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**Australian Institute of
Health and Welfare**

Medications prescribed for people with obstructive airways disease

Antibiotics and inhaled corticosteroids

WOOLCOCK 
INSTITUTE of MEDICAL RESEARCH

ACAM
Australian Centre for
Asthma Monitoring



Australian Government

**Australian Institute of
Health and Welfare**

*Authoritative information and statistics
to promote better health and wellbeing*

Medications prescribed for people with obstructive airways disease

Antibiotics and inhaled corticosteroids

Australian Institute of Health and Welfare
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Abbreviations

AB	antibiotic
ABS	Australian Bureau of Statistics
AIHW	Australian Institute of Health and Welfare
ASGC	Australian Standard Geographical Classification
ATC	Anatomic Therapeutic Chemical
BEACH	Bettering the Evaluation and Care of Health
CI	confidence interval
COPD	chronic obstructive pulmonary disease
GP	general practitioner
ICS	inhaled corticosteroids
LABA	long-acting beta-agonists
LRTI	lower respiratory tract infection
LSAC	Longitudinal Study of Australian Children
NPS	National Prescribing Services, Better Choices, Better Health
OCS	oral corticosteroids
PBS	Pharmaceutical Benefits Scheme
RR	relative risk
RTI	respiratory tract infection
SAAC	short-acting anticholinergic
SABA	short-acting beta-agonists
SEIFA	socio-economic indices for areas
SES	socioeconomic status
URTI	upper respiratory tract infection

Summary

Appropriate use of medications is important in maximising health benefits for patients, minimising the negative effects of medications, and controlling health costs. This report focuses on the appropriate use of certain medications for the management of obstructive airways disease, including asthma and chronic obstructive pulmonary disease (COPD).

Data in this report suggest that antibiotics are commonly used among patients with asthma and COPD, and that supply patterns for inhaled corticosteroids (ICS) are often not consistent with treatment guidelines for the management of these conditions.

Use of antibiotics by people with obstructive airways disease

Antibiotics may be life-saving when used appropriately, and are recommended for treatment of bacterial infections, exacerbations of COPD, and some other respiratory conditions. However, they occasionally cause side effects. Widespread use is costly for the community and promotes the emergence of resistant strains of bacteria.

Upper and lower respiratory tract infections are a common trigger of exacerbations of asthma and COPD. Many of these are caused by viral infections and, therefore, do not respond to treatment with antibiotics.

This study has found high rates of dispensing of antibiotics to people with conditions such as asthma and COPD. In 2008, 75% of concession card holders dispensed any respiratory medication were also dispensed oral antibiotics.

Antibiotics are commonly indicated for treatment of acute exacerbations of COPD. In the cohort of people most likely to have COPD (aged 55 and over, dispensed tiotropium at least once in 2008), 78% were also dispensed oral antibiotics.

There was little difference in the dispensing of antibiotics to children with or without asthma, at about 80% in 2008.

In interpreting these findings, it is important to note that the available information does not allow us to assess the appropriateness of prescribing antibiotics in these populations.

Co-prescribing of antibiotics and one-off inhaled corticosteroids

The use of short courses of ICS as treatment for respiratory tract infections in patients without obstructive airways disease is neither supported by available evidence nor recommended in treatment guidelines.

Data in this report suggest that one-off courses of ICS are commonly co-prescribed with antibiotics, presumably for the management of symptoms of respiratory tract infections. In 2008, 44% of individuals whose dispensing record did not include any evidence that they had obstructive airways disease were co-dispensed one-off ICS with oral antibiotics.

Inappropriate prescribing of ICS increases the risk of adverse events for the patient as well as creating unnecessary cost to the public. It is estimated that in 2008 prescribing of ICS outside treatment guidelines for asthma and COPD cost the Australian Government at least \$2.7 million, with a further \$200,000 cost to patients.

The data presented here about prescribing practices also suggest that new strategies may be needed to assist in the diagnosis of patients presenting with respiratory symptoms in primary care. Improved diagnostic accuracy may minimise the likelihood that clinicians prescribe medication (or other therapy) that covers a number of possible diagnoses.

1 Introduction

There is evidence to suggest that inappropriate use of antibiotics is common both in the general community and in people with obstructive airways disease. The National Prescribing Service and World Health Organization state that antibiotics are overused in the general community and their widespread use has been shown to be a major cause of the development of antibiotic-resistant bacteria worldwide (NPS 2012; WHO 2012; Levy & Marshall 2004; Neu 1992). In 2008, antibiotics were commonly prescribed in Australia: oral antibiotics accounted for 3 of the top 10 drugs by prescription counts (DoHA 2009).

Amoxicillin was the second most prescribed drug with more than 6.5 million scripts, while cephalexin (sixth) and amoxicillin with clavulanic acid (tenth) also made the top 10.

Australian data from the Bettering the Evaluation and Care of Health (BEACH) survey in 2010–11 revealed that the most frequently prescribed medications in general practice were the antibiotics amoxicillin (3.8% of prescriptions) and cephalexin (3.2%) (Britt et al. 2011). Similar results were reported in 2008–09, the period covered by this analysis, when amoxicillin and cephalexin represented 4.1% and 2.9% of prescriptions, respectively (AIHW: Britt et al. 2009).

Use of antibiotics for the general population represents a substantial cost to the health system, and any inappropriate prescribing poses a burden both in terms of cost and consequences of their use.

Box 1.1: Respiratory tract infections

Respiratory tract infections (RTIs): RTIs are infectious diseases involving the respiratory tract. These are usually further classified into upper respiratory tract infections (URTIs) and lower respiratory tract infections (LRTIs).

URTIs: The upper respiratory tract includes the nasal cavity, pharynx, and larynx. Common conditions caused by URTIs include the common cold, laryngitis, pharyngitis, tonsillitis, otitis media, and sinusitis. They are often caused by viruses but may also be due to bacteria. Some typical symptoms of URTIs include cough, runny nose, headache, nasal congestion, sore throat and fever.

