through the Services Australia. This intervention is sent to all GPs who had prescribed over $1,000 of medicines on the PBS over a 3-month period.

The print version of NPS MedicineWise news: Chronic pain was distributed in June 2015 to over 70,000 health professionals, including GPs, pharmacists and specialists. The top three Chronic pain print resources ordered by health professionals over the life of the program were; *Biopsychosocial management of chronic pain plan (tear-off pad), Pain communication card* and *Headaches diary*. The total quantity ordered for all resources to health professionals was 19,013 as at March 2017.

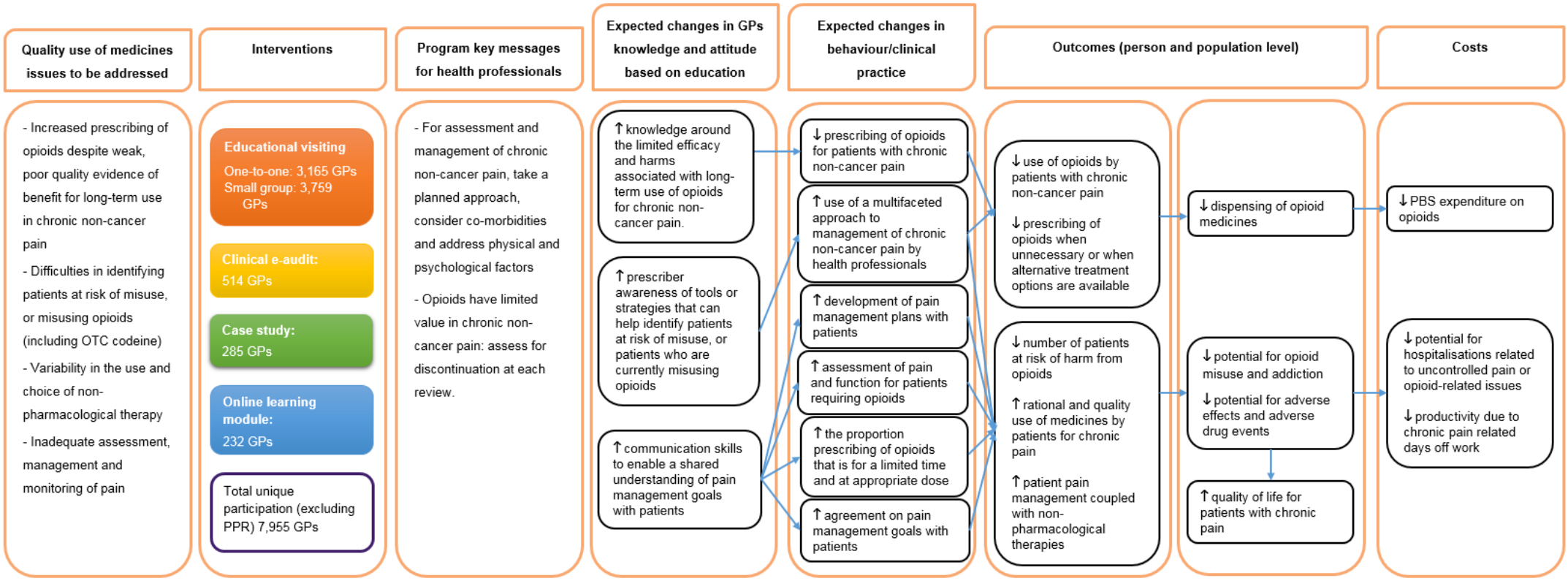
Chronic pain print resources were also ordered by consumer and consumer organisations such as community pharmacy and community health centres. The two resources ordered by consumers and consumer groups were the; *Headaches Diary* and factsheet *Chronic Pain: what can I do?* The total quantity ordered for resources to consumers was 17,339 as at March 2017.

Expected program outcomes

Based on key messages, educational materials, and current prescribing and patient management patterns the expected outcomes of the program were:

- Reduce the number of opioid prescriptions for the patients with chronic non-cancer pain
- Reduce the number of patients with chronic non-cancer pain inappropriately prescribed opioids
- Improve pain management for patients with chronic non-cancer pain.

Figure 1: EXPECTED OUTCOMES OF THE 2015 NPS MEDICINEWISE CHRONIC PAIN PROGRAM



Program evaluation

The impact of the 2015 Chronic Pain Program on health professionals' attitudes, confidence, knowledge and self-report practices has previously been evaluated using a GP survey and analysis of the clinical e-audit.

The GP survey involved a participant survey sent to a random sample of 1,356 GPs who had participated in a 1-1 educational visit or small group case-based visit as part of the Chronic Pain Program. A control survey was also sent to a random sample of 912 GPs who had not actively participated in the Chronic Pain Program but had engaged in NPS MedicineWise educational activities previously. The surveys were self-completion, online-based questionnaires. The surveys were conducted approximately 12 months after program launch and were in field for a period of six weeks. The initial distribution of surveys occurred in June 2016, followed by two reminder e-mails sent at 2-week intervals. The response rates for the participant and control surveys were 14% and 17% respectively.(12)

The clinical e-audit is an educational intervention available for GPs to gain feedback on their management of patients. The Clinical e-audit available for the Chronic Pain Program used 10 key indicators related to the management of chronic pain. Participating GPs enter information about a sample of their patients at two time points. Paired-samples t-test were conducted to examine the impact of the NPS MedicineWise activity on the number of patients meeting each indicator pre and post the intervention. Data from 514 participating GPs was analysed for the program evaluation.(12)

GP survey results

Participation in the program resulted in significant improvements in GP knowledge in line with key messages. The program was effective at increasing GP use of the 5A's assessment tool, pain management plans and opioid contracts with patients with chronic (non-cancer) pain. The 5A's referred to in the assessment tool were defined as; analgesia, activity, adverse effects, affect and aberrant behaviour.

Several knowledge questions relating to program key messages were asked. The proportion of participant GPs who agreed/strongly agreed that GPs should agree on pain management goals with their patients significantly increased ($p<0.001$) after participation in an educational visit, with an absolute increase of 12%. The program was also effective at significantly increasing the proportion of GPs who regularly reviewed patients on opioid therapy using the 5A's assessment tool (+57%). There was an increase of 32% ($p<0.001$) in the proportion of participant GPs who agreed that the use of opioids should be discontinued after a 4-week trial if no improvement was observed in patient wellbeing. These findings suggest that the program succeeded in conveying these messages to GPs.

Participant GPs were asked to assess the level of change in their practice as a result of their participation in the NPS MedicineWise educational activity. The proportion of participant GPs who always/often assessed pain and function in relevant patients significantly increased ($p<0.001$) after participation in an educational visit, with an absolute increase of 32%. A 25% increase was observed in the proportion of GPs who routinely used a validated pain assessment tool to assess pain levels in relevant patients.

The program message about non-pharmacological strategies prompted a significant increase in GP use of 'dietary changes' (+24%), 'cognitive behavioural therapy' (+37%) and 'mindfulness-based approaches' (+47%) in the management of chronic pain. The proportion of GPs who discussed using pain management plans and opioid contracts with their patients increased by 56% and 35% respectively.

The survey asked GPs about how they responded to the prescribing (PBS) feedback intervention which was sent to them. Just over half of participant GPs felt that this activity provided a useful tool for comparing their pattern of prescribing with their peers. A significantly higher proportion of participant GPs indicated that the prescribing feedback helped them to reflect on their prescribing of opioid

medicines. Over one quarter of participant GPs (31%, n=57) stated that the prescribing feedback prompted a change in their prescribing of opioid medicines.

Clinical e-audit results

The chronic pain clinical e-audit generated significant improvements in GP practice in six of the indicators analysed (Table 2). The clinical e-audit was particularly effective at increasing the use of pain management plans (+28%) and the 5A's assessment tool (+33%).

Table 2: CLINICAL E-AUDIT RESULTS

Clinical indicators (eligible GPs included)	% of Patients (n)		
	Initial audit phase	Review audit phase	Difference
3. Adopted a multidisciplinary approach to chronic non-cancer pain management (n = 416)	94.1 (3,917)	97.5 (4,955)	+3.4 p<0.0001
4. Discussed and agreed on realistic pain management goals with your patients (n = 411)	92.6 (3,807)	97.8 (4,021)	+5.2 p<0.0001
5. Agreed to and documented a pain management plan, outlining pain management goals with the patient (n = 356)	65.2 (2,320)	93.2 (3,320)	+28.0 p<0.0001
8. Used oral modified-release formulations or transdermal preparations (n = 321)	87.6 (2,457)	92.7 (2,600)	+5.1 p<0.0001
9. Patient achieving pain management goals (n = 374)	79.9 (2,392)	91.7 (2,745)	+11.8 p<0.0001
10. Regularly reviewed patients by using the 5As to assess if ongoing opioid therapy is needed (n = 237)	64.0 (1,435)	97.0 (2,175)	+33.0 p<0.0001

Note: No data was presented for 4 of the 10 clinical indicators (i.e. Indicators 1, 2, 6 and 7), due to patient drop out at the audit review phase or no patients being audited against the specified indicators.

STUDY ONE: POPULATION LEVEL ECONOMIC EVALUATION

This study involved an economic evaluation at the population level. The program effectiveness was evaluated using a time series analysis of national administrative data from the Pharmaceutical Benefits Scheme (PBS). Total program costs were used to conduct a cost-benefit analysis.

Stage 1: Program effectiveness

Methods

The program effectiveness of the 2015 NPS MedicineWise Chronic Pain Program on the prescribing of opioid medications was evaluated using time series analysis of the national administrative data from the PBS dispensing data.

Data sources

The provider level dispensing and reimbursement data for opioid medications listed on the PBS (See Table 3) were obtained from Services Australia. The data provided covered the period from 1 January 2006 to 30 June 2017. Services Australia supplied the PBS data in aggregate form at the GP level. The PBS data comprises the number of subsidised prescriptions prescribed, both original and repeats, with a breakdown by general and concessional beneficiary entitlement levels. Repatriation Pharmaceutical Benefits Scheme (RPBS) data were not included.

The PBS data were supplied according to the following specifications:

- Vocationally Registered General Practitioners (VRGPs) and Other Medical Practitioners (OMPs)
- PBS prescribing by scrambled provider number
- Date of prescribing and date of supply of medicine
- Price and net benefit of prescriptions by PBS medication item code.

Opium alkaloids (hydromorphone, morphine, oxycodone, codeine), phenylpiperidine derivatives (fentanyl), diphenylpropylamine derivatives (methadone), oripavine derivatives (buprenorphine), and other opioids (codeine with paracetamol, tapentadol and tramadol) were extracted from PBS data by selecting dispensing records for the PBS item numbers listed in Table 3.

Table 3: PBS ITEM CODES USED IN THE FINANCIAL IMPACT ANALYSIS OF THE 2015 CHRONIC PAIN PROGRAM

Medicine	PBS item numbers (2006-April 2017)
Buprenorphine	8865N, 8866P, 8867Q, 10746N, 10755C, 10756D, 10770W
Codeine	1214X
Codeine + paracetamol	1215Y, 6032L, 8785J
Fentanyl	5265D, 5277R, 5278T, 5279W, 5280X, 5437E, 5438F, 5439G, 5440H, 5441J, 8337T, 8338W, 8339X, 8340Y, 8878G, 8891Y, 8892B, 8893C, 8894D
Hydromorphone (long acting)	9299K, 9406C, 9407D, 9408E, 9409F
Hydromorphone (short acting)	8420E, 8421F, 8422G, 8423H, 8424J, 8541M, 8542N, 8543P,
Morphine (long-acting)	1653B, 1654C, 1655D, 1656E, 2839K, 2840L, 2841M, 8035X, 8146R, 8305D, 8306E, 8349K, 8453X, 8454Y, 8489T, 8490W, 8491X, 8492Y, 8493B, 8494C

Medicine	PBS item numbers (2006-April 2017)
Morphine (short-acting)	1607N, 1644M, 1645N, 1646P, 1647Q, 2122Q, 2123R, 2124T, 2332R, 2333T 6039W, 6047G, 6048H, 6049J, 8669G, 8670H, 9014K, 9015L, 9016M, 9017N
Oxycodone (long-acting)	8385H, 8386J, 8387K, 8388L, 8681X, 9399Q, 9400R
Oxycodone (long-acting with naloxone)	8000C, 8934F, 8935G, 8936H, 10757E, 10758F, 10776E
Oxycodone (short-acting)	2481N, 2622B, 6043C, 6044D, 6063D, 6070L, 6071M, 6078X, 8464L, 8501K, 8502L, 8644Y
Tapentadol	10091D,10092E, 10094G, 10096J, 10100N
Tramadol	2527B, 6072N, 6073P, 6074Q, 8455B, 8523N, 8524P, 8525Q, 8582Q, 8611F, 8843K, 9199E, 9200F, 9201G

Time series analysis

1) A time series model was fitted to the monthly dispensing data of medicines of interest (referred to as the 'actual' series).
2) The model forecasted what the series of dispensing would have been had the program of interest not taken place (referred to as the 'counterfactual series')
3) The two series were compared (subtracted) to obtain a monthly series of saved prescriptions
4) The number of saved prescriptions in each month was multiplied by the medicine's average subsidy in the same month; giving a monthly series of saved expenditure
5) The series of saved expenditure was summed over the months of interest to produce an estimate of expenditure savings.(13)

The outcome was the number of dispensed prescriptions summed by month across all opioid groups listed in Table 3. This produced a single time series of monthly opioid dispensing running from January 2006 to June 2017 (11.5 years). Between 2006 and 2017, the average price of opioid medications was continually above the general co-payment threshold. We therefore analysed the total number of prescriptions dispensed to general and concessional beneficiaries.

