International Journal of Drug Policy 74 (2019) 170–173

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Short Report

Changes in Australian prescription opioid use following codeine rescheduling: A retrospective study using pharmaceutical benefits data

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ARTICLE INFO

Keywords:
Codeine
Pharmaceutical benefits scheme
Prescription opioid
Rescheduling

ABSTRACT

Purpose: In February 2018, Australia up-scheduled the 'weak' opioid codeine to a prescription only medication. This study aimed to analyse the change in prescribing trends for codeine and other commonly prescribed opioids in Australia following this policy change to determine if removal of over-the-counter codeine resulted in an increase in opioid prescribing.

Methods: Data was obtained through the Australian Government Department of Human Services statistics website, and contained monthly data about subsidised national prescription numbers for codeine, oxycodone, oxycodone–naloxone, tapentadol, tramadol, morphine, and fentanyl, from January 2016 to December 2018. Segmented linear regression accounting for autocorrelation was used to assess the effect of codeine rescheduling on the supply trends of these opioids.

Results: Rescheduling codeine to remove over-the-counter (non-prescription) supply does not appear to have had an immediate effect on the prescription rates of codeine, and there is no significant change in these rates in the months following. Analysis of data showed decreasing trends for codeine and most other schedule 8 prescription opioids, with no increase in any prescribed opioids associated with codeine up scheduling.

Conclusions: Despite concerns, substitution of over-the-counter codeine with higher strength prescribed codeine has not been observed at a population level, nor has a shift to other prescribed opioids occurred. Overall, opioid prescribing in Australia has been decreasing since 2016, both for strong and weak opioids.

Introduction

Many countries are considering strategies to reduce prescription opioid-related harm in response to increasing opioid-related deaths (Fischer, Jones, Urbanoski, Skinner & Rehm, 2013; Center for Disease Control, 2018; Fischer, Rehm & Tyndall, 2016; Roxburgh, Dobbins, Degenhardt & Peacock, 2018; Seth, Scholl, Rudd & Bacon, 2018). Codeine, a 'weak' opioid, is one of the most widely available and commonly used opioids in the world for pain relief (International Narcotics Control Board, 2015). Yet, considerable harms have been documented with its use including dependence and associated mortality (Nielsen, Macdonald & Johnson, 2018; Roxburgh et al., 2015). These harms are frequently associated with use of low-dose combination over-the-counter (OTC) products containing ibuprofen and paracetamol (Nielsen et al., 2018). In response, many countries have considered, or already put in place, policy changes on supply. In Australia in February 2018 codeine was up-scheduled to a prescription opioid medicine (Therapeutic Goods Administration, 2016). One concern expressed with this move was, given the high rate of OTC codeine use (15.5 million packets sold in 2013 (Gisev et al., 2016)), that a large increase in higher-dose prescribed codeine, or other prescribed opioids, would result, and that this may be associated with significant healthcare costs and inconvenience for people needing to see a doctor for an opioid prescription (McCoy, Bruno & Nielsen, 2018).

To examine if this concern was realised, this study aimed to analyse the change in Australian national supply of: (i) codeine, and (ii) other common pharmaceutical opioids available in Australia, over a three year period covering the two years leading up to codeine rescheduling in Australia, and the 11 months following.

Methods

The primary focus of this study was to assess if the policy change around codeine scheduling led to a change in prescription rates for codeine, with a secondary focus on if codeine rescheduling affected the prescriptions rates for other commonly prescribed opioids in Australia. The opioids assessed were oxycodone, oxycodone-naloxone, tapentadol, tramadol, morphine, and fentanyl.

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https://doi.org/10.1016/j.drugpo.2019.08.008

Supply data for each opioid was obtained through the Australian Government Department of Human Services (DHS) Medicare Statistics website (Australian Government, 2019) that includes Pharmaceutical Benefits Schedule item statistics reports, and covered prescription medications dispensed under the pharmaceutical benefits scheme (PBS) and repatriation pharmaceutical benefits scheme (RPBS) schemes nationally from January 2016 to December 2018. Supply was analysed through PBS and RPBS prescription data processed by DHS during the month of interest, and includes all PBS prescriptions even if they are below the threshold for subsidy. This dataset does not include prescriptions that have not been filled or are not covered under the PBS and RPBS schemes (e.g. private prescriptions). Supply was converted to oral morphine equivalent (OME) (Nielsen, Degenhardt, Hoban & Gisev, 2016), to allow for comparison between differing strength opioids, using information regarding each item codes pack size, strength and administration method with final units in kg/month. An aggregated combined opioid variable was created to assess the overall trend in opioid supply. Segmented linear regression models using Newey–West standard errors and adjusting for seasonal trends were used to estimate the trend in supply over time as well as the immediate effect of rescheduling Codeine and the post-rescheduling change in trend. Each opioid was assessed individually as well as the combined total. To determine if any temporal supply patterns were unique to opioids, trends with three common non-psychoactive pharmaceuticals, amoxicillin, atorvastatin and pantoprazole were also examined.