LRTIs: The lower respiratory tract includes the trachea, bronchi, and lungs. LRTIs may be caused by viral and/or bacterial infection. Infections of these areas of the respiratory tract (such as pneumonia, which is often bacterial) are generally more serious than URTIs.

Bacterial infections: Bacterial infections are, as the name suggests, infections caused by bacteria. Antibiotics are used for treating clinically important bacterial infections, for example, streptococcal pharyngitis, or for conditions that are highly likely to be caused by bacteria, for example, acute otitis media.

Viral infections: Viral infections are infections caused by viruses. They often cause similar symptoms to bacterial infections. Antibiotics have no effect in treating viral infections, such as the common cold.

Over the last decade there has been a concerted effort by government agencies and other organisations to discourage the use of antibiotics in the treatment of URTIs (Box 1.1) in the general population (NPS 2009). Data from the BEACH survey suggest that between 1990–91 and 2002–03 there was a decrease in the overall rate of antibiotic prescribing for URTIs (Pan et al. 2006). This was evident in both adults (58.2 to 40.0 per 100 URTI problems managed; $p < 0.001$) and children (39.0 to 24.4; $p < 0.001$) presenting to GPs with URTIs during this time. The rate of antibiotic prescribing for the treatment of other respiratory problems remained unchanged in the same period.

There has been little further change in the rate of antibiotic prescribing in general practice in Australia since 2003–04. In 2009–10, the rate of antibiotic prescribing remained high in the general population, specifically in the management of respiratory infections (AIHW: Britt et al. 2010).

The impact that campaigns to discourage the use of antibiotics for the treatment of RTIs in the general population has had on GP prescribing for patients with obstructive airways disease is not known. See Box 1.2 for definitions of obstructive airways diseases.

Box 1.2: What is obstructive airways disease?

Obstructive airways disease encompasses both asthma and chronic obstructive pulmonary disease (COPD).

Asthma is a common chronic inflammatory condition of the airways. People with asthma experience episodes of wheezing, breathlessness and chest tightness due to widespread narrowing of the airways. The symptoms of asthma are usually reversible, either spontaneously or with treatment (GINA 2009).

COPD is a serious long-term lung disease that mainly affects older people. It is characterised by airflow limitation that is not fully reversible with bronchodilator medications. Some people with COPD also have frequent cough with sputum due to excessive mucus production in the airways. This condition is often referred to as 'chronic bronchitis'. People with COPD may also have evidence of destruction of lung tissue with consequent enlargement of the air sacs and further impairment of lung function. This condition is known as 'emphysema' (Thurlbeck 1990). The terms COPD, emphysema and chronic bronchitis tend to be used interchangeably.

Exacerbations of asthma and COPD are characterised by a worsening of the patient's symptoms that is beyond their normal day-to-day variation, and requires a change in treatment.

Antibiotics and asthma

All patients with asthma, whether it is well or poorly controlled, may experience severe exacerbations in association with RTIs (Reddel et al. 1999).

Viral infections (see Box 1.1), such as rhinovirus, coronavirus, respiratory syncytial virus (RSV), influenza virus, and adenovirus, are associated with about 80% of asthma exacerbations in school-age children (Johnston et al. 1995) and up to 75% in adults (Wark et al. 2002). Bacteria are rarely implicated as a primary cause of asthma exacerbations. See Box 1.2 for the definition of asthma.

People with asthma are more likely to experience wheezing cough, and mucus production after respiratory virus infection than people without asthma (Corne et al. 2002). In people with asthma, as in the general population, these LRTI symptoms are occasionally due to secondary bacterial infection. However, people with asthma are no more prone to bacterial infection (see Box 1.1) than the general population.

Current national guidelines for the management of asthma state that antibiotics are rarely indicated in the treatment of asthma exacerbations in children or adults, unless a bacterial infection is present (NAC 2006). However, some of the symptoms of asthma exacerbations, such as cough or mucus production, may be similar to the symptoms of RTIs. People with asthma may be prescribed antibiotics for these symptoms, even if they are not, in fact, attributable to an infection. Hence, one would expect that antibiotic prescribing and dispensing would be common among people with asthma, particularly those with severe or poorly controlled asthma.

The relationship between the use of medications specifically to treat asthma and the use of antibiotics is likely to be complex and the evidence is conflicting. Frequent use of antibiotics by patients with asthma may reflect suboptimal asthma control and greater frequency of exacerbations, rather than frequent bacterial infections. In this context, the frequent use of antibiotics is probably not beneficial to the patient.

In France, people with poorly controlled asthma were more likely to be dispensed antibiotics for an exacerbation of asthma than people with well-controlled asthma (Laforest et al. 2008). In a socioeconomically deprived area of the United Kingdom, improving overall asthma control was associated with a decrease in antibiotic use (Moudgil et al. 2000). In a managed care organisation in the United States, antibiotic use was correlated with use of both bronchodilator and anti-inflammatory medication (Glauber et al. 2001).

Although the interpretation of data for antibiotic use in asthma needs to proceed with caution, monitoring of antibiotic dispensing is important to evaluate the extent of use, and as a first step in assessing appropriateness of treatment.

Antibiotics and COPD

Among people with COPD, acute exacerbations are commonly triggered by bacterial or viral infections. It has been estimated that 78% of COPD exacerbations are infectious in origin: 30% related to bacteria, 23% related to viruses, and 25% were due to bacterial and viral co-infection (Celli & Barnes 2007). See Box 1.2 for the definition of COPD.