The impact of the program was estimated as an interaction term between the monthly cumulative number of participating GPs and the dispensing trend over time. This term models the program's effect as a gradual decline in the monthly dispensing rate of opioid medicines as an increasing number of GPs participate in the program. The term was chosen in preference to a cumulative count of GP participation based on a comparison of diagnostic measures of goodness-of-fit.

The model also incorporated two additional terms—one to account for the anomalous decline in dispensing that began in January 2016 and another to account for a decline that was likely related to a price change in some opioid medicines in January 2017. Both declines were accounted for by including a step change in the model. Comparisons of model diagnostics suggested that accounting for each event with a step change resulted in a better model fit than if both, or either, were accounted for by a trend change.

Results

PBS utilisation

Following the launch of the program, there was a statistically significant decline in the rate of opioid dispensing with increasing GP participation. Figure 2 shows the modelled number of dispensed prescriptions (red line) juxtaposed against the number of prescriptions that would have occurred had

the program not taken place (green line). As decay and non-decay models fit the actual dispensing data equally well, results were averaged from the two models. These are presented in Table 4. The resulting cost savings were calculated by multiplying each of the monthly prescription savings by the respective monthly average benefit paid for opioid prescriptions, and then summing the result.

Figure 2: TIME SERIES ANALYSIS OF MONTH COUNT OF OPIOID MEDICINE DISPENSING, JAN 06-JUN17 (NON-DECAY MODEL SHOWN)

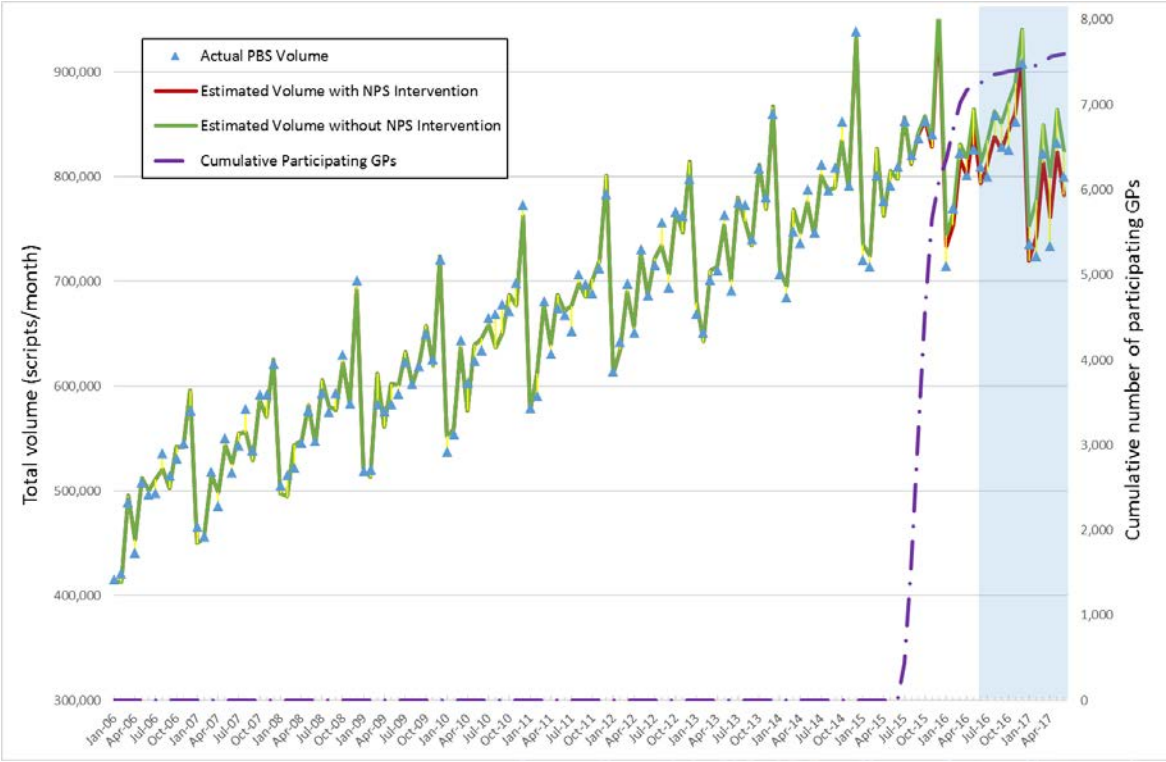


Table 4: SUMMARY OF RESULTS FROM TIME SERIES ANALYSIS

	Decay model	Non-decay model	Average
Volume	509,155	494,640	501,898
% decrease in volume	2.59%	2.52%	2.56%
Cost savings	13,934,907	13,527,448	13,731,177

Using the average between the decay and non-decay model, the program was associated with 501,898 (95% CI: 44,903 - 958,893) fewer opioid prescriptions dispensed than expected had the program not occurred. This represents a 2.56% decrease in volume and is associated with an estimated savings to the PBS of $13,731,177.

Stage 2: Economic evaluation

Method

Evaluation design

A ***cost benefit analysis*** was used to compare the cost and benefits of the NPS MedicineWise 2015 Chronic Pain Program expressed in monetary terms. The measures used in this analysis are:

- The **cost** of the resources required to deliver the 2015 program (outlined in Table 6)
- The **benefits** of the program expressed as the monetary value of the effects generated by the program. In this analysis the benefits are restricted to the direct estimated savings associated with the reduction in opioids dispensed on the PBS

Other economic benefits are possible due to the side effects of opioid use and the potential other outcomes of the program. These have been excluded from the analysis at this time.

The cost-benefit analysis was conducted by calculating the program net benefit and the benefit-cost ratio. The *net benefit* is calculated as the difference between the benefits and the costs. Values higher than zero indicate that the benefits exceed the costs. The *benefit-cost ratio* is calculated as the ratio of benefits to costs. Values higher than one indicate that the benefits exceed the costs.

A ***cost-effectiveness analysis*** was undertaken to compare the costs and effects of the NPS MedicineWise Chronic Pain Program against the alternative of no program. The cost-effectiveness was conducted by calculating incremental cost effectiveness ratio (ICER) for the outcome of averted opioid prescriptions dispensed. The ICER is calculated using the formula below.(14)

$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta\, Cost}{\Delta\, Effect}$$

Time frame

The timeframe for the evaluation of program effectiveness and benefit was the 24 months post-program, July 2015 to June 2017.

Perspective

The Australian Government Department of Health (DoH), funds both the Quality Use of Medicines (QUM) program at NPS MedicineWise and the PBS. Only monetary costs and benefits associated with DoH funding to the NPS MedicineWise QUM program were including in this economic evaluation.

Discounting and cost standardisation

Program costs began to occur in the 2013-14 financial year. A discounting rate of 5% p.a. was applied to all costs, benefits and effect that occurred after this year. All program costs were adjusted to 2016-17 currency, the last year that costs and benefits occurred, using the Australian Consumer Price Index (CPI) published by the Australian Bureau of Statistics (ABS).(15)

Decision tree

A simple decision tree was created in TreeAge Pro(16) with the costs and effects for the outcome of dispensed opioids averted associated with the NPS MedicineWise intervention compared to no NPS MedicineWise intervention. Table 5 describes the decision tree variables implemented.

Figure 3: DECISION TREE FOR COST-EFFECTIVE ANALYSIS, OUTCOME AVERTED OPIOID DISPENSING

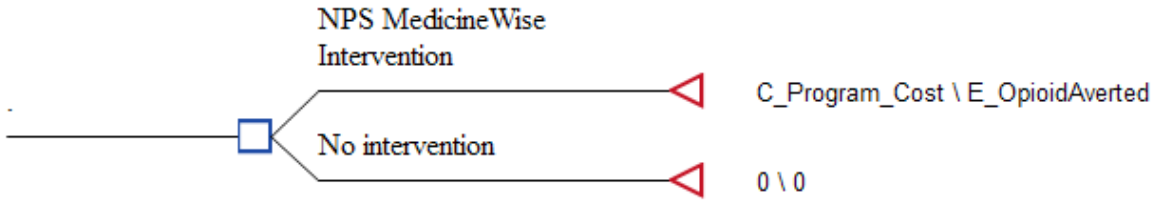


Table 5: DESCRIPTION OF DECISION TREE VARIABLES

Decision tree variables	Description
C_program_cost	The cost of implementing the Chronic Pain Program
E_OpioidAverted	The number of dispensed opioids averted due to the Chronic Pain Program

Uncertainty

Sensitivity analysis was conducted for the cost-benefit and cost-effectiveness analysis by calculating the net benefit, cost-benefit ratio and ICER for the four possible combinations of estimated maximum and minimum cost, benefit and effect based on variation data.

Probabilistic sensitivity analysis was conducted for cost-effectiveness analysis using TreeAge Pro.(16)

Data Sources

The economic evaluation is based on the program effectiveness results presented previously and program cost data collected from NPS MedicineWise organisational records.

Invoiced costs for the program were sourced directly from NPS MedicineWise's internal finance department. Timesheet data completed by staff and salary data were used to estimate the staff costs directly associated with the design and implementation of the program. NPS MedicineWise applied a 24% increase to total staff costs, to account for the cost of infrastructure and support services used.

The delivery of face-to-face visits to GPs by Educational Visitors was costed by multiplying the cost per face-to-face visits with a GP for the 2015-16 financial year (FY) by the total number of face-to-face visits with a GP for the Chronic Pain Program, which was a proportion of the total visits delivered in that year. The average cost per face-to-face visits with a GP was calculated by dividing the total expenditure of the NPS MedicineWise educational visiting program by the total number of face-to-face visits with GPs for any program for that financial year. Factors such as travel, particularly in remote locations, and the ratio of GPs to Educational Visitors in a visit vary the cost per individual visit with a GP.

Variation for sensitivity analysis

Uncertainly around the estimates of program impact used to calculated *effect* and *benefit* of the program were estimated using the 95% confidence intervals from the time-series analysis of the PBS opioid dispensing volume data.

Estimates of variation for invoiced costs and staff resource costs were derived from three national NPS MedicineWise visiting programs that occurred at a similar time to the 2015 Chronic Pain Program and involved a similar intervention product suite. These programs were the 2015 Blood Pressure program, the 2015 Chronic Pain Program and the 2016 Depression program. The Blood Pressure program did not include a PBS feedback intervention, which the other comparison programs included. To account for this difference, the invoiced cost of the PBS feedback in the Chronic Pain Program was added to the invoiced cost total of the Blood Pressure program. All costs were adjusted to the same

financial year equivalent value, using Australian CPI values published by the ABS(15) and discounted at a rate of 5% per year after the first year to calculate a standard deviation. See details in the *Discounting and cost standardisation* section. Variation estimates were calculated by varying the base case by the standard deviation of the four similar programs' costs.

The estimate of variation for the cost of delivery of visiting was derived from the average cost per GP face to face visits for the three financial years 2013/14, 2014/15 and 2015/16. There was a 15% reduction in this cost from 2014/15 to 2015/16 (Table 7). This change was due to change in delivery model; from delivery primarily through contracts with Medicare locals to a majority in-house workforce delivery model.

