

Relationship between antimicrobial-resistance programs and antibiotic dispensing for upper respiratory tract infection: An analysis of Australian data between 2004 and 2015

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Abstract

Objective: NPS MedicineWise aims to ensure that medicines are prescribed and used in a manner consistent with current evidence-based best practice. A series of nationwide educational and advertising interventions for general practitioners and consumers were implemented in Australia between 2009 and 2015 with the aim of reducing antibiotic prescriptions for upper respiratory tract infections (URTI). The work described in this paper quantifies the change in antibiotic dispensing following these interventions.

Methods: Antibiotic dispensing data between 2004 and 2015 were obtained from a national claims database. A Bayesian structural time series model was used to forecast a series of antibiotic dispensing volumes expected to have occurred if the interventions had not taken place. These were compared with the volumes that were actually observed to estimate the intervention effect.

Results: On average, 126,536 fewer antibiotics were dispensed each month since the intervention programs began in 2009 (95% Bayesian credible interval = 71,580–181,490). This change

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represents a 14% total reduction in dispensed scripts after the series of intervention programs began in 2009.

Conclusions: Continual educational intervention programs that emphasise the judicious use of antibiotics may effectively reduce inappropriate prescribing of antibiotics for the treatment of URTIs at a national level.

Keywords

Evaluation, antimicrobial resistance, intervention, antibiotic dispensing, general practitioners, primary health care

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Introduction

Antimicrobial resistance (AMR) is a global public health concern.¹ Patients with antimicrobial-resistant infections are less responsive to standard treatments, are infectious for longer times, and place larger economic burdens on health care systems.^{2,3} The evolution of AMR is accelerated by the widespread use of antibiotics in primary health care.^{1,4} Consequently, national strategies have been adopted by many countries to foster judicious prescribing and consumption of antibiotics.⁴⁻⁶

In Australia, NPS MedicineWise implements nationwide intervention programs that aim to ensure that medicines are prescribed, dispensed, and used in accordance with evidence-based best practice. The interventions cover many therapeutic topics and adopt a mix of interventions to communicate key messages to health care professionals, their patients, and the community.⁷ A mix of intervention activities has been shown to effectively change medicine-prescribing behaviours.^{8,9}

Inappropriate antibiotic use is a national topic¹⁰⁻¹³ of ongoing concern given the high rate of antibiotic use in Australia compared with similar countries.¹⁴ In 2014, 46% of the Australian population was prescribed at least one antibiotic, and at least half of these prescriptions may have

been unnecessarily issued.¹⁴ Antibiotics for upper respiratory tract infections (URTIs) are particularly over-prescribed.^{14,15} Recently, 47% of patients diagnosed with an acute URTI were prescribed an antibiotic despite guidelines indicating an acceptable range of 0% to 20%.¹⁴ Given that URTIs account for one-third of all antibiotics dispensed annually,¹⁶ bringing current prescribing rates in line with recommendations can substantially reduce antibiotic consumption.

Since 1999, NPS MedicineWise has addressed the problem of inappropriate antibiotic prescribing in primary health care with nationwide educational and advertising interventions.¹⁷ The educational components of the interventions are designed for health professionals, particularly general practitioners (GPs), and encourage judicious antibiotic use, especially for URTIs. The number of GPs participating in these educational interventions has increased since NPS MedicineWise launched its first AMR programs. In 2012, almost one-third of Australian GPs participated in an educational activity. The activities that constituted the educational interventions involved academic detailing through information products, case studies, clinical audits, face-to-face educational outreach, and feedback regarding the prescribing of antibiotics. The feedback component

was provided by direct mail to every registered practicing GP in Australia in addition to those participating in an educational intervention. Advertising interventions were aimed at the community and encouraged the symptomatic management of colds and flu over antibiotic use.

An analysis of national dispensing claims between 1999 and 2003 demonstrated that educational and advertising interventions reduced the rate at which certain classes of antibiotics were dispensed.¹⁸ However, few studies have examined the impact of such interventions on the overall volume of antibiotics dispensed.

The objective of this study was to evaluate whether the dispensing volume of antibiotics commonly prescribed for URTIs changed since implementation of the national AMR programs in 2009.