A Cochrane review has found that treatment of exacerbations of COPD with antibiotics is associated with reduced mortality, reduced treatment failure, and reduced purulence of sputum (coloured mucus coughed up from the chest, indicative of bacterial infection) (Ram et al. 2009). Adding antibiotics to oral corticosteroid treatment among people with an acute exacerbation of COPD presenting to primary care reduces the risk of subsequent exacerbations and mortality (Roede et al. 2009). On the basis of this evidence, Australian guidelines for the management of COPD encourage early use of antibiotics in the management of infective exacerbations of COPD (McKenzie et al. 2010).

There is research interest in the long-term use of low doses of one particular class of antibiotic (macrolides) to reduce the risk of exacerbations in patients with COPD (Albert et al. 2011; Seemungal et al. 2008). The beneficial effect of this treatment is believed to occur through an anti-inflammatory and immune modulatory mechanism rather than through an antibacterial action. However, Australian treatment guidelines do not currently support long-term antibiotic use for COPD.

Although most patients with exacerbations of COPD present to, and are managed by, general practitioners, little is known about the use of antibiotics for exacerbations of COPD in this setting.

RTIs may also be an adverse effect of therapy in patients with COPD. There is evidence that treatment of patients with COPD with the inhaled corticosteroid (ICS) fluticasone is associated with an increased risk of LRTI, including pneumonia (Crim et al. 2009; Ernst et al. 2007). This may, in turn, lead to the increased use of antibiotics.

Although the same effect has not been seen with the ICS budesonide in COPD (Sin et al. 2009) and is not seen in patients with asthma treated with fluticasone or budesonide (O'Byrne et al. 2011), this finding has raised concerns about the adverse effects of this class of medication in people with COPD.

It is not clear whether this effect is specific to fluticasone or a class effect related to higher ICS dose or potency. In the study by Crim et al., the highest recommended dose of fluticasone was used (1000 mcg/day). Although not all episodes were radiologically confirmed as pneumonia, the fact that the events were reported as such suggested that they represented clinically significant LRTIs.

If there is a clinically important increased incidence of pneumonia in patients with COPD treated with ICS, this could be associated with an increased rate of prescription of antibiotics in these patients.

To better understand the risks and benefits of these medications for people with COPD, it is important to monitor their use. However, interpreting the relationship between use of ICS for patients with COPD and the use of antibiotics is difficult and complex, as ICS are only recommended for use in COPD patients with more severe disease and frequent exacerbations (McKenzie et al. 2010).

Inhaled corticosteroids and antibiotics

As well as concern about the use of antibiotics for respiratory conditions, there is also concern about the use of medications containing ICS contrary to treatment guidelines for the management of asthma and COPD.

Long-term regular use of ICS is an important component of the management of obstructive airways disease, based on evidence of their effectiveness in persistent asthma and in moderate to severe COPD. However, among children and young adults dispensed ICS in Australia, more than half are dispensed these medications only once in a calendar year. Among adults aged 65 and over, 23% of those receiving any ICS have the medication dispensed only once in a year, contrary to the long-term regular use recommended for the management of the disease (AIHW: ACAM 2008).

This dispensing pattern is often attributed to poor adherence to regularly prescribed preventer treatment regime by patients with persistent asthma, COPD, or other chronic respiratory conditions. It may reflect use by patients with intermittent asthma, for which regular treatment is not required, particularly in children. However, it could also be attributable to inappropriate prescribing of medications containing ICS for patients who do not have obstructive airways disease.

One possible explanation for inappropriate prescribing of medications containing ICS is that some patients with no history of obstructive airways disease are prescribed this medication and an antibiotic together for short-term treatment of an RTI. Evidence to support the effectiveness of this practice is lacking, and it is not recommended in treatment guidelines for RTIs, asthma (NAC 2006), or COPD (McKenzie et al. 2010).

Monitoring of such dispensing patterns may provide useful insight into prescribing patterns. The co-dispensing of one-off ICS and oral antibiotics is investigated in this report to provide insight into the use of single courses of ICS.

Rationale for this report

Given the worldwide increase in microbial antibiotic resistance (Levy & Marshall 2004; Hoban et al. 2001), the public health impact of over-using antibiotics among people with asthma and/or COPD – as among the general population – may be a cause for concern. While antibiotics are indicated early in the treatment for infective COPD exacerbations (McKenzie et al. 2010), and in the small proportion of asthma exacerbations in which primary or secondary bacterial infection appears to be delaying recovery (NAC 2006), there is not persuasive evidence for their use more broadly in acute exacerbations of obstructive airways disease.

Reducing unnecessary antibiotic treatment and, hence, the risk of antibiotic resistance, adverse events, morbidity, and mortality is an important challenge. This report examines antibiotic use in people who are taking treatment for obstructive airways diseases such as asthma and COPD. It assesses the association of antibiotic use with sociodemographic variables, such as age, sex, socioeconomic status, remoteness of residence and season, and with use of other medications, particularly medications containing ICS (Chapter 3). A first step to establishing whether the use of antibiotics in patients with asthma or COPD is appropriate is to measure the level of usage.

This can be achieved using the Pharmaceutical Benefits Scheme (PBS) data on dispensing of antibiotics and medications approved for treatment of asthma and/or COPD. Conversely, antibiotic dispensing data can be used to provide insight into potentially inappropriate use of medications containing ICS for isolated RTIs by examining co-prescribing of these classes of medications in patients who did not receive other respiratory medications within the same year and who are unlikely to have obstructive airways disease. Chapters 2 and 6 provide details of the methods used to examine dispensing patterns and data limitations.

This knowledge is important for our understanding of these medicines in people with asthma and COPD in Australia. People with COPD may have different requirements for the use of antibiotics than the general population, and for this reason the PBS analysis is limited to those dispensed medications used for treatment of obstructive airways disease, with additional analysis for patients who are most likely to have COPD as indicated by age (55 or over) and dispensing of tiotropium (Chapter 4).