Table 6: NPS MEDICINEWISE PROGRAM COSTS

Year	Type	Invoice costs	Staff costs	Infrastructure/ support services	Delivery of face-to-face visits	TOTAL
2013/14	Raw	-	75,382	25,127	-	100,509
	Adjusted to 16/17$	-	79,060	26,353	-	105,414
2014/15	Raw	130,908	580,725	193,575	1,969,532	2,875,309
	Adjusted to 16/17$	134,983	598,800	199,600	2,030,835	2,964,805
2015/16	Raw	84,737	220,122	73,374	-	378,233
	Adjusted to 16/17$	86,185	223,882	74,627	-	384,694
2016/17	Raw	-	3,896	1,299	-	5,195
	Adjusted to 16/17$	-	3,896	1,299	-	5,195
Total	Raw	215,645	880,125	293,375	1,969,532	3,358,677
	Adjusted to 16/17$	221,168	905,639	301,880	2,030,835	3,459,521
	Adjusted + discounting (5% pa applied)	206,727	855,780	285,260	1,934,128	3,281,895

Table 7: ESTIMATES OF VARIATION OF PROGRAM COST

	Base case	Standard deviation from similar programs	Upper estimate of variation	Lower estimate of variation
Invoiced costs	206,727	65,300.71	272,028	141,426
Staff costs (plus 25% Infrastructure/ support services)	(855,780 + 285,260) = 1,141,040	31,413.82	(887,194 + 295,731) = 1,182,925	(824,366 + 274,788) = 1,099,155
Delivery of face-to-face visits	1,934,128	33.06 per face-to-face nb * 6924 occurrences	2,163,036	1,705,221
Total	3,281,895		3,617,989	2,945,802

NB: based on differences between FY rather than differences between programs

The costing scenarios for sensitivity analysis will be calculated using these limits as follows:

- Base Case: Point estimates of the program cost, the effect and the benefit
- Scenario 1 **Maximum costing**: The upper confidence limit of the program cost per GP, the upper confidence limit of the effect and the highest cost attributed to averted scripts and encounters
- Scenario 2 **Minimum costing**: The lower confidence limit of the program cost per GP, the lower confidence limit of the effect and the lowest cost attributed to averted scripts and encounters
- Scenario 3 **Least Favourable costing**: The upper confidence limit of the program cost per GP, the lower confidence limit of the effect and the lowest cost attributed to averted scripts and encounters
- Scenario 4 **Most Favourable costing**: The lower confidence limit of the program cost per GP, the upper confidence limit of the effect and the highest cost attributed to averted scripts and encounters

Table 8 presents the results from the program effectiveness evaluation.

Table 8: PROGRAM EFFECTIVIENSS DATA SUMMARY TABLE

Outcome	Raw value	Adjusted to 16/17 $AUD and discounted (base case)	Variation
Number of opioid dispensing averted	501,989	438,740	Raw - 95% CI (44,903-958,893) Discounted - 95% CI (39,251-838,229)
Cost of opioid dispensing averted	$13,787,170	$12,053,870	Adjusted and discounted 95% CI ($1,078,375-$23,029,365)

Results

Cost-benefit analysis

The Chronic Pain Program aimed to reduce cost to the Australian health care system via a reduction in inappropriate use of opioids. Table 9 presents the results of the cost-benefit analysis of the program. The net benefit and benefit to cost ratio are used to compare the cost of the program to the benefit gained from savings to the PBS.

Table 9: COST-BENEFIT ANALYSIS OF NPS MEDICINEWISE IMAGING FOR CHRONIC PAIN 2015 PROGRAM

Parameter	Benefit: Savings from opioid dispensing averted	Cost of program	
Total cost of intervention	$12,053,870	$3,281,895	
Net Benefit			$12,053,870 - $3,281,895 = $8,771,975
Benefit to cost ratio			$12,053,870 / $3,281,895 = 3.67

The net benefit is the difference in the cost of changing dispensing patterns and the costs of the program, i.e. $12,053,870 - $3,281,895= **$8,771,975**. This represents a net saving as a result of the program.

The benefit to cost ratio is calculated by dividing the estimated cost of changing dispensing patterns by the cost of the NPS MedicineWise program. The benefit to cost ratio is $12,053,870 / $3,281,895 = **3.67**. Values higher than one indicate that the benefits exceed the costs. The value of 3.67 indicates that for every dollar spent on the program, $3.67 was gained in monetary benefit.

Cost effectiveness analysis

The program aimed to reduce inappropriate opioid use in chronic non-cancer pain. A reduction in the net national dispensing of opioid prescriptions was a positive outcome based on the current environment and QUM issues discussed in the background section of this report. A cost effectiveness analysis was used to assess the relationship between the program costs and effect on reducing net national dispensing of opioid prescriptions. For this analysis the monetary benefit from savings to the PBS is not included as the volume of opioids dispensed is the primary outcome.

An incremental cost effectiveness ratio (ICER) was calculated for the program (a) with the alternative of no program (b).

$$ICER = \frac{Cost_a - Cost_b}{Effect_a - Effect_b} = \frac{\Delta\, Cost}{\Delta\, Effect}$$

$$ICER = \frac{3{,}281{,}895-0}{438{,}740-0} = 7.48$$

The ICER for an opioid dispensing averted is 7.48. For every $7.48 spent on the program, one opioid prescription was not dispensed as a result. The cost was offset by the savings to the PBS from the averted opioid prescription, which was on average $27.

Sensitivity analysis

Table 10 presents uncertainty around the net benefit, benefit to cost ratio and ICER by using four different scenarios based on estimated maximum (upper confidence limit) and minimum (lower confidence limit) values for program cost, benefit and effect. In the most favourable scenario, in which the minimum program costs and the maximum benefit and effect were used, the net benefit was $20,083,563, the benefit to cost ratio was 7.82 and the ICER was 3.51. In the least favourable scenario, in which the maximum program costs and the minimum benefit and effect were used, there was a net loss (rather than benefit) of $2,539,614, the benefit to cost ratio was 0.30 and the ICER was 92.18.

Table 10: SENSITIVITY ANALYSIS – BASE-CASE AND FOUR SCENARIOS

	Base-case	Scenario 1 (Maximum costing)	Scenario 2 (Minimum costing)	Scenario 3 (least favourable costing)	Scenario 4 (most favourable costing)
Cost of program variation	3,281,895	3,617,989	2,945,802	3,617,989	2,945,802
Benefit: savings from averted opioid dispensing variation	12,053,870	23,029,365	1,078,375	1,078,375	23,029,365
Effect: averted opioid dispensing variation	438,740	838,229	39,251	39,251	838,229
Net Benefit	8,771,975	19,411,376	-1,867,427	- 2,539,614	20,083,563
Benefit to cost ratio	3.67	6.37	0.37	0.30	7.82
ICER	7.48	4.32	75.05	92.18	3.51

Probabilistic sensitivity analysis

A probabilistic sensitivity analysis was performed on the cost-effectiveness analysis for the outcome of averted opioid prescriptions dispensed. This sensitivity analysis simulates multiple scenarios incorporating all inputs above (and their lower and upper limits) to see the impact varying these inputs have on the ICER calculated.

Uncertainty around the program costs was included using a triangular distribution and the confidence intervals estimated from the range presented in Table 11. The uncertainty around the effectiveness of the program was included using a normal distribution and standard error from the time series analysis presented in Table 8. A willingness to pay threshold of $27 was used to represent the average savings to the PBS from each opioid dispensing averted. The probabilistic sensitivity analysis was run with 1000 samples. The results are presented in Figure 4 below and in Table 11.

In 92.6% of iterations the NPS intervention was effective at reducing opioid dispensing and at a cost less than the average PBS reimbursement.

Figure 4: INCREMENTAL COST-EFFECTIVENESS, NPS MEDICINEWISE INTERVENTION VS NO INTERVENTION

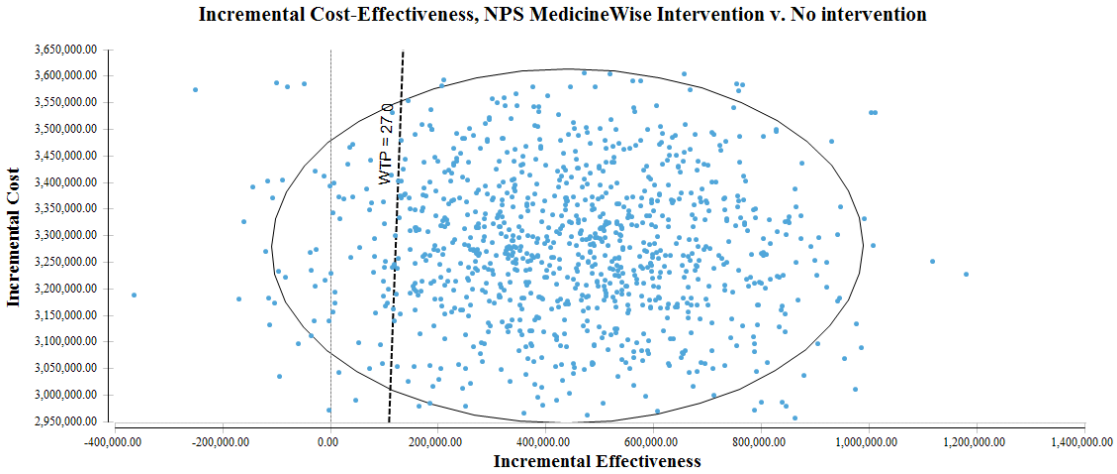


Table 11: RESULTS FROM INCREMENTAL CE PLOT REPORT

Sensitivity Analysis Scenario	Result of Iterations
NPS intervention more effective, ICER less than $27	92.6% of iterations
NPS intervention more effective, ICER greater than $27	4.4% of iterations
NPS intervention inferior - less effective and greater cost	3.0% of iterations

Discussion

The economic evaluation of the NPS MedicineWise Chronic Pain Program found that:

- The Chronic Pain Program was effective at reducing dispensing of opioids prescribed by GPs by a relative 2.56%. In the two-year period after the program there was an estimated 501,989 fewer prescriptions dispensed. This corresponded to an estimated mean savings to the PBS of $13,787,170.
- At a population level from the perspective of the Australian Government Department of Health, the Chronic Pain Program had a benefit to cost ratio of 3.67 and a net benefit of $8,771,975.
- The cost-effectiveness analysis found that for every $7.48 spent on the program, one dispensing of an opioid prescription was averted. The cost was offset by the savings to the PBS from the averted opioid prescriptions, which was on average $27 per prescription.

Based on the findings of this economic evaluation, the NPS MedicineWise 2015 Chronic Pain Program was successful at reducing the dispensing of opioid prescriptions and the net effect of the program resulted in a monetary benefit to the payer, the Australian Government Department of Health.

The sensitivity analysis demonstrated that the estimates of net benefit, benefit of cost ratio and ICER were highly dependent on the uncertainty in the estimate of impact on the PBS from the time-series analysis. The conclusion was supported by the probabilistic sensitivity analysis, which showed that in 92.6% of iterations the NPS intervention was both effective at reducing opioid dispensing and at a cost less of than the average PBS reimbursement. The positive impact of the program on reducing opioids was supported by the findings from previous evaluations of the program. A program evaluation survey and clinical audit completed by GPs, reported improvements in GPs' self-reported use of a 4-week trial of opioids and reviewing patients using the 5As to assess if ongoing opioid therapy was needed.(12)

The monetary benefit of the program used in this analysis was restricted to only direct benefit from savings to the PBS from reduced dispensing of opioids. Other monetary benefits may include reduced costs associated with opioid-related harms. However, the causal link between the reduction of opioid dispensing associated with this program and an impact on opioid-related harms could not be estimated using the data and methods available for this study.

A limitation of the evaluation was the lack of measurement of the appropriateness of the behaviour change in relation to best practice evidence. The data and method used to assess the impact of the program cannot be used to assess whether the appropriateness of prescribing of opioids has improved, only the net changes in dispensing of these medications. Evidence from the previous evaluations of the program, information about the current patterns of opioid use and the theoretical program logic of the Chronic Pain Program, support the assumption that the reduction observed in the PBS data represents a positive QUM outcome for the community. Further analysis could improve our understanding of how the program has impacted on prescriber behaviour regarding opioids and the downstream outcomes of these.