Methods

Interventions

The AMR interventions evaluated in this study were launched in July 2009, followed by a more intensive 5-year program between 2012 and 2017. For an educational visiting program, educational activities of each intervention were implemented over a period of 12 to 18 months, depending on the type of activities involved (Table 1). In the early months of each intervention, the number of GPs participating in educational activities was generally small, with peak participation generally occurring 6 months after an intervention's launch date. Nationally, 17,000 GPs participated in an educational intervention between 2009 and 2015, and around one-third of Australian GPs (10,021) participated in 2012. The 2009 and 2012 programs were also followed by direct mail-out of a personalised prescribing feedback to about 22,000 registered practicing GPs in Australia. The mail-out of the feedback reports was coordinated with the

Australian Government Department of Human Services (DHS) by using a national administrative claims database, the Pharmaceutical Benefits Scheme (PBS). The PBS feedback presented GPs with their prescribing patterns for antibiotic drugs, which were filled by the patient at the pharmacy, in comparison with their peers. It also contained points for reflection relevant to the GPs' practice and messages regarding the appropriate use of antibiotics. Advertising interventions for consumers were timed to coincide with the cold and flu season. Their key messages were disseminated through GP practices, community pharmacies, and mass media channels.

Data source

The prescriber-level PBS and Medicare Benefit Schedule (MBS) databases were the primary data sources and were obtained from DHS. The PBS data contained the number of prescriptions dispensed to general and concessional beneficiaries for each PBS item code (see Table 2 for examples) grouped by individual prescriber and month of dispensing from January 1997 to June 2015. From the PBS database, we extracted the data for 13 antibiotics commonly prescribed for URTIs (Table 2), as suggested by clinical experts and the literature,¹⁹ that were only dispensed to concessional beneficiaries. Before April 2012, drugs that did not incur a government subsidy were not included in the PBS database. This resulted in the data being less representative for drugs priced below the general beneficiary co-payment threshold, with coverage for concessional beneficiaries being the most complete data available from the PBS. Concessional beneficiaries are primarily older, sicker, and poorer and include, for example, single-parent pensioners, health care card holders, and commonwealth seniors health card holders. For these patients, drugs are provided at a lower cost or for free if incurred expenditure for a patient in the calendar year exceeds a safety

Table 1. Summary of NPS MedicineWise’s AMR interventions between 2009 and 2014

Program name	Key messages to clinicians	Examples of activities conducted in programs
Antibiotics in respiratory tract infections (2009)	<ol style="list-style-type: none"> 1. Antibiotics are only appropriate for an acute cough if a chest X-ray suggests pneumonia, or for exacerbations of COPD with sputum purulence plus increased sputum volume and/or dyspnoea 2. Antibiotics are only appropriate for a sore throat if all four diagnostic criteria (fever, exudate, lymphadenopathy, and absence of cough) for streptococcal infection are present 3. Use penicillin V (phenoxymethylpenicillin) for 10 days for an uncomplicated sore throat that appears to be streptococcal 4. When treating respiratory tract infections, reserve macrolides for patients with pertussis or penicillin hypersensitivity 5. Antibiotics have limited efficacy against the common cold or flu 6. Provide advice to patients regarding appropriate symptomatic relief 	<ul style="list-style-type: none"> – Comparative prescribing feedback to all GPs – Case vignettes for discussion with pharmacists, nurses, and GPs – Clinical audit and feedback for GPs – Multiple publications/newsletters mailed to GPs and community pharmacists – Decision support tools and resources (e.g., symptomatic management pad) – Translation of resources for other common language groups
Antibiotic resistance (2012)	<ol style="list-style-type: none"> 1. Antibiotic resistance is an issue that requires balancing treatment of the individual against public health problems at the population level 2. Establish patient’s beliefs and expectations about antibiotics for acute respiratory tract infections and tailor communication strategies accordingly 3. Encourage self-management of acute respiratory tract infections and explain why antibiotics may not be appropriate 4. Consider the issue of resistance when prescribing antibiotics 	<ul style="list-style-type: none"> – Comparative prescribing feedback forms to GPs – Face-to-face educational outreach conducted one-on-one or in small group peer discussion groups – Case vignettes for discussion with pharmacists, nurses, and GPs – Clinical audits and feedback for GPs – Multiple publications/newsletters mailed to GPs and community pharmacists – Shared decision making tools and resources (e.g., updated symptomatic management pad) – Interactive Workshops for RACFs – Webinars for GPs and practice nurses – Mass audience advertising campaign aimed at limiting antibiotic consumption for cold and flu – Large number of point-of-care resources distributed through all community pharmacies – Targeted resources for seniors, early childhood day care centres, and multiple language groups – Phone application with antibiotic reminder functionality