This report also investigates dispensing of one-off ICS, using the co-dispensing of an antibiotic to identify events that may have been considered by the prescriber to represent a RTI. Results from this analysis may also assist in reducing inappropriate use of medications containing ICS (Chapter 5).

Chapter 3 also investigates the use of antibiotics in children with and without parent-reported doctor-diagnosed asthma using data from the Longitudinal Study of Australian Children (LSAC).

2 Methods

Data sources

Pharmaceutical Benefits Scheme data

In Australia, information on reimbursements for the purchase of some prescription medications is available from the PBS and the Repatriation Pharmaceutical Benefits Scheme (RPBS) databases. The PBS subsidises the cost of about 80% of prescription medications dispensed in Australia (DoHA 2010).

PBS prescriptions include Medicare numbers. Use of the Medicare number has created the capacity for anonymously identifying the prescription history of individuals within the PBS data set and also for linking that information with data on age group, gender, and postcode of residence. Hence, the PBS and RPBS represent an invaluable source of information about the patterns of use of medications in Australia.

Limitations of PBS data for studying obstructive airways disease

Even for items that are covered by the PBS or RPBS, subsidies are only paid, and recorded in the database, where the cost of the medication is more than the patient co-payment amount. As the co-payment for concession card holders is much lower than for general beneficiaries, a wider range of medications are subsidised by the PBS (and included in the PBS database) for patients who are concession card holders.

Most inhaled corticosteroid preparations and long-acting beta-agonist preparations, and all combined long-acting beta-agonist and inhaled corticosteroid preparations, are dispensed at a price that is higher than all PBS co-payments. Short-acting beta agonists, oral corticosteroids, and oral antibiotics, however, cost less and are only subsidised by the PBS when the patient is a concession card holder (see Table 2.1 for a description of the medications used for obstructive airways disease). For this reason and to ensure complete coverage of the relevant medications, analyses in this report have been limited to prescriptions dispensed to concessional patients. While this improves the completeness of the data, it does somewhat limit the general application of the results.

About 64% of people receiving medications for the treatment of asthma and COPD through the PBS hold a card that entitles them to the concessional rate (PBS data; AIHW: ACAM 2011).

Short-acting beta agonists are also available over the counter, that is, without a prescription. However, the over-the-counter cost is greater than the co-payment for a concession card holder who uses a prescription, which means there is a financial incentive for concession card holders to purchase short-acting beta agonists with a doctor's prescription. Therefore, it is assumed that most short-acting beta agonists dispensed to concessional patients are supplied with a prescription and recorded on the PBS database. A cross-sectional study of randomly selected pharmacies in Victoria (Douglass et al. 2012) confirms this assumption – 84% of health care or pension card holders purchased their short-acting beta agonists with a prescription rather than over the counter, compared with 35% of those without a health care or pension card.

The PBS data set in general excludes medications dispensed in the public hospital system, so does not include medication dispensed to patients who are admitted to a public hospital for management of an acute exacerbation.

PBS study population

Study cohorts were defined within the PBS data set for the period 1 January 2008 to 31 December 2008 based on their use of specific medications. They comprised:

- individuals who were dispensed any of the following respiratory medications used to treat obstructive airways disease: inhaled corticosteroid, long-acting or short-acting beta agonists, long-acting or short-acting anti-cholinergics, leukotriene receptor antagonists, theophylline or cromones (see also Table 2.1)
- individuals who were dispensed tiotropium bromide. In Australia, the long-acting anti-cholinergic inhaled medication tiotropium bromide (Spiriva™) is approved and subsidised only for use in the treatment of COPD. Since COPD is most common among people aged 55 and over, limiting the cohort to those in this age group who were dispensed this medication once or more during 2008 increases the likelihood that the cohort is comprised of people with COPD.

Only those medications dispensed and subsidised by the PBS to concession card holders are in this report. If an individual held a government health concession card at any time during 2008, they were included in the analysis.

The Longitudinal Study of Australian Children

The LSAC was initiated and is funded by the Australian Government Department of Families, Housing, Community Services and Indigenous Affairs and aims to explore a range of research questions about children's development and wellbeing.

The study began in 2004 with a sample of about 10,000 children recruited from the Medicare enrolments database. The sample is broadly representative of Australian children in each of two age cohorts:

- those born between March 2003 and February 2004 (infant cohort)
- those born between March 1999 and February 2000 (kindergarten cohort).

Both cohorts are followed up every 2 years (termed a Wave). The LSAC provides information on parent-reported current asthma among children in each cohort.

In this report, we used data from the LSAC for 2004 (Wave 1) to 2008 (Wave 3) to investigate specific questions related to the treatment of asthma in children. Data from the LSAC were linked to the PBS and MBS databases by the individual child health insurance commission identification number to enable access to information on the dispensing of medications. This allowed comparison of the use of antibiotics and respiratory medications among children with and without diagnosed asthma or recent asthma symptoms.

LSAC study population

The study populations were from two cohorts of Australian children aged 0–1 and 4–5 at baseline (2004) that were followed up in 2006 and 2008 (infant and kindergarten).

Children were classified as having asthma if their parents had responded 'Yes' to 'Ever told by a doctor they have asthma' and 'Yes' to 'In the last 12 months, has child had an illness

with wheezing in the chest which lasted for a week or more or taken any medication for asthma?' at any one of three interviews over the 4-year observation period.

Parents of those children in the infant cohort were not asked about the diagnosis of asthma in the baseline interview.

Data analysis

Pattern of antibiotic use among people dispensed any medications for obstructive airways disease

Within the PBS cohorts described above, we investigated the type, frequency and seasonality of antibiotic dispensing.

The factors which were analysed in relation to their effect on the nature and frequency of antibiotic dispensing include:

- sociodemographic characteristics
- use of specific respiratory medications
- frequency of use of inhaled corticosteroids
- season/time of year.