Results

Prescription rates in OME (kg/month) are displayed in Fig. 1. There appears to be no increasing trend for codeine or combined opioid supply (Fig. 1(A) and (B)). A decreasing trend can be seen for most Schedule 8 opioids excepting tapentadol and oxycodone-naloxone (Fig. 1(D)), which appear to be increasing over time.

Table 1 displays the regression results for each opioid individually and the combined opioid model. Codeine appears to be decreasing at a rate of 0.031 OME kilograms per month (95% CI: decrease of 0.01–0.05). There are also decreasing trends for oxycodone, tramadol, morphine and fentanyl and these appear to be at a greater rate of decrease. Oxycodone–naloxone and tapentadol prescription rates are increasing over time, with tapentadol (1.35 OME kilograms per month) increasing at a greater rate than oxycodone–naloxone (0.54 OME kilograms per month).

No significant changes were seen in the immediate effect on the prescription rates of codeine, or in the months following rescheduling codeine to remove over-the-counter (non-prescription) supply. Similarly, no effect on supply of any other opioid was observed, either immediately after, or in the months following rescheduling, except for tapentadol and oxycodone–naloxone. Immediately after codeine rescheduling a drop in prescription rates of tapentadol was observed (change: −3.1 OME kilograms, 95% CI: −4.93 to −1.01), however there was no long-term effect on the increasing rate of tapentadol prescriptions. Oxycodone–naloxone prescriptions saw a decrease in rate following codeine rescheduling (change: −0.71 OME kilograms, 95% CI: −1.20 to −0.22).