(continued)

Table 1. Continued

Program name	Key messages to clinicians	Examples of activities conducted in programs
Reducing antibiotic resistance (2014)	<ol style="list-style-type: none"> 1. Antibiotic resistance begins with the individual and impacts the population 2. Quality antibiotic prescription and consumption can extend the longevity of existing antibiotic treatments 3. Apply the following principles when prescribing: allow microbiology to guide the chosen therapy, use evidence-based indications for antibiotics, use narrow-spectrum antibiotics where possible, ensure the dosage is appropriate for the site and type of infection, minimise the duration of antibiotic treatment, and use monotherapy for most infections 4. Establish patient beliefs and expectations about antibiotics and discuss when necessary 5. Educate and use prevention strategies including vaccination and hand and respiratory hygiene 	<ul style="list-style-type: none"> – Comparative prescribing feedback forms to GPs – Case vignettes for discussion with pharmacists, nurses, and GPs – Clinical audit and feedback for GPs – Webstercare® Quality-Use-of-Medicine reports for use in RACFs to benchmark and encourage quality improvement activities – Mass audience campaign aimed at limiting antibiotic consumption and taking a Facebook® pledge to only use antibiotics responsibly – Large number of point-of-care resources distributed through all community pharmacies

AMR, antimicrobial resistance; GP, general practitioner; COPD, chronic obstructive pulmonary disease; RACF, residential aged care facilities

net threshold set by the government for that year. For example, in 2017, the PBS general beneficiary co-payment is \$38.80 with an annual safety net threshold of \$1,494.90, and the concessional beneficiary co-payment is \$6.30 with an annual safety net threshold of \$378.00. Because the price of most included antibiotic drugs are below the general beneficiary co-payment, the small fraction of antibiotics dispensed to general beneficiaries who reached the safety net were excluded to ensure that our data captured the full dispensing history of each patient for the duration of the study. Thus, the data contained only scripts that were dispensed to the concessional beneficiaries.

All prescribers in the data were allocated into two groups: GPs and other health practitioners, according to their specialties. The specialty and the number of

consultations (used for the rate calculations) per prescriber per month were obtained from the MBS database. They were then linked to the PBS data by a scrambled provider identification number to distinguish between GPs and other health practitioners. The GP group comprised registered GPs, GP trainees, and non-vocationally recognised doctors. The other health practitioners were those not classified as GPs. The top five other health practitioners who contributed 50% of the dispensed antibiotics were unknown/unspecified specialists, general surgeons, thoracic medicine specialists, dermatologists, and paediatricians. We excluded dentists' data from this group because the approved antibiotic PBS item codes that can be prescribed by dentists are different from those listed in Table 2.

Table 2. Antibiotics commonly prescribed for URTIs¹⁹ included in the analysis of dispensing volumes

Drug	PBS Item Code [†]
Doxycycline	10176N, 1800R, 2702F, 2703G, 2707L, 2708M, 2709N, 2711Q, 2714W, 2715X, 6015N, 6016P, 6023B, 6024C, 6026E, 6027F, 6081C, 6082D, 9105F, 9106G, 9107H, 9108J
Amoxicillin/amoxicillin with clavulanic acid	1878W, 1883D, 1884E, 1886G, 1887H, 1888J, 1889K, 8581P, 8705E, 9714G, 1890L, 1891M, 1892N, 1893P, 8254K, 8319W
Phenoxyethylpenicillin	1702N, 1703P, 1705R, 1786B, 1787C, 1789E, 2354X, 2356B, 2965C, 3028J, 8976K, 8977L, 9143F
Benzathine	2267H, 1766Y, 8167W, 8743E, 9002T, 9003W, 1767B
Cefaclor	1155T, 1169M, 2460L, 2461M
Cephalexin	3058Y, 3094W, 3095X, 3119E, 2655R
Cefuroxime axetil	8292K, 5499K
Erythromycin	1395K, 1399P, 1400Q, 1402T, 1404X, 1397M, 1398N, 1401R, 1403W, 2425P, 2610J, 2423M, 2499M, 2424N, 2428T, 2750R
Roxithromycin	1760P, 8016X, 8129W
Azithromycin	2484R, 8200N, 8201P, 8336R
Clarithromycin	8318T, 9192T
Trimethoprim with sulfamethoxazole	2949F, 2951H, 3103H