To address this question specifically in children, we used data from the LSAC linked to the PBS. Rates of antibiotic dispensing for all children receiving ICS prescriptions in 2008 were compared for those with and without diagnosed asthma.

It should be noted that asthma and COPD can be difficult to distinguish in clinical practice as their definitions are not mutually exclusive and both have similar manifestations.

Long-acting beta-agonists and inhaled corticosteroids and their combination are often used in the treatment of asthma as well as COPD, and the PBS record does not include the indication for prescription.

For these reasons, this data source is unable to distinguish medications dispensed for asthma alone.

Co-dispensing of an antibiotic with a one-off inhaled corticosteroid

We also investigated whether ICS are being used for the treatment of RTIs, using PBS data.

If antibiotics are prescribed at the same time as a one-off ICS-containing medication, this might indicate inappropriate prescribing of inhaled corticosteroids for the management of RTIs in patients without evidence of asthma or COPD.

First, we defined a cohort of subjects who were dispensed only one ICS-containing medication in 2008 (Figure 3.1). We excluded those who had any ICS scripts dispensed in adjacent years within 6 months (before or after) of the one-off ICS dispensing in 2008. In this way, we excluded those who may have started taking ICS-containing medication in the latter part of 2008 and continued taking the medication regularly throughout 2009. Also, people who were dispensed one ICS in the early half of 2008 but were taking the medication at regular intervals in the previous calendar year would be excluded from our analysis. In doing this, we ensured that the study population only included those who were dispensed ICS once in a period of one year.

From this cohort we further excluded subjects who were dispensed any other respiratory medications within 6 months before or after the date the ICS were dispensed (except within the period 7 days before or after this event). With this exclusion we have defined a cohort of people who are unlikely to have obstructive airways disease.

We then identified those members of the cohort who were dispensed antibiotics within 7 days before or after the one-off ICS dispensing date (that is, who were co-dispensed these medications). Our assumption is that this defines a cohort of people who are unlikely to have obstructive airways disease (including asthma or COPD) and have probably been prescribed this combination of medications, that is, antibiotics and ICS, for management of a RTI.

Cost to Government

We calculated the cost to Government of one-off ICS prescriptions when co-dispensed with antibiotics by multiplying the number of one-off prescriptions dispensed for each of the ICS drugs by the total cost of each of the ICS drugs. The cost of the ICS drugs used in the calculations was that listed in the 2008 PBS Schedule. It should be noted that we subtracted the concessional co-payment (\$5 in 2008) from the total cost of each drug so that the total cost to Government excluded the cost paid by the patient. We separately estimated the cost of the one-off ICS prescriptions to the patient.

Definitions

Concession card holders

We defined concession card holders as those with patient category codes of:

- C0 – concessional safety net
- C1 – concessional non-safety net
- R0 – repatriation safety net or
- R1 – repatriation non-safety net.

If a patient was a concession card holder at any time during the study period (2008), they were included in the analysis.

Medications for obstructive airways disease

The following were classified as medications used by people with obstructive airways disease:

- short-acting beta agonists (SABA)
- long-acting beta agonists (LABA)
- any inhaled corticosteroids (ICS, either alone or in combination with long-acting beta agonist)
- short-acting anticholinergics
- long-acting anticholinergics
- xanthines (theophylline)
- cromones
- leukotriene receptor antagonists and/or
- oral corticosteroids (these were only included if the individual was also dispensed one or more other respiratory medications).

A description of the mode of action of these medications is in Table 2.1.

Antibiotics

Only oral antibiotics that may be used for short-term treatment of respiratory infections were included in the analyses. Antibiotic formulations approved for long-term use, defined as those prescribed with five repeats (for example, doxycycline for bronchiectasis or severe acne) were excluded.

We have included information about antibiotics down to the Anatomic Therapeutic Chemical (ATC) level 5 since the different antibiotics prescribed reflect the different nature of infections in people with COPD compared with people with other obstructive airways diseases.

Table 2.1: Medications for obstructive airways disease and their mode of action

Type of medication	Description
Short-acting beta-agonists (SABA)	These are fast-acting bronchodilators; their effects are evident within 5 minutes and last for about 3 hours. They are used to relieve bronchoconstriction and are known in Australia as 'reliever' medications. Short-acting beta-agonists should only be used for intermittent symptom relief. Frequent use indicates poorly controlled asthma. Examples include salbutamol and terbutaline.
Long-acting beta-agonists (LABA)	Long-acting beta-agonists (available as eformoterol and salmeterol) relax the muscles that surround the airways and allow for easier breathing. In asthma management, long-acting beta-agonists are only recommended for use in combination with inhaled corticosteroid therapy. In COPD, these medications may be used on their own. Eformoterol has an onset of action of 1–3 minutes and salmeterol 10–20 minutes. The action of these long-acting beta-agonists lasts at least 12 hours.
Inhaled corticosteroids (ICS)	Inhaled corticosteroids are widely used in the treatment of airways disease (including asthma and moderate to severe COPD) to reduce bronchial inflammation and hyper-responsiveness. They reduce symptoms, improve lung function, and reduce the risk of exacerbations. Inhaled corticosteroids are most effective when used on a regular basis, either twice or once daily. In Australian asthma guidelines, inhaled corticosteroids are termed 'preventers'. Examples include beclomethasone, budesonide and fluticasone.
Short-acting anti-cholinergics	Short-acting anti-cholinergics are bronchodilators; their peak effect is not reached for 1.5–2 hours and the duration of action is about 6 hours. This type of medication is not normally used for immediate relief of symptoms. It is mainly used in acute exacerbations of COPD and sometimes in the emergency situation for acute, severe asthma. (Ipratropium bromide is the only example of this class of drugs available in Australia.)
Long-acting anti-cholinergics	Inhaled anti-cholinergic drugs work by relaxing the muscles that surround the airways. This tends to open the airways and relieve breathlessness. The duration of action is more than 24 hours and the onset of action is about 30 minutes. The only long-acting anti-cholinergic drug available in Australia is tiotropium bromide. It only needs to be taken once per day.
Xanthines (theophylline)	Xanthines are bronchodilators that are administered orally and have a highly variable half-life of about 8 hours in adults and 4 hours in children.
Cromones	Cromones are administered by inhalation and are occasionally used as preventer treatment of asthma. Cromones must be taken regularly to produce optimal effect but they will not relieve acute symptoms. Although the mechanism of action of these drugs is not fully understood, they are thought to block allergen-induced bronchoconstriction, and may be useful in asthma associated with allergic factors. They may also be used to prevent exercise-induced asthma. Examples include cromoglycate and nedocromil.
Leukotriene receptor antagonists	The leukotriene receptor antagonist is orally administered and acts by reducing airway inflammation mediated by leukotrienes. In Australia, this type of treatment is used as a preventer medication for asthma, mostly in children. It may also play a role in the management of aspirin-sensitive asthma and exercise-induced bronchoconstriction. An example is montelukast.
Oral corticosteroids (OCS)	During episodes of marked worsening of asthma symptoms (known as severe exacerbations), oral corticosteroids are sometimes used for short-term treatment. Corticosteroids act to reduce inflammation and swelling in the airways. A small number of people with severe asthma that is not controlled with maximal inhaled therapy need long-term treatment with oral corticosteroids to control their disease. Unlike inhaled corticosteroids, oral corticosteroids are carried to all parts of the body and are more likely to cause side effects, particularly if they are used for more than 2 weeks. Prednisone is the most commonly used formulation.