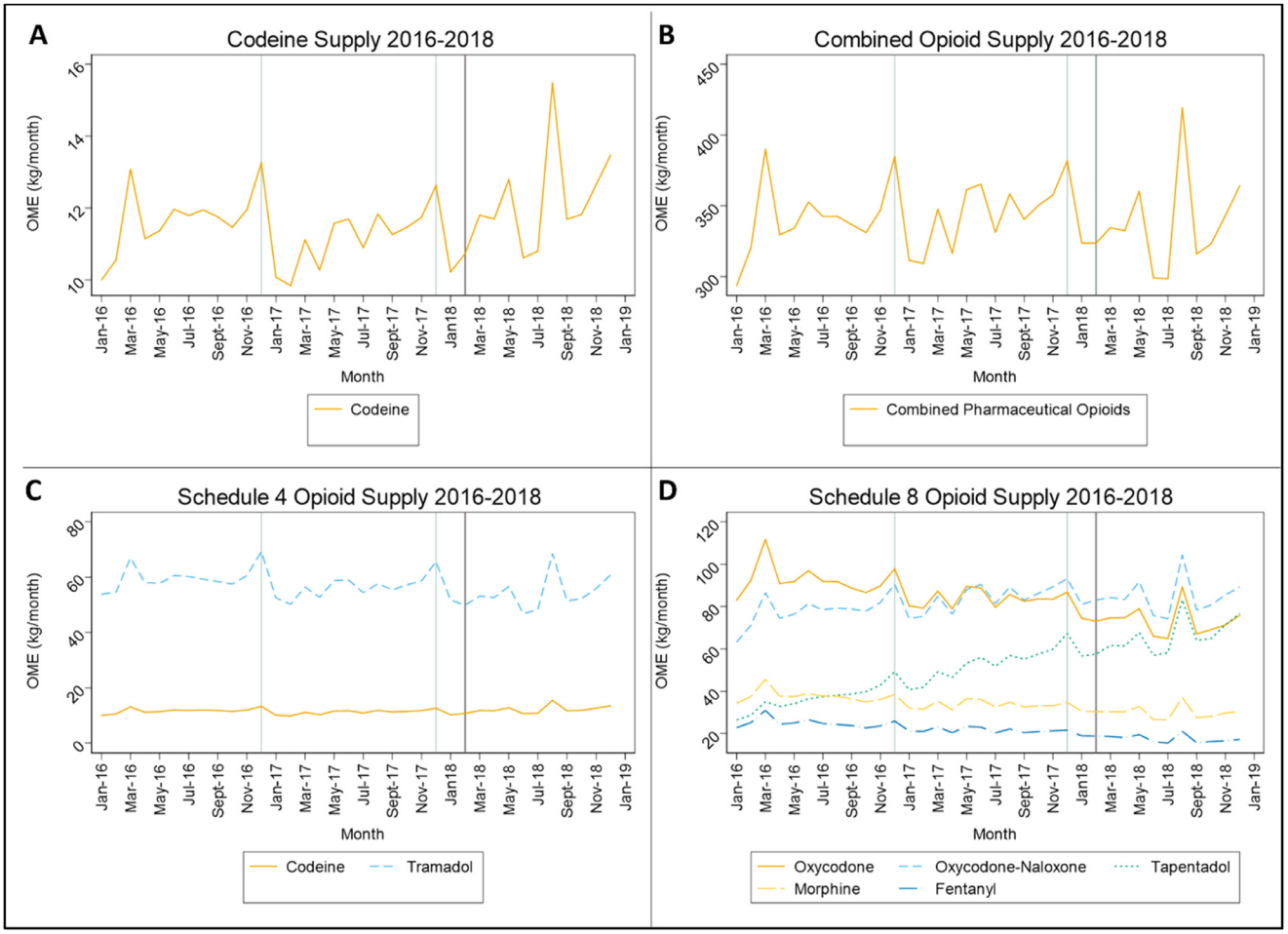

Fig. 1. Supply trends for pharmaceutical opioids commonly prescribed in Australia from January 2016 to December 2018. Panels depict the trend in (a) Codeine, (b) all pharmaceutical opioids combined, (c) schedule 4 opioids, and (d) schedule 8 opioids, before and after Codeine rescheduling (February 2018).

Table 1
Regression estimates for the time trend in pharmaceutical opioid supply, the immediate effect of Codeine rescheduling and the change in trend post rescheduling.

Opioid/coefficient	β	95% confidence	p-value
Codeine			
Time trend	−0.031	−0.053 to −0.009	0.008
Immediate effect	0.848	−0.016 to 1.712	0.054
Change in slope	0.045	−0.036 to 0.127	0.261
Oxycodone			
Time trend	−0.676	−0.887 to −0.495	<0.001
Immediate effect	−4.464	−12.771to 3.843	0.276
Change in slope	0.149	−0.708 to 1.007	0.721
Oxycodone w Naloxone			
Time trend	0.536	0.422 – 0.650	<0.001
Immediate effect	−3.276	−8.395 to 1.843	0.197
Change in slope	−0.707	−1.195 – −0.218	0.007
Tapentadol			
Time trend	1.349	1.269 to 1.429	<0.001
Immediate effect	−3.102	−4.704 to −1.499	0.001
Change in slope	−0.243	−0.483 – 0.078	0.148
Tramadol			
Time trend	−0.230	−0.322 to −0.138	<0.001
Immediate effect	−0.644	−4.436 to 3.149	0.728
Change in slope	0.065	−0.341 to 0.470	0.743
Morphine			
Time trend	−0.302	−0.391 to −0.212	<0.001
Immediate effect	−1.157	−4.750 to 2.436	0.510
Change in slope	0.108	−0.273 to 0.489	0.562
Fentanyl			
Time trend	−0.262	−0.316 to −0.208	<0.001
Immediate effect	−1.015	−3.341 to 1.311	0.375
Change in slope	−0.014	−0.244 to 0.216	0.902
All opioids combined			
Time trend	0.384	−0.159 to 0.928	0.156
Immediate effect	−12.810	−37.357 to 11.738	0.290
Change in slope	−0.556	−3.190 to 2.079	0.665

Time Trend: The supply trend prior to February 2018; Immediate effect: level change occurring as a result of codeine rescheduling; Change in slope: change in supply trend following February 2018.

Unexpected temporal trends in opioid supply observed in June - August 2018 were explored through analysing supply patterns for other high-volume prescription items. These analyses revealed that similar patterns were observed with amoxicillin, atorvastatin and pantoprazole (see Supplementary Material), confirming that these reflected systematic anomalies with PBS data.

Discussion

Our study examined changes in opioid supply following the policy change relating to codeine scheduling. We found no evidence of increased prescribing of codeine, or any other opioid, associated with the removal in over-the-counter codeine availability. In fact, these analyses show clear trends of decreasing opioid prescribing in Australia. This suggests that, despite concerns that over-the-counter codeine products would be substituted for stronger variants (McCoy et al., 2018), at a population level, substitution with prescribed codeine has not been observed, nor has a shift to other prescribed opioids occurred. This is despite the considerable use of OTC codeine amongst the community prior to the change (Gisev et al., 2016). The rate of prescriptions for oxycodone–naloxone began to decrease immediately following the rescheduling, while tapentadol was the only opioid where an ongoing increase in prescribing was observed.