[†]Item codes listed between January 1997 and June 2015 were included in this study. The item code is an administrative code to assist in claims processing. Multiple item codes can represent the same antibiotic drug. Further information related to each PBS item code for each antibiotic drug can be accessed at www.pbs.gov.au.

For our analysis, the data were summarised as the total number of dispensed scripts across the groups of GPs or other health practitioners, respectively, within each month. We also calculated the monthly data of the mean dispensing rate per GP or per other health practitioner, and the rate per 1,000 consultations for each group.

Statistical analysis

We implemented a Bayesian structural time series model (BSTM)²⁰ to examine and quantify the association between the series of NPS MedicineWise AMR interventions and the changes in the antibiotic dispensing volume of the GP group. First, we modelled the GP time series data from January 2004 to June 2009 with dispensing data from other health practitioners as a predictor. We then forecasted the

remaining data from July 2009 to June 2015 as the expected dispensing volume had the interventions not taken place. The estimated change in the dispensing volume following the sequence of interventions was calculated from the monthly differences between the observed and expected antibiotic dispensing volumes. The statistical significance of each monthly effect was assessed by observing whether its 95% Bayesian credible interval (Bayesian CI₉₅) contained zero.

The BSTM used in this study modelled the behaviour of the linear predictor and set up prior distributions for unknown quantities in the model for the data before the interventions. The time series components of the BSTM incorporated the trend and seasonality of dispensing volumes with a basic structural model containing a regression component with a static coefficient.

The basic structural time series model used was as follows:

$$\begin{aligned}
 y_t &= \mu_t + \gamma_t + \beta x_t + \varepsilon_t & \varepsilon_t &\sim N(0, \sigma_\varepsilon^2) \\
 \mu_t &= \mu_{t-1} + \eta_{\mu,t} & \eta_{\mu,t} &\sim N(0, \sigma_{\eta_\mu}^2) \\
 \gamma_t &= -\sum_{j=1}^{S-1} \gamma_{t-j} + \eta_{\gamma,t} & \eta_{\gamma,t} &\sim N(0, \sigma_{\eta_\gamma}^2)
 \end{aligned}$$

for $t = 1, \dots, n$ and $S = 12$, where y_t is the monthly dispensing volume of antibiotics prescribed by GPs; μ_t is a trend component; γ_t is a seasonal component; βx_t is a regression component with coefficient β and linear predictor x_t of the monthly dispensing volume prescribed by other health practitioners; ε_t 's, $\eta_{\mu,t}$'s and $\eta_{\gamma,t}$'s are mutually independent and normally distributed error terms for the observed data, trend and seasonal components with zero means and constant variances σ_ε^2 , $\sigma_{\eta_\mu}^2$, and $\sigma_{\eta_\gamma}^2$, respectively. The BSTM used in the present study was implemented using the ‘‘CausalImpact’’ package in R.^{21,22} A detailed discussion of prior specification and elicitation for the unknown parameters in the model can be found in its associated publication.²⁰

The validity of including dispensing volumes from other health practitioners in forecasting volumes for GPs was dependent on the following assumptions. First, from an intervention perspective, the prescribing behaviour of other health practitioners was less likely to be influenced by the interventions. We thought this was a reasonable assumption because other health practitioners did not ‘‘actively’’ participate in the AMR interventions and were not the recipients of the PBS prescribing feedback reports. Second, from the observed data, a stationary relationship (similar trend and seasonal pattern) in dispensing volumes between GPs and other health practitioners could be established prior to the

interventions. Stationarity prior to the interventions was the primary assumption of our modelling approach.²⁰

Results

Figure 1(a) illustrates the time series of the dispensing volumes for GPs, the dispensing volumes predicted by the model, and the expected dispensing volumes if no interventions had been implemented. The dispensing volumes from other health practitioners, which were used as a predictor, are shown in Figure 1(b). The estimated changes in the monthly dispensing volumes following all interventions are shown in Figure 1(c).