Co-dispensing of an antibiotic and one-off inhaled corticosteroids

We defined 'co-dispensing of an antibiotic' as dispensing of an antibiotic within 7 days before or after dispensing of one-off ICS. We chose 7 days as the cut-off to identify medications likely to have been used to treat the same clinical event.

This is substantially shorter than the typical duration of LRTIs (median 18 days, mean 24 days) (Ward et al. 2005). If anything, therefore, the extent of co-prescribing of one-off ICS with antibiotics for such clinical episodes would have been under-estimated.

'One-off' ICS was defined as the dispensing of an ICS-containing medication to a patient who received no other respiratory medications in the previous 6 months or the subsequent 6 months, apart from within 7 days before or after the index prescription of ICS.

Statistical procedures

The relationship between the various explanatory factors and antibiotic use was quantified as rate ratios. The rate ratios were estimated using a generalised linear model (Proc GenMod in SAS, v9.2) with a binomial distribution and log link.

The factors sex, age, socioeconomic status and remoteness of area of residence were included in the model where antibiotic use was the dependent variable of interest.

All the models were unadjusted and no multivariate analyses were performed.

3 Pattern of use of antibiotics in people with obstructive airways disease

This section describes the pattern of use of antibiotics among people with obstructive airways disease using data from the PBS and the LSAC. The PBS study population is limited to concession card holders, to ensure complete coverage for the relevant medications (see Chapter 2).

Pattern of use of antibiotics among people taking any respiratory medications

In 2008, there were 1,109,322 individuals who were dispensed medications that are usually prescribed for obstructive airways disease (from now referred to as 'respiratory medications') at the concessional rate (see 'Definitions' in Chapter 2).

Of these, 826,836 (75%) were also dispensed oral antibiotics at any time in the same year (Table 3.1).

It is not possible to assess the appropriateness of the antibiotic prescriptions, and no published data are available for the proportion of the general Australian population who are prescribed antibiotics in any year, for comparison with these results.

Table 3.1: Frequency of oral antibiotic prescriptions among concession card holders who were dispensed any respiratory medication during 2008

Number of oral antibiotic prescriptions dispensed	Number of persons (%)
None	282,486 (25.5)
1	180,588 (16.3)
2	172,582 (15.6)
3–4	204,020 (18.4)
5–8	172,149 (15.5)
9 and over	97,497 (8.8)
Total	1,109,322 (100)

Source: ACAM analysis of PBS data.

Among concession card holders who were dispensed respiratory medication(s) during 2008, a slightly higher proportion of females (77.5%) than males (72.1%) were dispensed oral antibiotics at some time during the year (Table 3.2). The proportion of this cohort who were dispensed antibiotics was highest among 0 to 4 year olds and lowest among 5 to 14 year olds. Dispensing of oral antibiotics in this cohort decreased with increasing remoteness of residence (Table 3.2) but did not differ meaningfully by socioeconomic status.

Table 3.2: Dispensing of oral antibiotics among concession card holders who were dispensed any respiratory medication, by demographic variables, 2008

Demographic variable (%)	Dispensed oral antibiotics (%)	Relative risk % (95% CI)
Sex		
Male (42.3)	334,495 (71.3)	1.0
Female (57.6)	491,366 (76.9)	1.08 (1.07–1.08)
Age group (years)		
0–4 (5.1)	47,303 (83.7)	1.22 (1.21–1.22)
5–14 (10.4)	78,908 (68.7)	1.0
15–34 (11.5)	91,078 (71.2)	1.04 (1.03–1.04)
35–64 (27.8)	228,036 (73.9)	1.07 (1.07–1.08)
65 and over (45.1)	380,536 (76.1)	1.10 (1.10–1.11)
Socioeconomic status (SES, from SEIFA)		
SES 1 (low SES) (22.5)	188,117 (75.4)	1.00 (1.00–1.00)
SES 2 (22.3)	180,919 (73.3)	0.97 (0.97–0.97)
SES 3 (21.2)	174,158 (74.2)	0.98 (0.98–0.99)
SES 4 (18.0)	149,517 (74.9)	1.00 (1.00–1.00)
SES 5 (high SES) (15.4)	128,728 (75.2)	1.0
Remoteness category (ASGC)		
Major cities (65.0)	551,436 (76.5)	1.0
Inner regional areas (23.0)	182,110 (71.2)	0.93 (0.93–0.94)
Outer regional areas (10.1)	78,615 (70.1)	0.92 (0.91–0.92)
Remote (1.1)	8,272 (68.0)	0.89 (0.88–0.90)
Very remote (0.3)	2,077 (63.2)	0.83 (0.80–0.85)
All ages	826,836 (75)	