In the future, analysis of linked health data may be used to examine the relationship between the impact of the program on opioid prescribing with opioid-related harms.

PBS dispensing data provides a national census of medicines reimbursed by the PBS, the data is not impacted by self-report bias, and NPS MedicineWise has a high level of expertise at conducting time series analysis using health administration datasets.

The findings from this evaluation demonstrate the cost-effective impact that a national visiting program can have on reducing the use of over-prescribed medicines by providing information on evidence-based best practice. Further analysis using MedicineInsight data (study two) provides additional insights into the impact of the Chronic Pain program on GPs' clinical practice.

STUDY TWO: GENERAL PRESCRIBER LEVEL ECONOMIC EVALUATION

This study provides an economic evaluation of the 2015 NPS MedicineWise Chronic Pain Program at the GP behaviour level. The program effectiveness was evaluated using a time series analysis of data extracted from GP clinical information systems which are available in the MedicineInsight dataset. Outcomes associated with improved pain management were evaluated in a cost benefit analysis.

Stage 1: Program effectiveness

About the intervention

The Chronic Pain Program aimed to:

- Reduce the volume of opioid medicines prescribed to patients with non-cancer pain;
- Reduce the number of patients with chronic non-cancer pain being initiated on opioids where opioids were not indicated;
- Reduce the number of patients with chronic non-cancer pain on opioids where opioids were not effective; and
- Improved patient pain management.

Method

Overall aim

To evaluate the impact and costs of the 2015 NPS MedicineWise Chronic Pain Program using MedicineInsight data.

Objectives

The objectives of Study 2 were to assess:

a) the impact of the 2015 Chronic Pain Program on:

- The volume of opioid medicines prescribed by GPs (medicine volume) to patients with chronic non-cancer pain
- The number of adult patients with chronic non-cancer pain who had an GP encounter (GP encounters)
- The number of new patients with chronic non-cancer pain initiated on an opioid (opioid initiations)

b) the costs of the programs (changes in medicine volume, GP encounters, opioid initiations).

Data source

This study uses general practice data from the MedicineInsight dataset and GP program participation data from the NPS MedicineWise client database. MedicineInsight is a national general practice data program developed and managed by NPS MedicineWise. It is a leading large-scale general practice data program in Australia that extracts longitudinal de-identified patient health records from the software GPs already use to manage patient records and write prescriptions. MedicineInsight includes 7% of general practices in Australia and contains approximately 3.5 million active patients.

MedicineInsight uses third-party data extraction tools to extract, de-identify, encrypt and securely transmit whole of practice data from the GP Clinical Information System of over 700 general practices.

Patient level data is de-identified ‘at source’ meaning the patients’ personal identifiers such as name, date of birth, and address are not extracted by the tool. The data held in the MedicineInsight database are anonymous. However, each patient has a unique identifying number which allows all the records (clinical, prescription, referral, etc.) held in the database for a particular individual over time to be linked.

MedicineInsight extracts data from general practices including: 1) patients’ demographic and clinical data (except for progress notes) for all encounters entered directly by GPs or practice staff into the system; 2) system generated data (e.g. start time and date of an encounter); and 3) GP identifiable information. De-identified patient data are extracted regularly from each participating practice, collated with de-identified GP information, and analysed centrally in the data repository held by NPS MedicineWise in an external, secure environment.

The following data tables from MedicineInsight were used for this study:

- Patient conditions
- Diagnosis
- Encounter (including reason for encounter)
- Prescription
- Prescription history
- Patient flags
- Patient (for year of birth and gender)
- Provider
- Site

Data was extracted from the MedicineInsight database between 1 June 2010 and 31 May 2018 for analysis. NPS MedicineWise participation data was used to identify if MedicineInsight GPs participated in one or more Chronic Pain Program ‘interactive’ interventions: clinical audit, educational visit, interactive case study and/or small group meeting (case-based).

Evaluation design and GP populations

Time series analyses were used to assess the impact of the interactive components of the 2015 NPS Chronic Pain Program on patients with chronic non-cancer pain who attended MedicineInsight practices. Time series analysis is appropriate for measuring a long-term change in the monthly volume of scripts and encounters. Longitudinal analysis was employed to measure the change in rate of opioid initiations, before and after the intervention period.

Study periods

GP Encounters and Opioid Medicine Volumes

- Prior to the Program: June 2010 - May 2015 (60 months)
- During and after the Program: June 2015 - May 2018 (36 months)

Initiations

- Before Program (pre-intervention): Jan 2014 – Dec 2014
- Year of the launch of Program (intervention): Jan 2015 – Dec 2015
- One year after launch of Program (post-intervention): Jan 2016 – Dec 2016
- Two years after launch of Program (post-intervention): Jan 2017 – Dec 2017

These dates for initiation periods correspond to seasonality evident in GP prescribing behavior. Each period is of equal length and ensures the capture of comparative seasons across these periods.

Study population

Patients were eligible for inclusion in the study if they:

- had chronic non-cancer pain recorded in the clinical system prior to 31 May 2018
- were 18 years or over at the date they had their first encounter to a MedicineInsight GP for chronic non-cancer pain during the study period.
- had at least one encounter with and/or were prescribed an opioid prescription by an eligible GP

Patients with cancer, or who were palliative were excluded, as opioids are indicated for the management of pain in these conditions.

Figure 5 describes the process for identifying eligible patients in MedicineInsight data for inclusion in the study.

Chronic non-cancer pain was defined as ever having a diagnosis, reason for encounter or reason for prescription of chronic pain (with body area specified or unspecified) or having multiple records of neuropathic pain or back pain suggesting that the pain was chronic i.e. pain mentioned for periods longer than three months.

Prescriptions prescribed and encounters with a MedicineInsight GP were searched for these patients in the study period defined. The relationship between a patient and a GP was defined through a record of an encounter and/or the prescribing of a prescription by unique provider id.

Eligible GPs were those who:

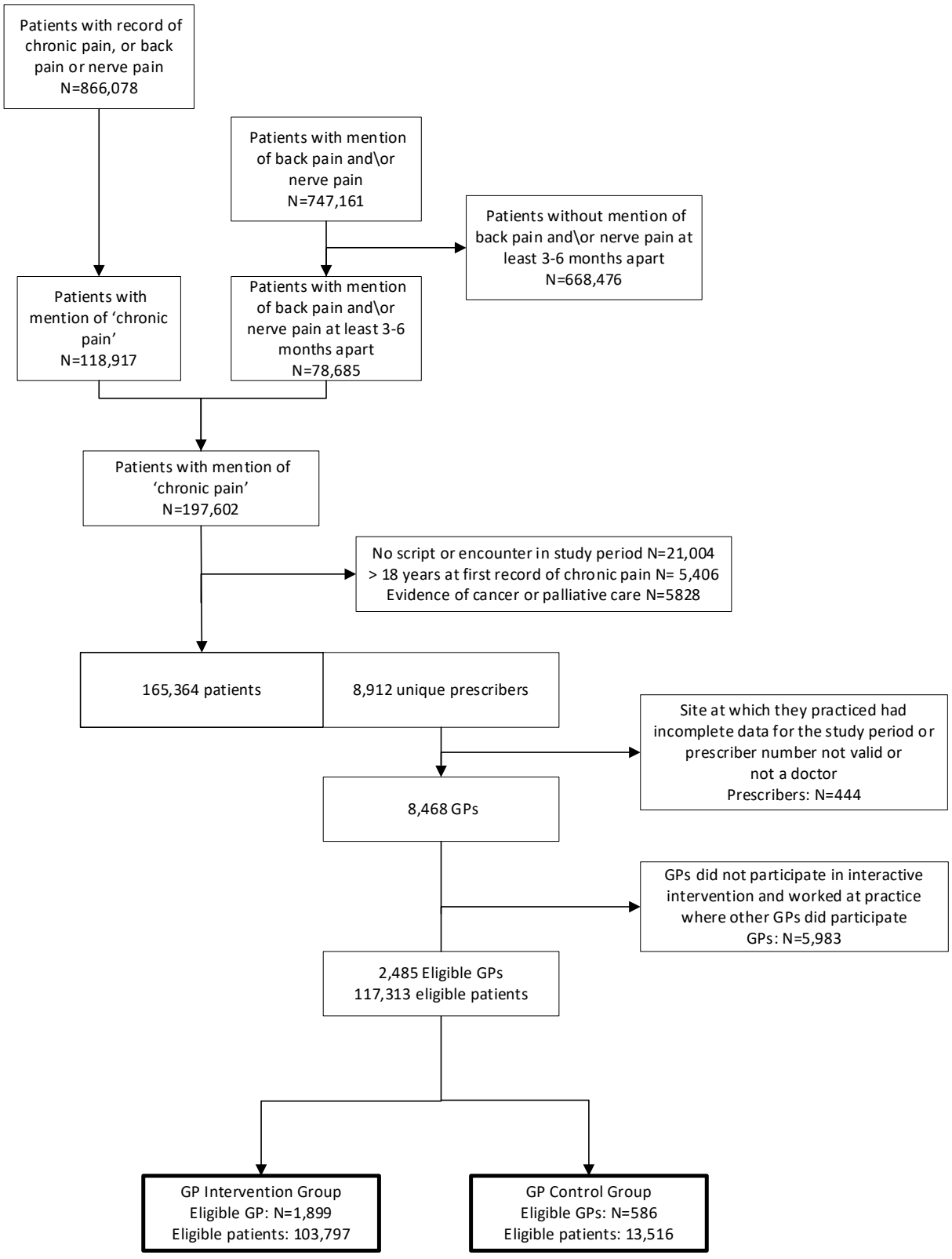
- Were classified as a doctor (Clinical_provider = doctor and/or Clinical_User_Type=1)
- Had a valid providerID (to ensure they can be tracked over time)
- Had a valid prescriber number (enables GPs to be assigned participating or non-participating)
- Attended a MedicineInsight practice which had complete data for the study period.

Exclusions: To remove the influence of contamination on our results, we excluded GPs if they had not participated in any interactive programs but had worked at a practice where other GPs had participated in these programs.

The eligible GPs were assigned to two groups:

- **GP intervention group:** GPs who participated in interactive components of the NPS Chronic Pain Program
- **GP control group:** GPs who did NOT participate in interactive components of the NPS Chronic Pain Program and did NOT attend a practice with one or more participating GPs.

Figure 5: PATIENT AND GP SELECTION PROCESS



Outcomes of interest

The outcomes of interest for this study were developed based on the Chronic Pain Program key messages and expected outcomes, and availability of data in the MedicineInsight database. The Chronic Pain Program aimed to address the quality use of medicines (QUM) issues of the inappropriate initiation and continuation of opioid prescribing for chronic non-cancer pain and aimed to improve pain control for patients. We expected the program to:

- Reduce the number of original opioid prescriptions (PBS and private) for the patients with chronic non-cancer pain.
- Reduce the number of patients with chronic pain attending general practices as a result of improved pain management
- Reduce the number of patients with chronic pain initiated on opioids.

We measured the impact of the intervention using the following indicators of these expected outcomes:

- The volume of opioid medicines prescribed by GPs for adult patients with chronic non-cancer pain (average monthly)
- The number of encounters with a GP for adult patients with chronic non-cancer pain (average monthly)
- The proportion of adult patients with chronic non-cancer pain newly prescribed an opioid medicine (opioid initiation). The initiation of an opioid was defined as where there were no prescriptions for any opioid-containing medicines of any formulation prescribed in the 24 months prior to the date of the initial prescription.

The results from the analysis compared the GP intervention group and the GP control group before and after the intervention.

Selected opioid medicines

The opioids investigated in this program were based on those targeted by the Program and used to conduct study one: codeine 30mg with paracetamol, fentanyl, hydromorphone, morphine and oxycodone and tapentadol (Table 12). Information on the prescribing of these medicines was extracted based on active ingredient and ATC recorded in the MedicineInsight data.

Exclusions: All injectable medicines and medicines where some formulations were approved for opioid dependence (buprenorphine and methadone).