After implementation of the programs in 2009, the dispensing volumes averaged 781,547 antibiotics per month (Figure 1(a)). Over the same time, the estimated dispensing volume (as if the intervention had not been implemented) averaged 908,083 antibiotics per month (Bayesian $CI_{95} = 853,130\text{--}963,040$), yielding an average reduction in dispensing of 126,536 antibiotics each month (Bayesian $CI_{95} = 71,580\text{--}181,490$). By June 2015, the overall reduction in the dispensed scripts of antibiotics was about 14% (Bayesian $CI_{95} = 8\%\text{--}20\%$).

Statistically significant reductions in the monthly dispensing volume emerged in August 2012 (Figure 1(c)). This was 6 months into the 2012 AMR intervention, when GP participation was at its peak and all registered GPs had been mailed the PBS prescribing feedback. Following this, the antibiotic dispensing volumes averaged 759,720 scripts per month and the expected volume averaged 944,162 scripts per month. On average, this was 184,442 fewer prescriptions dispensed every month after the peak of GP participation since the 2012 intervention. From August 2012 to June 2015, the overall reduction in the dispensed scripts of antibiotics was about 19.5%.

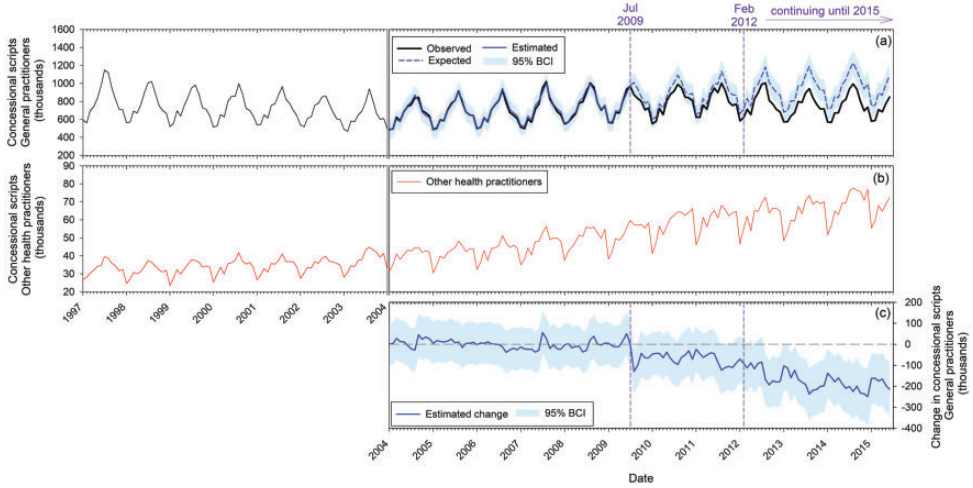


Figure 1. (a) Observed (black) vs. estimated (solid blue) dispensing volumes of GP-prescribed antibiotics vs. expected (dashed blue) dispensing volumes as if without the interventions. (b) Time series of dispensing volumes prescribed by other health practitioners (used as a predictor) and (c) estimated monthly reduction in antibiotic dispensing volume. Additional panels on the left of (a) and (b) show the dispensing volumes of GP-prescribed and other health practitioner-prescribed antibiotics prior to the study period. The blue shaded areas are the 95% Bayesian credible intervals (95% BCI). The dashed vertical lines indicate the launch of the programs. The right-arrow at the top of panel (a) indicates that the 2012 intervention was ongoing beyond the end of the study period in June 2015.