Notes

1. Relative risk describes the risk (or probability) of being dispensed oral antibiotics according to each demographic variable.
2. For each demographic variable we have estimated the risk of being dispensed oral antibiotics compared with the reference group, which has a relative risk of 1.0 and is shown in bold.
3. Demographic variable percentages may not add up to 100% due to missing values.

Source: ACAM analysis of PBS data.

The most commonly dispensed antibiotic within this cohort was amoxicillin (19.2% of all antibiotic scripts in this population), followed by amoxicillin with clavulanic acid (18.4%) and cephalexin (17.1%) (Table 3.3).

Table 3.3: Number of scripts for oral antibiotic dispensing among concession card holders who were dispensed any respiratory medication, by type of antibiotic (ATC level), 2008

Antibiotic group (ATC level 3/4)	Number of scripts	Per cent of scripts (n=3, 545,506)
Tetracycline	170,144	4.80
Beta-lactam antibacterials, penicillins	1,360,696	38.38
Other beta-lactam antibacterials	796,060	22.50
Sulfonamides and trimethoprim	175,085	4.94
Macrolides, lincosamides and streptogramins	850,758	24.00
Quinolone antibacterials	87,304	2.46
Other antibacterials	105,459	2.97

Note: Refer to Appendix A for a more detailed analysis.

Source: ACAM analysis of PBS data.

Frequency of dispensing of oral antibiotics and inhaled corticosteroids among children

Within the LSAC cohort in 2008, ICS were dispensed to 126 children (24.9%) who were eligible to receive prescriptions at the concessional rate and whose parents reported that they had ever been diagnosed with asthma.

In comparison, 25 (3.3%) eligible children who had never been diagnosed asthma were dispensed any ICS in 2008 ($p < 0.0001$).

In terms of oral antibiotic prescriptions, there was no difference in the proportion of children dispensed oral antibiotics according to asthma status. In 2008, 80.2% of children with asthma were dispensed oral antibiotics compared with 80% of children without a parent-reported diagnosis of asthma. These data show that most children will be prescribed an antibiotic in any given year, irrespective of whether they have asthma.

In the PBS data set, among children receiving ICS medications at the concessional rate, more than half (53.2%) were dispensed one ICS prescription during that year while few had more than 6 ICS prescriptions dispensed (Figure 3.1). This is as expected given the intermittent nature of asthma in children (AIHW: ACAM 2008). It should be noted that no diagnostic information is available in the PBS data set.

The majority of children aged 0 to 4 (82.8%) and 5 to 14 (68.4%) who were dispensed any ICS in 2008 were dispensed oral antibiotics at least once in the same year.

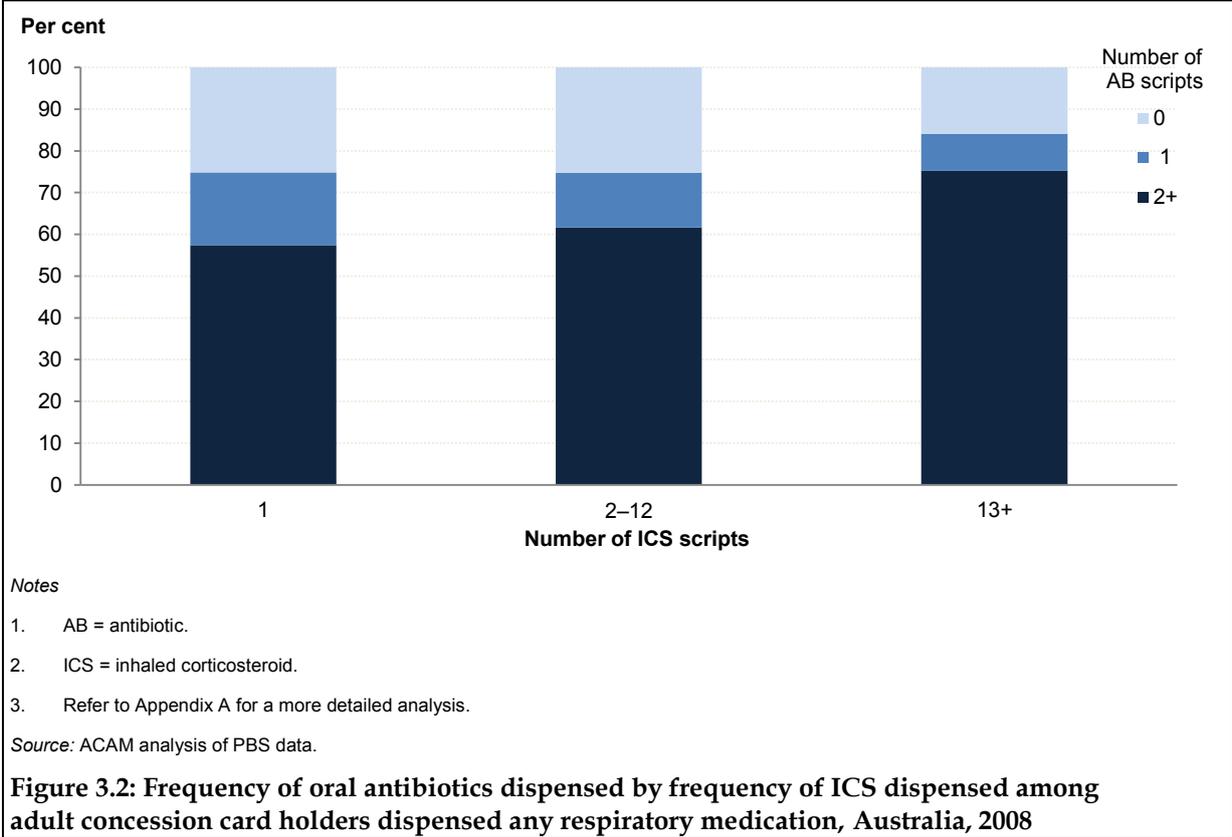
In the majority of cases, more than one course of oral antibiotics was dispensed during the year, with 18.8% of children aged 0–4 and 24.5% of children aged 5–14 having a single prescription for oral antibiotics dispensed in 2008 (Figure 3.1).