Table 12: MEDICINES USED IN THE FINANCIAL IMPACT ANALYSIS (PART 2) OF THE 2015 CHRONIC PAIN PROGRAM

Medicine	ATC codes	Exclusions
Codeine 30mg + paracetamol	N02AJ06	Codeine formulations with less than 30mg
Fentanyl	N02AB03	Injectables
Hydromorphone (long acting)	N02AA03	Injectables
Hydromorphone (short acting)	N02AA03	Injectables
Morphine (long-acting)	N02AA01	Injectables
Morphine (short-acting)	N02AA01	Injectables
Oxycodone (long-acting)	N02AA05	
Oxycodone (long-acting) with naloxone	N02AA55	
Oxycodone (short-acting)	N02AA05	
Tapentadol	N02AX06	

Comparing intervention and control GPs and their patients

Table 13 describes the methods for calculating demographic characteristics of eligible patients and socio-demographics of GPs. No data are available about the demographic characteristics of the GPs in MedicineInsight, so GP demographics were based on the site at which they practice.

Statistical analysis of the difference between mean and median values of demographic variables for the GP intervention group and the GP control group was calculated using nonparametric tests. Comparisons of differences between proportions used Pearson chi-square tests.

Table 13: SUMMARY OF THE METHODS FOR CALCULATING SOCIODEMOGRAPHIC CHARACTERISTICS OF PATIENTS AND GPS

Characteristic	How operationalised
Patient Age	Prior to the intervention: 2014 - Year of birth After the intervention: 2016 - Year of birth Excludes patients with missing year of birth Calculated estimated mean and medians
Patient Gender	As recorded in the clinical Information system of the practice site (Male, Female, Indeterminate) Calculated the proportion of males and females of whole sample (including those with missing gender)
GPs: State/Territory	State/Territory was assigned based on the postcode for the GP's practice site
GPs: Rurality	Assigned ASGS Remoteness Areas 2011,[17] using the ABS mapping of the postcode for the GP's practice site (2012)
GPs: Socioeconomic status (SEIFA)	Assigned the Index of Relative Socioeconomic Disadvantage (IRSD),[18] using the ABS mapping of postcode of the GP's practice site (2012).

Time series analysis

For the first two outcomes of interest (opioid prescription volume and the number of encounters), a time series of the volume of the outcome of interest was calculated at a month time-step. The analyses were conducted using the Causal Impact package of R.(16) The intervention was defined as starting from one time point, June 2015.

Data were obtained from the NPS MedicineWise participation database to analyse the impact of active participation in the Chronic Pain Program. GPs were allocated to the GP intervention group or the GP control group.

A counterfactual time series was constructed for the intervention group on what the outcome of interest would have been had this group *not* actively participated in the Chronic Pain program. This counterfactual time series was constructed using data on the pre-intervention behaviour of the GP intervention group and the pre- and post-intervention behaviours of the GP control group.

For the third outcome measure (initiations of opioid medicines), a generalized linear model (GLM) was used to estimate the expected average ratio of patients initiated on an opioid medicine for each of the four initiation periods using PROC GENMOD in SAS v9.3. The use of this model is appropriate for this analysis as there were repeated measurements on individual participants at different time points and this model specification estimates the within-subject and between-subject correlation.

Results

MedicineInsight data from 2,485 eligible GPs were available for this evaluation. The GP intervention group included 1,899 GPs. This represents 26% of all Australian GPs who participated in an interactive intervention as part of the 2015 Chronic Pain Program. An additional 586 GPs were

assigned to the GP control group, representing 10% of the 6,569 GPs that had data in the MedicineInsight database for the study period and did not actively participate.

There were 117,313 eligible patients with chronic non-cancer pain who had encounters with eligible GPs during the study period. A total of 103,797 eligible patients were included in the GP intervention group and 13,516 eligible patients in the GP control group.

Patient demographics

The demographics of patients with chronic non-cancer pain one year prior to the intervention period (2014) and one year after the intervention (2016) is presented in Table 14. Overall patients' age and gender were similar between the two groups for both periods. A very small, not practically significant, but statistically significant difference in mean and median age was found between the two groups both prior to the intervention and after the intervention. The proportion of females in both groups and during and following the intervention ranged between 58.2% and 59.7% in both groups.

Table 14: PATIENT DEMOGRAPHIC CHARACTERISTICS BEFORE AND AFTER INTERVENTION, GP INTERVENTION AND CONTROL GROUPS

Demographic Characteristic	Prior to the intervention (2014)		Following the intervention (2016)	
	GP intervention group N=54,040	GP control group N=8,867	GP intervention group N=57,506	GP control group N=9,576
Mean Age (95% CI)	57.39 (57.24, 57.54)	59.09 (58.73, 59.45) ∞	58.11 (57.97, 58.25)	59.35 (59.00, 59.70) ∞
Median Age	58	60∞	59∞	60∞
Gender – Female	59.72%	59.17%	59.06%	58.15%∞
Gender – Male	40.28%	40.83%	40.67%	41.85%

* based on the demographic information of patients with chronic non-cancer pain

∞ P<0.05

GP socio-demographics and service characteristics

The socio-demographics and service characteristics of GPs one year prior to the intervention period (2014) and one year after the intervention (2016) are presented in Table 15. The demographic and practice profile of each GP group was consistent over the two periods. However, there were marked differences between the GP intervention and GP control groups. The GP control group were more likely to practice in NSW compared with the GP intervention group (2014: 51% vs 30%%; 2016: 49% vs 30%). A larger proportion of the GP control group worked at practices in major cities compared to the GP intervention group (2014: 74.5% vs 58.1%; 2016: 74.4% vs 61.4%). The practices of the intervention GP group were more likely to be in socio-economically disadvantaged areas compared with the control GP group.

On average, the GP intervention group had more patients with chronic non-cancer pain than the GP control group and as might be expected had a greater number of encounters per GP with patients with chronic non-cancer pain (Table 15).

Table 15: GP SOCIODEMOGRAPHIC AND SERVICE CHARACTERISTICS BEFORE AND AFTER INTERVENTION, GP INTERVENTION AND CONTROL GROUPS

GP Characteristics	Prior to the intervention (2014)		Following the intervention (2016)	
	GP intervention group N=1,140	GP control group N=340	GP intervention group N=1,303	GP control group N=402
State*				
ACT	1.49%	5.29%	2.29%	4.98%
NSW	29.62%	51.47%	29.95%	48.51%
NT	0.61%	0.29%	0.31%	0.75%
QLD	20.25%	12.06%	19.02%	13.68%
SA	2.54%	3.53%	2.83%	4.48%
TAS	8.15%	1.76%	7.33%	1.74%
VIC	28.48%	12.65%	28.11%	12.94%
WA	8.85%	12.94%	10.16%	12.94%
Remoteness*				
Major cities	58.10%	74.49%	61.37%	74.44%
Inner regional	27.19%	17.89%	25.63%	17.12%
Outer regional	13.59%	7.33%	12.32%	7.69%
Remote/ very remote	1.13%	0.29%	0.68%	0.74%
SEIFA disadvantage*				
1 most disadvantaged	16.84%	12.61%	15.14%	10.17%
2	16.92%	13.49%	16.17%	13.40%
3	24.49%	14.37%	24.89%	15.14%
4	19.02%	19.65%	19.50%	20.60%
5 least disadvantaged	22.39%	36.36%	23.93%	36.72%
Not Recorded	0.34%	3.23%	0.37%	3.97%
Service characteristics				
Mean no. of eligible patients per GP (95% CI)	76.64 (72.82, 80.45)	48.02 (43.40, 52.64) ∞	74.56 (71.20, 77.92)	44.93 (40.82, 49.04) ∞
Mean no. of encounters with eligible patients per GP (95% CI)	87.91 (83.36, 92.45)	54.2 (48.86, 59.55) ∞	86.00 (82.01, 89.98)	50.73 (46.05, 55.41) ∞
Median no. of encounters with eligible patients per GP	68	42∞	69	40∞

* based on the demographic information of the site at which the GP practiced

∞ P<0.05

Outcome measure 1: Prescribing behaviour: Volume of prescriptions prescribed to patients with chronic non-cancer pain

There were 51,584 unique patients who were prescribed a relevant opioid prescription by 1,899 intervention GPs and 8,560 unique patients who received a relevant opioid prescription by 586 control GPs during the study period.

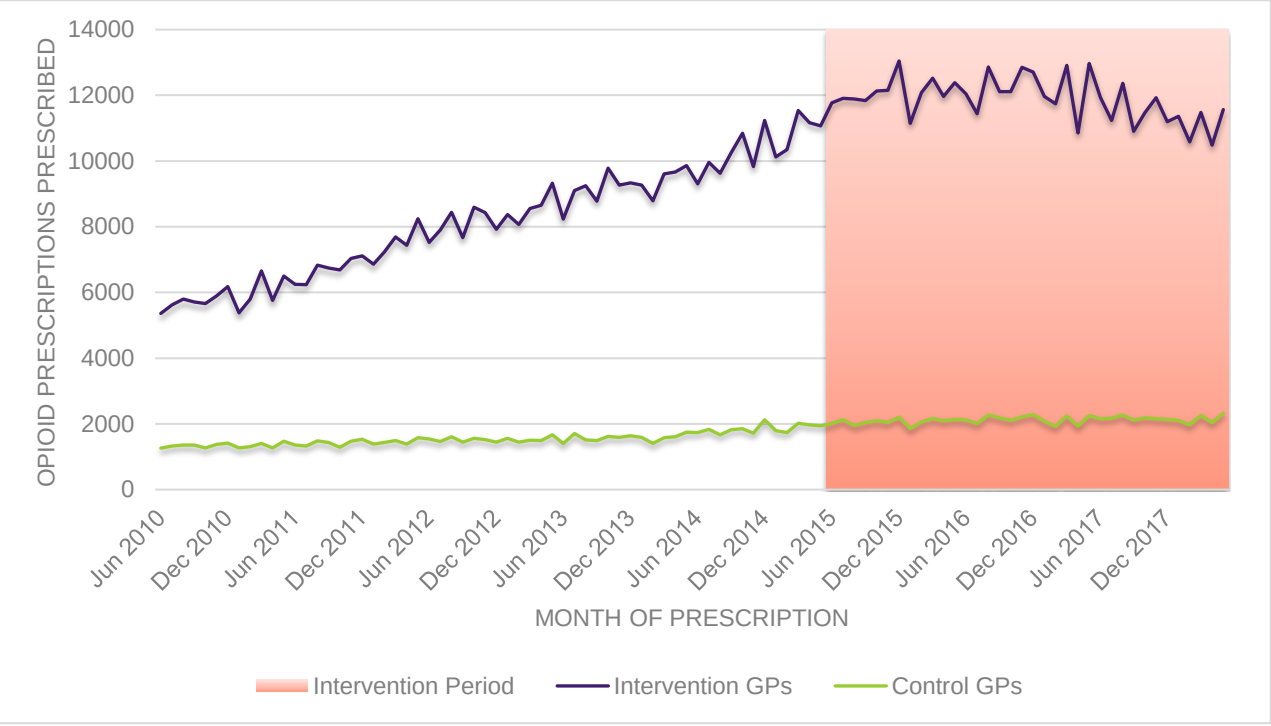
The average monthly change in volume of opioid prescriptions for patients with chronic pain decreased between the pre-intervention period and the post-intervention period from 2.76% to 0.02% in the GP intervention group and from 1.78% to 0.71% in the GP control group (Table 16).

Table 16: AVERAGE MONTHLY CHANGE IN VOLUME OF OPIOID PRESCRIPTIONS FOR PATIENTS WITH CHRONIC PAIN, PRE AND POST THE INTERVENTION, GP INTERVENTION AND CONTROL GROUPS

Indicator	GP Intervention Group		GP Control Group	
	Prior to the intervention (2014)	Following the intervention (2016)	Prior to the intervention (2014)	Following the intervention (2016)
Average monthly change in volume of opioid prescriptions prescribed to eligible patients	2.76%	0.71%	1.78%	0.02%

Figure 6 shows the monthly volume of prescriptions dispensed to patients with chronic pain by GP group. There was a significant reduction in the volume of opioid prescriptions prescribed in the patients of intervention GPs following the intervention.

Figure 6: VOLUME OF OPIOID PRESCRIPTIONS DISPENSED TO PATIENTS WITH CHRONIC PAIN, GP INTERVENTION AND CONTROL GROUPS



During the post-intervention period, the GP intervention group had an actual average monthly opioid prescription volume of 11,820. The time series model estimated the modelled average monthly volume of prescriptions should the intervention have not occurred was 12,780 (95% CI: 12,170-13,380) (Table 17; Figure 7).