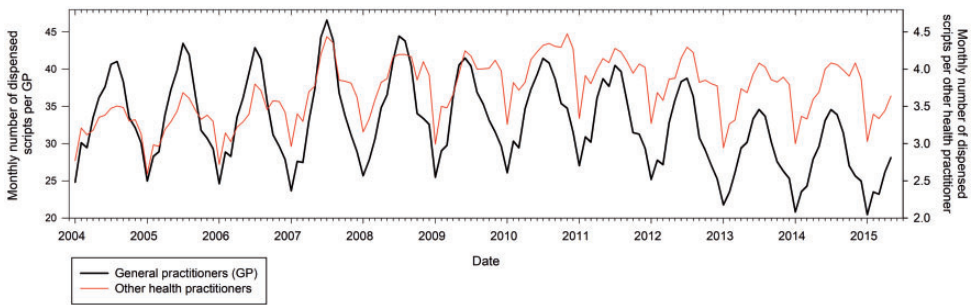


Figure 2. Mean antibiotic dispensing rates per GP (black) and per other health practitioner (red). The launch of the programs is indicated by the dashed vertical lines. The right-arrow at the top of the panel indicates that the 2012 intervention was ongoing beyond the end of the study period in June 2015.

Discussion

Management of AMR includes using antibiotics in a manner consistent with established guidelines regarding the quality use

of medicine. According to our analyses, the antibiotic dispensing volumes of concessional beneficiaries were reduced by 14.0% for the entire intervention period under consideration following implementation of

the AMR program since 2009 and by 19.5% since August 2012. These findings add to a growing body of evidence showing that educational and advertising programs can be an effective means of addressing the overuse of antibiotics in primary health care.^{23–25} Previous research in Australia has demonstrated the effectiveness of similar programs for reducing antibiotic consumption at local or regional levels.^{26,27} The results of the present study suggest that such programs, when implemented on a broader scale, may also reduce national antibiotic consumption, at least among concessional beneficiaries.

A statistically significant monthly reduction in the dispensing volumes was observed from August 2012 onward in terms of the estimated difference between the observed and expected data (Figure 1(c)). This was after the launch of the first 5-year AMR program and the distribution of the PBS prescribing feedback reports. The delay between the intervention launch and effect can be attributed to the progressive roll-out of educational activities and PBS prescribing feedbacks. It is likely that the dispensing volumes changed gradually as the cumulative number of participating GPs and consumer reach increased.

Numerous changes to government pricing policies and medicine expenditures occurred during the study period (2004–2015).²⁸ However, these changes are unlikely to have confounded our results because we limited the analysis to concessional beneficiaries. Furthermore, any change in pricing or policy during the study period would have likely affected the dispensing volumes from other health practitioners in the same way as the volumes from GPs. Because of this, pricing or policy-related changes in dispensing volumes could be controlled for when forecasting the expected dispensing volumes of the GP group by the predictor of other health practitioners. Thus, the reductions in antibiotic

dispensing observed in our study are unlikely to have been confounded by policy or pricing changes.

The time range of the data we selected in the analysis was from January 2004 onward because of an observed stationary relationship in the volume data between GPs and other health practitioners from 2004 to 2009. However, this was not clear prior to 2004 (see first additional panels in Figure 1(a) and (b)). A potential explanation for this is the hospital policy reforms that commenced in Victoria, Western Australia and Queensland between 2001 and 2003. These policy changes allow PBS-listed medicines to be dispensed to both hospital outpatients and inpatients upon discharge. Antibiotics subsequently issued by other health practitioners (possibly coming from hospitals) are captured by the PBS in a manner that makes them predictive of dispensed antibiotics issued by GPs.

The decrease in antibiotic dispensing accompanying the series of AMR interventions between 2009 and 2015 may also reduce the burden on Australia's health care system by slowing the development of antibiotic-resistant bacteria and extending the longevity of current antibiotic treatments. Because a reduced number of dispensed scripts is associated with fewer re-consultations,²⁹ the interventions may have partially reduced the overall patient load on GPs and the Australian health care system in general.

This study was observational and data-driven; therefore, causality cannot be confirmed despite the statistical method and software used. However, literature searches and discussions with clinical experts and researchers in AMR revealed no other significant interventions or policies at the national level to possibly account for the observed reduction in the data. In addition, the rate calculation of the number of scripts per GP, per other health

practitioner, or per 1,000 consultations showed similar reduction patterns (e.g., Figure 2), especially since 2012 (analysis not shown), providing another perspective regarding the changes in antibiotic use. Therefore, it appears that the reduction in antibiotic dispensing to concessional beneficiaries is attributable to the NPS MedicineWise AMR programs.