Our findings appear to differ from an examination of prescription trends following the up-scheduling of hydrocodone in the United States, where a large increase in prescribed tramadol and codeine was observed following hydrocodone up-scheduling (Seago, Hayek, Pruszynski & Newman, 2016). However, when these changes were measured as changes in OME, the increase equated to 3%. As this study only examined two discrete time periods, it is possible that the changes may have been explained by seasonal trends or other unmeasured confounders.

There are some important caveats in understanding the data. PBS data do not cover all supplied opioids, however a study examining underestimation of PBS data determined that in the time period studied 88% of opioid supply is captured via PBS data (Gisev et al., 2018). This proportion is likely to be higher now as OTC codeine accounted 6% of the 12% of opioid supply previously not captured by PBS data. Due to many low-dosage codeine products being discontinued following the policy change, and stock shortages reported with low-dose codeine products that may been prescribed on private prescriptions, it is also unlikely that the inclusion of private prescriptions would change the results significantly (Haggan, 2018). This is supported by the findings from a recent IQVIA report showing that supply of all codeine-containing products, not limited to those covered under PBS, in 2018 has been significantly lower than the previous four years, despite including 1 month of over-the-counter supply (January 2018) (Australian Government Department of Health, 2019b). There are small differences in date of supply and reporting, as the month is determined by the date of processing with Medicare, rather than the time of supply by the pharmacy; however due to frequent processing of the data, these differences are unlikely to effect the conclusions drawn. In Jan 2018, the PBS dataset shifted from reporting prescriptions based on date of processing to date of supply. Furthermore, from March 2018, changes have affected the availability of data supplied by the department of human services to the department of health. This has resulted in an approximate increase of 1.5% in the number of prescriptions reported (Australian Government Department of Health, 2019a), but is unlikely to affect our conclusions given the downward trend observed in opioid supply. Finally, an unexpected peak in opioid supply was observed in August 2018. This peak is not limited to opioids, with a similar trend seen for the most common PBS medications (amoxycillin, atorvastatin and pantoprazole). This peak follows an unexpected trough during June–July 2018. Given these three mediations are prescribed generally for three different illness categories, separate from opioids in pain management, are non-psychoactive and not subject to misuse, it is reasonable to assume that this trend is related to an event with Medicare and/or the PBS scheme rather than the change in opioid scheduling, though we have not been able to identify the cause of this trend. Finally, the minimum number of time points suggested for interrupted time serious was just exceeded. As such, results should be interpreted cautiously as the limited number of time points means the anomaly occurring in June to August could have unprecedented weight on the post-rescheduling effect.

We recommend replicating these analyses when additional data are available, and for future studies to include other indicators of the impact of the rescheduling change including GP consultations and costs, treatment, hospital and mortality data, to provide a more comprehensive understanding of the impact of this regulatory change, though these data will not be available for some time. Notwithstanding, this study demonstrates that a widely purported effect of the change, a large increase in people attending doctors to receive prescription codeine or other prescribed opioids was not observed.

In summary, these are the first analyses to suggest that, at the population level, codeine rescheduling did not lead to a measurable increase in opioid prescribing. Understanding how these changes affected individuals through linked data and cohort studies will provide additional understanding of regulatory changes as a policy lever to reduce opioid-related harm. Analysis of trends in sales of non-opioid over-the-counter analgesics may provide further details as to how consumers responded to this change.

CRediT authorship contribution statement

Melissa Middleton: Data curation, Formal analysis, Software,

Validation, Visualization, Writing - original draft, Writing - review & editing. **Suzanne Nielsen:** Conceptualization, Funding acquisition, Project administration, Supervision, Writing - original draft, Writing - review & editing.

Ethics statement

The authors state that no ethical approval was needed due to use of publically available non-identifiable datasets.

Acknowledgement

SN is a current recipient of an NHMRC research fellowship [#1163961]. No other funding was received to support this work. SN is a named investigator on research grants from Indivior (research on treatments for opioid dependence) and Seqirus (examining a population level indicators of opioid-related harm). These are unrelated to the current work. SN has delivered training on opioid dependence for Indivior for which honoraria were paid to her institution. SN has participated in an advisory board meeting Mundipharma relating to intranasal naloxone for which a sitting fee was declined.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2019.08.008.

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