The relative intervention effect was calculated as the difference between the modelled (predicted) and the actual monthly volume and showed a reduction of 960 prescriptions per month (95% BCI: -1,560, -360). This translates to an overall reduction in the post-intervention period of 34,575 prescriptions (95% BCI: -56,138, -12,815). On average the monthly volume of opioid prescriptions

prescribed was 7.5% lower for the GP intervention group compared to the GP control group following the start of the Chronic Pain program (95% BCI = -12%, -3%, p = 0.002) (Table 17).

Table 17: IMPACT OF THE INTERACTIVE COMPONENTS OF THE CHRONIC PAIN PROGRAM ON OPIOD PRESCRIBING

Intervention level analysed	Actual average monthly volume of prescriptions after intervention (June 2015–May 2018)	Modelled average monthly volume of prescriptions after intervention (June 2015 –May 2018) had the intervention not occurred (BCI 95%)	Relative intervention effect (BCI 95%)
Intervention GP (participated in Interactive interventions)	11,820	12,780 (12,170- 13,380)	-7.5% (-12%, -2.8%)*

* p=0.002

The first panel of Figure 7 presents the actual data and the predicted volume with 95% Bayesian credible intervals (light blue) of prescriptions. The second panel plots the difference between the actual data and the predicted data, known as the pointwise causal effect attributed to the program. The third panel adds up these pointwise contributions at each data point from the second panel which results in a cumulative effect of the intervention. The 95% Bayesian credible interval of the causal effect is plotted in this panel.

Figure 7: MODELLED MONTHLY VOLUME OF PRESCRIPTIONS AND ESTIMATED CAUSAL EFFECT

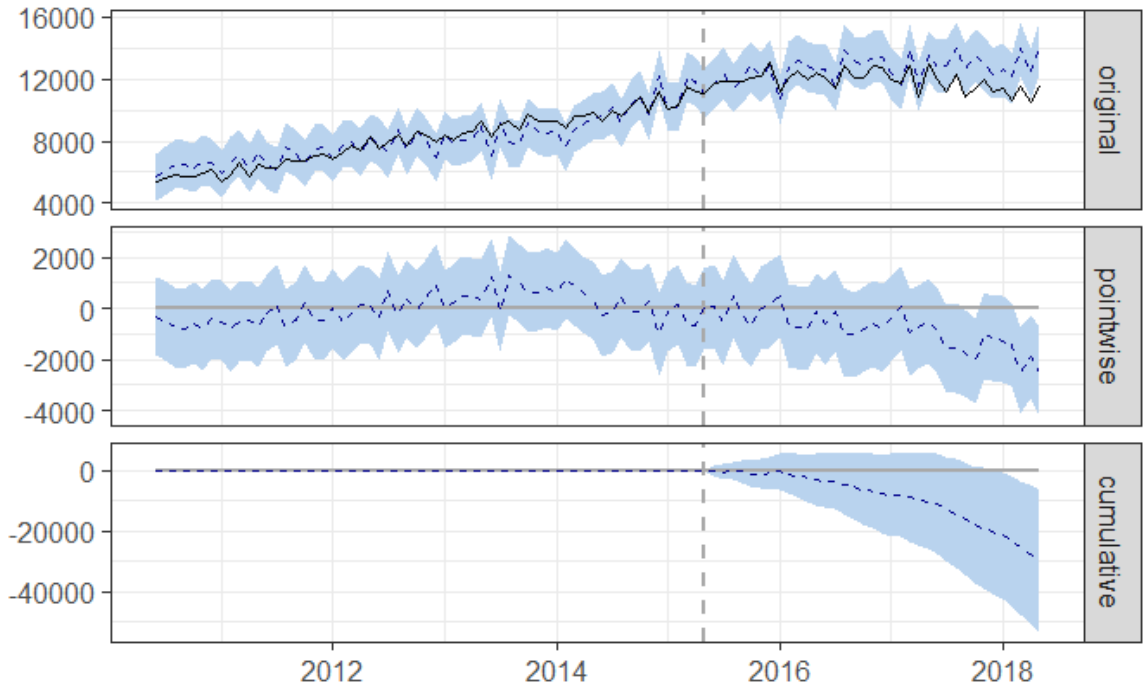


Table 18 shows the GP opioid prescribing behaviour by active medicine ingredient for adult patients with chronic non-cancer pain, before and after the intervention program. There was a significant relative decrease of the average monthly volume of oxycodone (including combinations with naloxone) and morphine. This relative intervention effect was a decrease of 5.2% (95% BCI: -9.9%, -0.41%) and 11% (95% BCI: -14%, -7.8%) respectively. There were no significant relative intervention effects seen in medicine types with active ingredients of codeine and paracetamol, fentanyl, dihydrocodeine and hydromorphone. The monthly volume of Tapentadol increased by 26% (95% BCI: 9.8%, 42%).

Table 18: IMPACT OF THE INTERACTIVE COMPONENTS OF THE CHRONIC PAIN PROGRAM ON OPIOD PRESCRIBING BY OPIOID ACTIVE INGREDIENT

Intervention level analysed	Active medicine ingredient	Actual average monthly volume of prescriptions post-intervention	Modelled average monthly volume of prescriptions post-intervention had the intervention not occurred (BCI 95%)	Relative intervention effect (BCI 95%)
Intervention GP (participated in Interactive interventions)	Codeine + Paracetamol	2,116	2,168 (2091, 2243)	-2.4% (-5.9%,1.1%)
	Fentanyl	704	701 (669, 733)	0.47% (-4.1%, 5%)
	Oxycodone (and combinations with naloxone)	6,955	7,333 (6,985, 7678)	-5.2% (-9.9%, -0.41%)*
	Morphine	756	847 (821, 871)	-11% (-14%, -7.8%)*
	Tapentadol	1,011	801 (670, 932)	26% (9.8%, 42%)*
	All other (Dihydrocodeine, Hydromorphone)	274	283 (244, 321)	-2.8% (-16%, 11%)

*p <0.05

Outcome measure 2: Number of encounters with patients with chronic non-cancer pain

There were 103,797 unique patients who recorded an encounter with an intervention GP and 13,516 unique patients who had an encounter with a control GP during the study period.

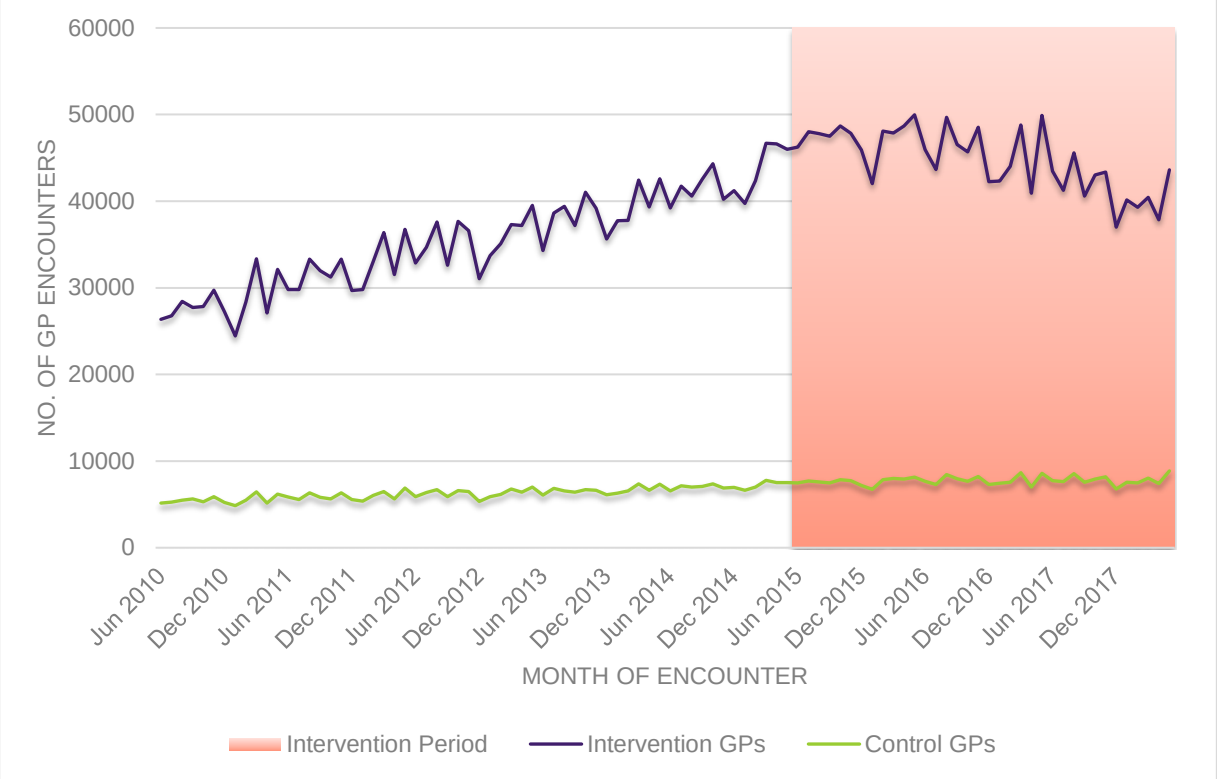
Table 19 presents the average monthly count of encounters for patients with chronic pain, pre and post the intervention for the two GP groups. The average monthly change in the count of encounters for patients with chronic pain decreased from a growth rate of 1.44% to -0.36% in the GP intervention group and from 1.40% to 0.56% in the GP control group.

Table 19: AVERAGE MONTHLY CHANGE IN NUMBER OF ENCOUNTERS FOR PATIENTS WITH CHRONIC PAIN, PRE AND POST THE INTERVENTION, GP INTERVENTION AND CONTROL GROUPS

	Intervention GPs		Control GPs	
Indicator	Prior to the intervention (2014)	Following the intervention (2016)	Prior to the intervention (2014)	Following the intervention 016)
Average monthly change in volume of encounters with eligible patients	1.44%	-0.36%	1.40%	0.56%

The trend in the number of unique encounters with the GP intervention group and the GP control group is presented in Figure 8. There was a significant reduction in the volume of encounters with the GP intervention group following the intervention.

Figure 8: VOLUME OF GP ENCOUNTERS WITH PATIENTS WITH CHRONIC NON-CANCER PAIN, GP INTERVENTION AND CONTROL GROUPS



During the post-intervention period, the GP intervention group had an average monthly number of encounters of 44,762. The time series model estimated the modelled average monthly number of encounters should the intervention have not occurred was 47,761 (95% BCI: 46,219, 49,321; Table 20; Figure 9).

The first panel of Figure 9 presents the actual data and the predicted volume with 95% Bayesian credible intervals (light blue) of prescriptions. The second panel plots the difference between the actual data and the predicted data, known as the pointwise causal effect attributed to the program. The third panel adds up these pointwise contributions at each data point from the second panel which results in a cumulative effect of the intervention. The 95% Bayesian credible interval of the causal effect is plotted in this panel.

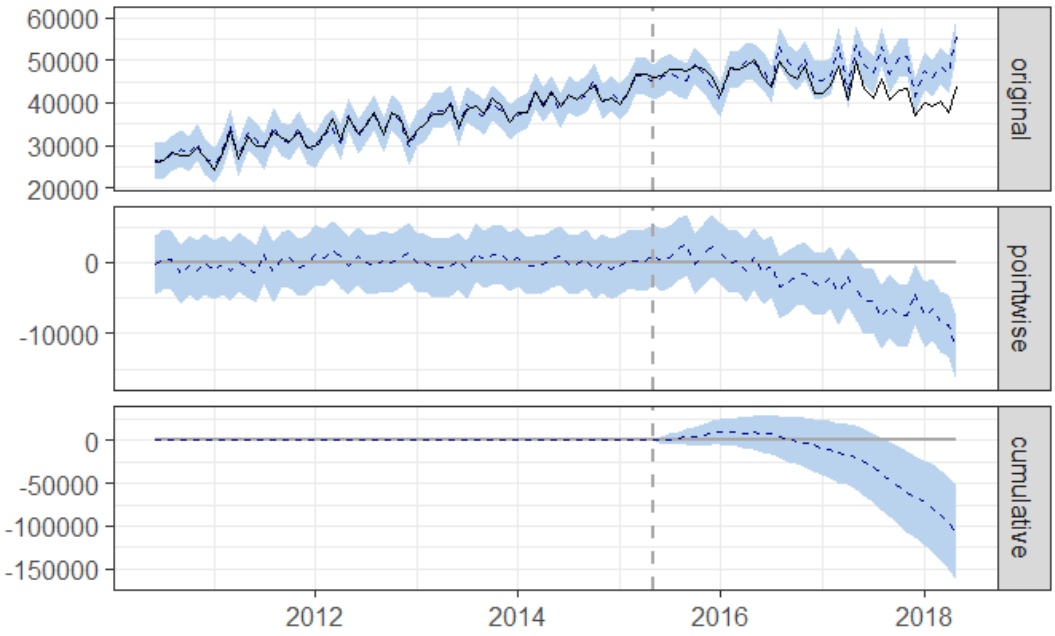
The relative intervention effect was calculated as the between the modelled (predicted) and the actual monthly number, showing a reduction in 2,998 encounters per month (95% BCI: -4,559, -1,457). This translates to an overall reduction in the post-intervention period of 107,938 encounters (95% BCI: -164,117, -52,438). On average the monthly number of GP encounters was 6.3% lower for the GP intervention group comparing to the GP control group following the start of the Chronic Pain program (95% BCI = -9.5%, -3%, p<0.001).