We view the present paper as a contribution to the suite of time series methods available for drug utilisation research. To date, BSTMs have not been used to analyse the effect of pharmacoepidemiological interventions. A recent systematic review³⁰ of time series analyses in drug utilisation studies showed that autoregressive integrated moving average models and segmented regression are the most widely used models. Structural time series models have an advantage over these methods because they do not require differencing to achieve stationarity of the outcome, which for a monthly time series may result in a loss of up to 13 months of data. Structural time series models accommodate non-stationarity by allowing trend and seasonal patterns in the outcome to change over time, thus avoiding the need for differencing and the accompanying loss of data. Moreover, modelling trend with a linear time predictor or misspecification of an autoregressive moving average error process in segmented regression may lead to inaccurate inference of an intervention's effect on drug utilisation. Structural time series models naturally accommodate non-linearity in trend and seasonality using random walks where $(\sigma_{\eta_\mu}^2, \sigma_{\eta_\gamma}^2) > 0$. This feature can be extended to allow the regression coefficients to vary when the relationship between the response variable and a predictor changes over time.²⁰

There were some limitations of the current study. First, we were not able to identify GPs in the PBS data who participated

in the active components of the interventions, who only received PBS prescribing feedback, or who did both. Therefore, comparable groups were difficult to establish, and measurement of the differential contribution of interventions was not feasible. Otherwise, the data can provide us with valuable information for planning future intervention programs.

Second, the PBS is an administrative database containing information to assist in claims and reimbursement processing. Clinical information such as the diagnosis and reason for a prescription is not available in the PBS data. Some of the PBS item codes for the included antibiotics can only be prescribed under a restricted benefit while others have no specific restrictions. Therefore, although the programs targeted the inappropriate use of antibiotic drugs for URTIs, the appropriateness of prescribing these drugs by GPs and other health practitioners could not be assessed with the PBS data. The results obtained when using other health practitioners as a control predictor must be cautiously interpreted, especially because the number of dispensed scripts issued by GPs was approximately 10 times greater than that issued by the other health practitioners, and the reason for prescribing antibiotics among other health practitioners could be entirely different.

Finally, the analysis only used the concessional beneficiary dispensing volumes. After completion of the analysis, we obtained the under-co-payment data from the DHS. It appeared that general beneficiaries were dispensed an average of 20% more antibiotics than concessional beneficiaries in the GP group and about 40% more in the other health practitioner group. These percentages were stable from July 2012, when the under-co-payment data became available to us, thus showing the same pattern as in the concessional data. However, because of the lack of previous

under-co-payment data with which to evaluate trends and seasonal patterns, we were not able to ascertain whether the same reduction would be observed for the entire Australia's population.

Conclusion

This study was able to quantify, for the first time in Australia, the impact of a series of AMR interventions on antibiotic dispensing for URTIs. Our analysis of PBS concessional beneficiary data suggests that ongoing educational and advertising interventions for GPs and consumers may reduce inappropriate antibiotic dispensing at the national level. The effects of the interventions are likely to be cumulative in nature, with each building on the success of previous interventions. The results of this study provide evidence that AMR interventions are improving the quality of antibiotic prescribing in primary health care.

Ethics approval

An ethics application was not warranted to conduct this study.

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Authors' contributions

JW designed the study, conducted the analysis, drafted and served as the principle editor for the current version.

DT wrote the first draft of the paper and served as the principle editor.

LO contributed to the study design and editing of the paper.

AH contributed to the design, development, and implementation of the NPS MedicineWise AMR programs and editing of the paper.

TM contributed to editing of the paper.

JD contributed to the design, development, and implementation of the NPS MedicineWise AMR programs and editing of the paper.

RH contributed to drafting of the paper.

LH conducted the literature review.

LW contributed to the design, development, and implementation of the NPS MedicineWise AMR programs and editing of the paper.

SB contributed to the study design, and editing of the paper.

Declaration of conflicting interests

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