Table 20: IMPACT OF THE INTERACTIVE COMPONENTS OF THE CHRONIC PAIN PROGRAM ON GP ENCOUNTERS FOR PATIENTS WITH CHRONIC NON-CANCER PAIN

Intervention level analysed	Actual average monthly volume of GP encounters post-intervention	Modelled average monthly volume of GP encounters post-intervention had intervention not occurred (BCI 95%)	Relative intervention effect (BCI 95%)
GP Intervention Group	44,762	47,761 (46,219, 49,321)	-6.3% (-9.5%, -3%)*

* p<0.001

Figure 9: MODELLED VOLUME OF ENCOUNTERS AND ESTIMATED CAUSAL EFFECT



Outcome measure 3: Proportion of patients with chronic non-cancer pain initiated on opioid medicines

The model used 1,755 subject levels of unique prescriber numbers and the within-subject group difference was estimated at the four time periods. Of these 1,755 prescribers (across GP intervention and GP control groups), 733 had some missing information. GPs were excluded completely or in certain initiation periods if there were no observations in the denominator, that is, no patients presenting themselves with suspected diagnosis of chronic non-cancer pain during any of the initiation time periods. The GP control group was used as the reference group, while Period 2 was used as the reference time period.

Table 21 presents the difference between the expected average proportion of initiated patients from period 1 (baseline) to period 4 for the Intervention and GP control groups. There was no significant difference between the 2 groups at the 4 time periods.

Table 21: IMPACT OF THE INTERACTIVE COMPONENTS OF THE CHRONIC PAIN PROGRAM ON OPIOD INITIATIONS

Intervention vs Control	Difference in expected Average Proportion of Initiated Patients (95% CI)	Standard Error	P-value
Period 1 - 2014	-5.55% (-14.40%, 3.31%)	0.05	0.22
Period 2 – 2015 (launch of program)	-0.27% (-8.52%, 7.98%)	0.04	0.95
Period 3 - 2016	7.99% (-1.49%, 17.48%)	0.05	0.10
Period 4 - 2017	0.87% (-7.55%, 9.29%)	0.04	0.84

Figure 10 presents the trend in the estimated average proportion of patients initiated on opioid medicines and the 95% confidence interval surrounding these estimates over the 4 time periods.

The score statistics produced in SAS for type 3 GEE analysis showed the intervention flag variable was not significant (p-value 0.80) and the intervention flag interacting with each time period (p-value 0.12) was non-significant.

Figure 10: PROPORTION OF PATIENTS INITIATED ON OPIOID MEDICINES, GP INTERVENTION AND CONTROL GROUPS

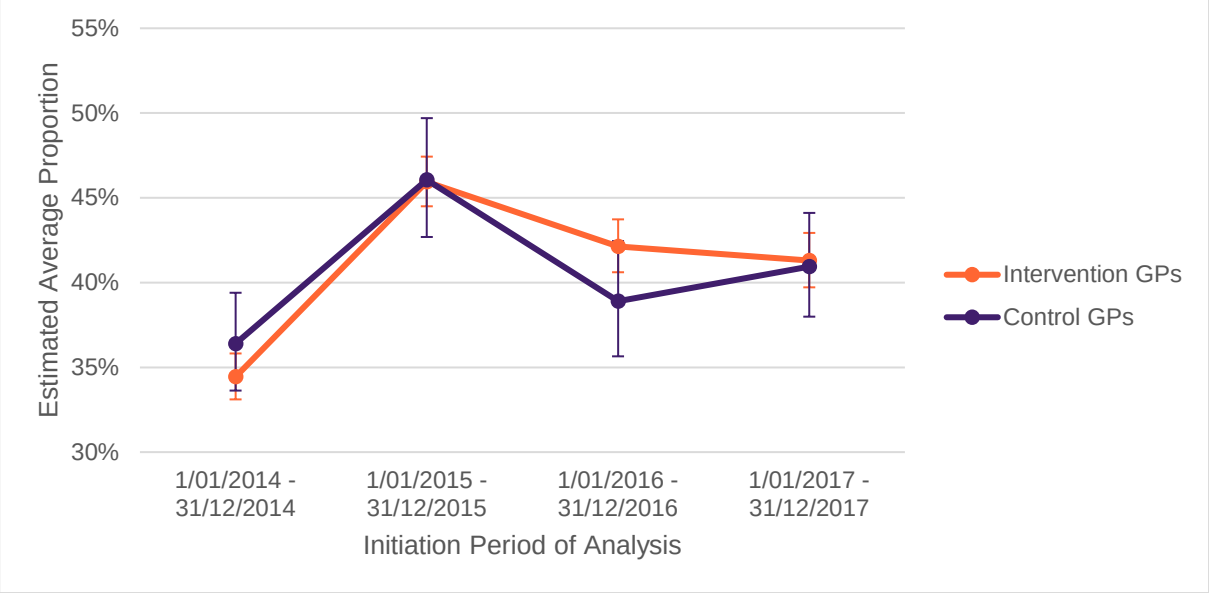


Table 22 presents difference in the average proportion of initiated patients for the GP intervention group and GP control group separately compared over the two periods (3 and 4) to the period of the launch of the program, period 2. The difference in the expected average ratio between period 1 and period 2, representing the baseline slope of the pre-intervention period, is an increasing rate of 28.82% (95% CI: 24.72% - 32.91%). There was a reduction in patients initiated on opioids for both GP intervention and GP control groups, suggesting that both groups may have been influenced by components of the national Program, such as the personalised Pharmaceutical Benefits Scheme (PBS) feedback report sent to all registered GPs.

Table 22: DIFFERENCE IN EXPECTED AVERAGE PROPORTION, POST-INTERVENTION

Group	Period comparison	Difference in expected Average Proportion of Initiated Patients (95% CI)	Standard Error	P-value
GP Intervention Group	Period 3 vs Period 2	-8.63% (-12.55%, -4.71%)	0.02	<.0001
	Period 4 vs Period 2	-10.65% (-14.69, -6.62%)	0.02	<.0001
GP Control Group	Period 3 vs Period 2	-16.89% (-27.56%, -6.22%)	0.05	0.00
	Period 4 vs Period 2	-11.79% (-21.82%, -1.76%)	0.05	0.02

Note: Period 2 = Launch of the program

Stage 2: Economic evaluation

Method

Evaluation design

A ***cost benefit analysis*** was conducted to compare the cost and benefits of the GPs participating in the interactive components (GP intervention group) of the NPS MedicineWise 2015 Chronic Pain Program using MedicineInsight data. The relationship between program costs and measurable outcomes is evaluated at the GP level and is based on the findings from the MedicineInsight GP level program effectiveness analysis in Stage 1 of this study.

The measures used in this analysis are:

- The cost of the resources required to deliver the 2015 program (outlined in Table 6)
- The benefits of the program expressed as the monetary value of the effects generated by the program. In this analysis, the benefits are restricted to the direct estimated savings associated with (1) the reduction in opioids prescribing per participating GP and (2) the reduction in encounters with the GP intervention group

Patient initiations on opioid medicines were excluded from this analysis given there was no significant difference between the GP intervention group and the GP control group in Stage 1.

The cost-benefit analysis was conducted by calculating the program net benefit and the benefit-cost ratio per intervention GP. The *net benefit* is calculated as the difference between the benefits and the costs per intervention GP. Values higher than zero indicate that the benefits exceed the costs. The *benefit-cost ratio* is calculated as the ratio of benefits to costs. Values higher than one indicate that the benefits exceed the costs.

Data sources

Program cost data is presented previously in Table 6. The total costs of the Chronic Pain program were $3,281,895. This was separated into a base cost for the program (**$1,504,134**; included all program development and the implementation of all non-visiting intervention) and cost of delivering the one-to-one and small group-based visiting to GPs (**$1,934,128**). Costs were calculated at the GP level for each outcome. See Table 23 for details of variables including costs and calculations.

As MedicineInsight data does not contain information on the individual PBS item numbers nor the costing and concession status at the time of prescribing for opioid prescriptions, we estimated the cost of an opioid prescription averted using the average cost to the PBS for dispensed opioid medicines, as calculated in Study 1, Stage 2. This weighted average cost is $27.36.

This cost of script averted was deemed appropriate because:

– pricing sensitivity analysis is limited given the patient's concessional status and the time it takes to reach the safety net threshold is difficult to account for in terms of prescriptions averted, and

– prescription item information in MedicineInsight is not linked to a PBS item code making further sensitivity analysis complicated.

Similarly, the cost information is not available for GP encounters and the type of encounter billed to MBS is only available for some practices. So, we used the cost of MBS item code 23 (standard consultation with a GP) at June 2017, $37.05, to estimate the cost of a GP encounter averted over the study period. This is discounted to a value of $32.01.

Table 23: VARIABLES USED IN COST-BENEFIT ANALYSIS FOR THE 2015 CHRONIC PAIN PROGRAM, PER INTERVENTION GP

Variables	
Total program costs (95% CI)	$3,281,895 ($2,945,802 - $3,617,989)
Number of GPs practicing in Australia at time of program who were sent the PBS feedback intervention	26,491
Number of GPs who participated in an interactive intervention	7,533
Number of GPs who participated in an interactive intervention – in the analysis	1,899
Number of months of evaluation (post intervention)	36
Program costs per participating GP (95% CI) (f=a/c)	$435.67 ($391.05, $480.28)
Estimated cost of opioid script (Discounted)- see Study 1 Stage 2	$27.36
Estimated cost of GP encounter (Discounted)	$37.05
Number of opioid prescription items prescribed averted for study 2 intervention GPs	34,575
Number of GP encounters averted for study 2 intervention GPs	107,938

Time frame

The timeframe for the evaluation of program effectiveness and benefit was the 36 months post-program, July 2015 to May 2018 inclusive. (Note: Stage 1 of this study calculated effectiveness over 36 months)

Perspective

The Australian Government Department of Health (DoH), funds both the Quality Use of Medicines (QUM) program at NPS MedicineWise and the PBS. Only monetary costs and benefits associated with DoH funding to the NPS MedicineWise QUM program were including in this economic evaluation.

Discounting and cost standardisation

A discounting rate of 5% p.a. was applied to all costs and benefits that occurred after the program began in 2013-14. All program costs were adjusted to 2016-17 currency, the last year that costs and benefits occurred, using Australia CPI published by the ABS.(15)

Costing prescriptions and GP encounters

The weighted average cost of an averted opioid medicine to the PBS was estimated at $27.36 in Study 1. A tolerance limit of -10%/+10% applied to this average cost produces a lower and upper weighted average cost of $24.62, $30.10 respectively.

The MBS Schedule contains pricing information as at June 2017 for the most common GP consultation codes. These codes were selected using the item category "Group A1 – General Practitioner Attendances to which no other item applies", which consists of services related to the professional attendance by a GP at consulting rooms.

Table 24 presents the proportion of GP encounter types billed as consultations with patients with chronic non-cancer pain derived from a sample of the intervention GP group (n=1,203) in the pre-intervention period. MBS item numbers 37, 47 and 23 represent 1.37% of the sample and have derived fees so were excluded from this analysis.

Table 24: MBS SCHEDULE CONSULTATION AND FEE INFORMATION, JUNE 2017

MBS Item No.	Fee as at June 2017	Benefit as at June 2017	Discounted	Proportion MedicineInsight Data
3	$16.95	Benefit: 100% = $16.95	$14.64	4.10%
23	$37.05	Benefit: 100% = $37.05	$32.01	75.83%
36	$71.70	Benefit: 100% = $71.70	$61.94	18.51%
44	$105.55	Benefit: 100% = $105.55	$91.18	1.57%
			Weighted Average Cost of GP Encounter	$37.77

Based on the approximate proportion of encounter types, the average weighted cost of a GP encounter was estimated as $37.77. This is calculated as the discounted value of a GP encounter by its proportion as estimated in MedicineInsight data.

Multivariate Sensitivity analysis

We conducted a sensitivity analysis to systematically examine how the outcome of cost-benefit analysis changes with variations in inputs and assumptions. We calculated multiple costing scenarios for the benefit and the confidence intervals surrounding the effects from each outcome. The scenarios focused on testing the assumptions of costing:

- Averted prescriptions
- Averted GP encounters
- Program costs per GP

Sensitivity analysis was based on the average cost to the PBS per opioid prescription dispensed, derived from Study 1 Stage 2 of this report. This approach takes into account the pricings of different opioid medicines, the concessional status and any safety net threshold a patient reaches. A tolerance limit of an increase and/or decrease in 10% to the average cost incurred to the PBS for dispensed opioid medicines was applied in this sensitivity analysis.

The cost of a GP encounter was tested using prescribing and encounter behaviour of the intervention GP group from MedicineInsight data. Site billing data in MedicineInsight was used to estimate the proportion of the type of GP encounters billed to patients with chronic non-cancer pain with participating GPs; MBS services for encounters are costed differently. Program costs, including an upper and lower limit have been calculated in Study 1, Stage 2 of this report.

The costing scenarios for the multivariate sensitivity analysis will be calculated using these limits as follows:

- Base Case: Point estimates of the program cost, the effect and the benefit
- Scenario 1 **Maximum costing**: The upper confidence limit of the program cost per GP, the upper confidence limit of the effect and the highest cost attributed to averted scripts and encounters
- Scenario 2 **Minimum costing**: The lower confidence limit of the program cost per GP, the lower confidence limit of the effect and the lowest cost attributed to averted scripts and encounters
- Scenario 3 **Least Favourable costing**: The upper confidence limit of the program cost per GP, the lower confidence limit of the effect and the lowest cost attributed to averted scripts and encounters
- Scenario 4 **Most Favourable costing**: The lower confidence limit of the program cost per GP, the upper confidence limit of the effect and the highest cost attributed to averted scripts and encounters.

Results

Table 25 presents the results from the cost benefit analysis of the Chronic Pain program. The total net benefit and benefit to cost ratio are used to compare the cost of the program to the benefit gained from the averted opioid prescriptions and GP encounters per intervention GP.

The total net benefit is the difference in the cost of changing prescribing and GP attendance patterns and the costs of the NPS MedicineWise program per participating GP, i.e. $2,317.30-$435.67 = **$1,881.63**. This represents a net savings as a result of the program.

The benefit to cost ratio is calculated by dividing the estimated cost of changing prescribing patterns by the cost of the NPS MedicineWise program. Benefit to cost ratio $2,317.30/$435.67 = 5.32. Values higher than one indicate that the benefits exceed the costs. The value of 5.32 indicates that for every dollar spent on the program, $5.32 was gained in monetary benefit.

Table 25: COST BENEFIT ANALYSIS RESULTS FOR 2015 NPS MEDICINEWISE CHRONIC PAIN PROGRAM

Outcome	Total outcomes 2015/16-2017/18 (95% CI)	Outcome per intervention GP (95% CI)	Benefit per intervention GP (95% CI)
Number of opioid prescription items prescribed averted	34,575 (12,815-56,138)	34,575/1,899 = 18.21 (95% CI: 6.75, 29.56)	18.21 x $27.36 =$498.14 ($184.63, $808.81)
Number of GP encounters averted	107,938 (52,438-164,117)	107,938/1,899 = 56.84 (95% CI: 27.61-86.42)	56.84 x $32.01 =$1,819.16 ($883.77, $2,123.34)
Total benefit per intervention GP			$2,317.30 ($1,068.41, $3,574.79)
Program cost per intervention GP			$435.67
Net benefit per intervention GP			$1,881.53 ($632.74, $3,139.12)
Benefit to Cost Ratio (Benefit/Program cost)			5.32 (2.45-8.21)

Multivariate Sensitivity analysis

A multivariate sensitivity analysis was performed to estimate the combination of changes in the effect and cost of scripts and encounters compared to program costs (Table 26).

Table 26: SENSITIVITY ANALYSIS – COST-BENEFIT RATIO

	Base-case	Scenario 1 (Maximum costing)	Scenario 2 (Minimum costing)	Scenario 3 (least favourable costing)	Scenario 4 (most favourable costing)
Cost of program variation per intervention GP	$435.67	$480.29	$391.05	$480.29	$391.05
Effect: averted opioid dispensing variation per intervention GP	18.21	29.56	6.75	6.75	29.56
Benefit: savings from averted opioid dispensing variation per intervention GP	$498.14	$889.756	$166.19	$166.19	$889.76
Effect: averted encounters per intervention GP	56.84	86.42	27.61	27.61	86.42
Benefit: savings from averted opioid dispensing variation per intervention GP	$1,819.16	$3,264.08	$883.80	$883.80	$3,264.08
Net Benefit	$1,881.53	$3,673.55	$658.93	$569.69	$3,762.79
Benefit to cost ratio	5.32	8.65	2.69	2.19	10.62

In the most favourable scenario, in which the minimum program costs and the maximum benefit and effect was used, the net benefit was $3,763 per intervention GP, with a benefit to cost ratio of 10.62. In the least favourable scenario, in which the maximum program costs and the minimum benefit and effect was used, there was a reduced net benefit of $569.69 per intervention GP, the benefit to cost ratio was 2.19.

Discussion

Using GP clinical data from the MedicineInsight database, this study found that that participation in the interactive interventions of the Chronic Pain Program had a significant impact on the GP intervention groups' prescribing of opioid prescriptions and encounters for patients with chronic non-cancer pain. This resulted in:

- 7.5% reduction in volume of opioid medicine prescriptions (n=12,780 scripts) and
- 6.3% reduction in the number of encounters with GPs for patients with chronic pain (n=47,761 encounters).

This program impact was associated with a benefit of $2,317 per intervention GP for the period July 2015 to June 2018. The cost of the development and delivery of the Chronic Pain program was $436 per intervention GP. The cost benefit analysis found a net benefit of the program of $1,882 from the perspective of the payer, the Australian Government Department of Health. The benefit to cost ratio of the program was 5.32. The value of 5.32 indicates that for every dollar spent on the program, $5.32 was gained in monetary benefit, and thus the program represents an efficient use of public resources.

When sensitivity analyses were conducted varying program costs; increases in costs to prescriptions and encounters; and the effect estimates of the Chronic Pain program on prescribing and GP encounters, the variation in benefit to cost ratio varied from 2.19 (least favourable scenario) to 10.62 (most favourable scenario). Attributing the highest program costs and the lowest effect estimates, a benefit to cost ratio of 2.19, is more than double the return on an investment of $1 per intervention GP.

The positive impact of the program on reducing opioid prescriptions was supported by the findings from Study 1 and previous evaluations of the program.

The strengths of cost-benefit analysis include the quality of the data sources used and the ability of the time series method to accurately estimate the attributable effect of the interactive components of the Chronic Pain program. We linked MedicineInsight data to NPS MedicineWise participation data enabling the identification of GP exposure to Chronic Pain program interventions. This allowed us to separate out GPs who participated in the NPS interactive interventions and to examine the effect that these interventions had beyond other aspects of the national program. The time-series analysis used the trend for GPs who did not participate in interactive interventions and who did not work at a practice where other GPs had participated in the interactive components as a covariant in the model to predict the participating GPs trend had they not participated in an interactive intervention. This allowed for the removal of the influence of any intervention GP on the control GP group.

MedicineInsight data is extracted directly from the GP clinical software. Data on prescriptions and GP encounters is well documented and is not influenced by recall or self-report biases. The dataset also captures information about the patient's condition which allows for a more targeted analysis of the impact on specific patient groups such as patients with chronic non-cancer pain.

Results should be interpreted with caution as not all confounding variables can be controlled for in this analysis. Although the age and gender distribution of patients was similar for both the GP intervention and GP control groups, there was significant variations in the socio-demographic variables and the average number of encounters and patients with chronic pain per GP. Some of this difference may be explained by GPs who manage patients with chronic pain being more receptive to participating in programs to support their patient management. General practitioners who participated in the MedicineInsight data collection program are also a self-selected group and the results from analysis using their data may have limited generalisability to the total GP population. The impact of patients of other intervention GPs not present in MedicineInsight data to obtain opioid prescriptions cannot be determined. The results from Study 1 support the reduction in opioid prescriptions found in this study.

In the future, consideration of other statistical techniques such as propensity score matching could be applied to estimate and account for potential confounding between the GP intervention and GP control groups, ultimately assisting in accounting for self-selection bias in an observational study. Weighting the control series to ensure similar characteristics between the two groups can also be considered. These statistical techniques would require feasibility and an assessment of its appropriateness in its application to MedicineInsight data.

DISCUSSION AND CONCLUSION

The effectiveness of the different levels of the intervention on a range of outcomes was consistent with the aims of these interventions. Study 1 showed the national Chronic Pain program, including interactive interventions such as one-to-one visiting and other interventions including prescribing (PBS) feedback and widespread information provision, was effective at reducing the dispensing of opioid prescriptions. Study 2 compared opioid prescribing, GP encounters and the opioid initiations in patients with chronic non-cancer pain for participating GPs (GP intervention group) and GPs who did not participate and did not work at practices with GPs that did participate (GP control group). Patients with chronic pain who attended intervention GPs had reduced rates of opioid prescribing and GP encounters than the GP control group. There was no significant difference between groups for initiation of opioids, however the rate of opioid initiations have decreased in both groups since the launch of the NPS MedicineWise 2015 Chronic Pain program. This is suggestive of the effect of other national Program activities targeting all GPs.

The economic evaluation of the national NPS MedicineWise 2015 Chronic Pain program found that:

- The Chronic Pain Program was effective at reducing dispensing of opioids prescribed by GPs by a relative 2.56%. In the two-year period after the program there was an estimated 501,989 fewer prescriptions dispensed. This corresponded to an estimated mean savings to the PBS of $13,787,170
- At a population level from the perspective of the Australian Government Department of Health, the Chronic Pain Program had a benefit to cost ratio of 3.67 and a net benefit of $8,771,975
- The cost-effective analysis found that for every $7.48 spent on the program, one dispensing of an opioid prescription was averted. The cost was offset by the savings to the PBS from the averted opioid prescriptions, which was on average $27 per prescription.

The interactive component of the Chronic Pain Program was effective at:

- reducing GP prescribing of opioids by a 7.5% (n=12,780 prescriptions) and reducing GP encounters by a 6.3% reduction (n=47,761 encounters).

This program impact was associated with:

- a benefit of $2,317 per intervention GP for the period July 2015 to June 2018
- a net benefit of the program of $1,882 per intervention GP based on PBS and MBS cost savings
- the benefit to cost ratio of the program was 5.32. For every dollar spent on the program, $5.32 was gained in monetary benefit.

The strengths of the study centre around the data sources used, the analysis methods used, and the results verified by the different studies. The studies conducted used two different data sources, PBS and MedicineInsight, to investigate the impact of the national and interactive components of the NPS Chronic Pain Program on opioid prescribing and dispensing patterns for general practice patients. The MedicineInsight analysis allowed the evaluation to explore benefits not available in the PBS dataset and explore the impact of the interactive interventions of the program.

The time series methods used in both studies allowed for the estimation of the attributable benefits and costs of the national and interactive components of the Chronic Pain program. The positive impact of the program on reducing opioid prescriptions was supported by the findings from Study 1, Study 2 and previous evaluations of the program.

Conclusion

This economic evaluation found that the national 2015 NPS MedicineWise Chronic Pain Program had economic benefit in terms of reducing costs to the PBS and had also had a positive impact on GPs who participated in the interactive components of the program.

The MedicineInsight analysis found important outcomes to be affected by different types of interventions included in the Chronic Pain Program. This evaluation highlights the value of multimodal programs to improve clinical practice when the quality use of medicine issues are complex and multifaceted.

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