The frequency of dispensing of antibiotics increased with the frequency of dispensing of ICS (Figure 3.1).

Frequency of dispensing of oral antibiotics and inhaled corticosteroids among adults

In the PBS data set, among concession card holders aged 15 to 64 who were dispensed any respiratory medication in 2008, 40% of those who were dispensed any ICS were only dispensed one ICS prescription during that year.

Among adults, rates of prescription of antibiotics increased with age and also with use of ICS (Figure 3.2).



The relationship between medication use and health-care use is complex. People with more severe disease are more likely to suffer from viral infections (Sin et al. 2009). They may also visit the GP more often and, as a result, are more likely to leave the GP’s office with a prescription.

Frequent users of ICS are dispensed more antibiotics than less frequent users. This relationship exists for both children (Figure 3.1) and adults (Figure 3.2).

The complex relationship between health-care use, disease severity and medication use means that it is not possible to assess the appropriateness of this pattern of medication use from the available data.

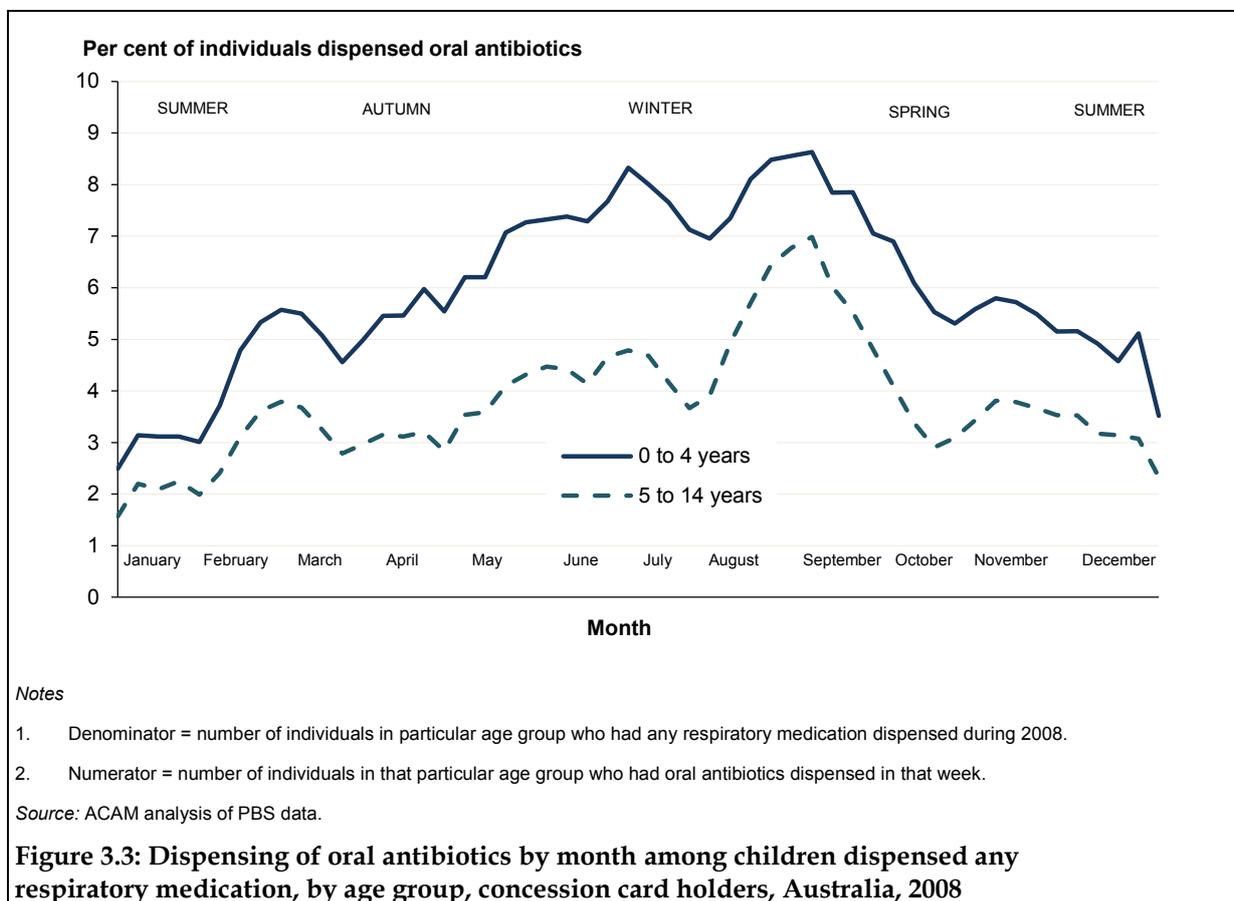
Seasonality

In 2008, among children taking respiratory medication, there was a small peak in oral antibiotic dispensing in late February and a gradual rise to larger peaks in early and then late winter or early spring (Figure 3.3).

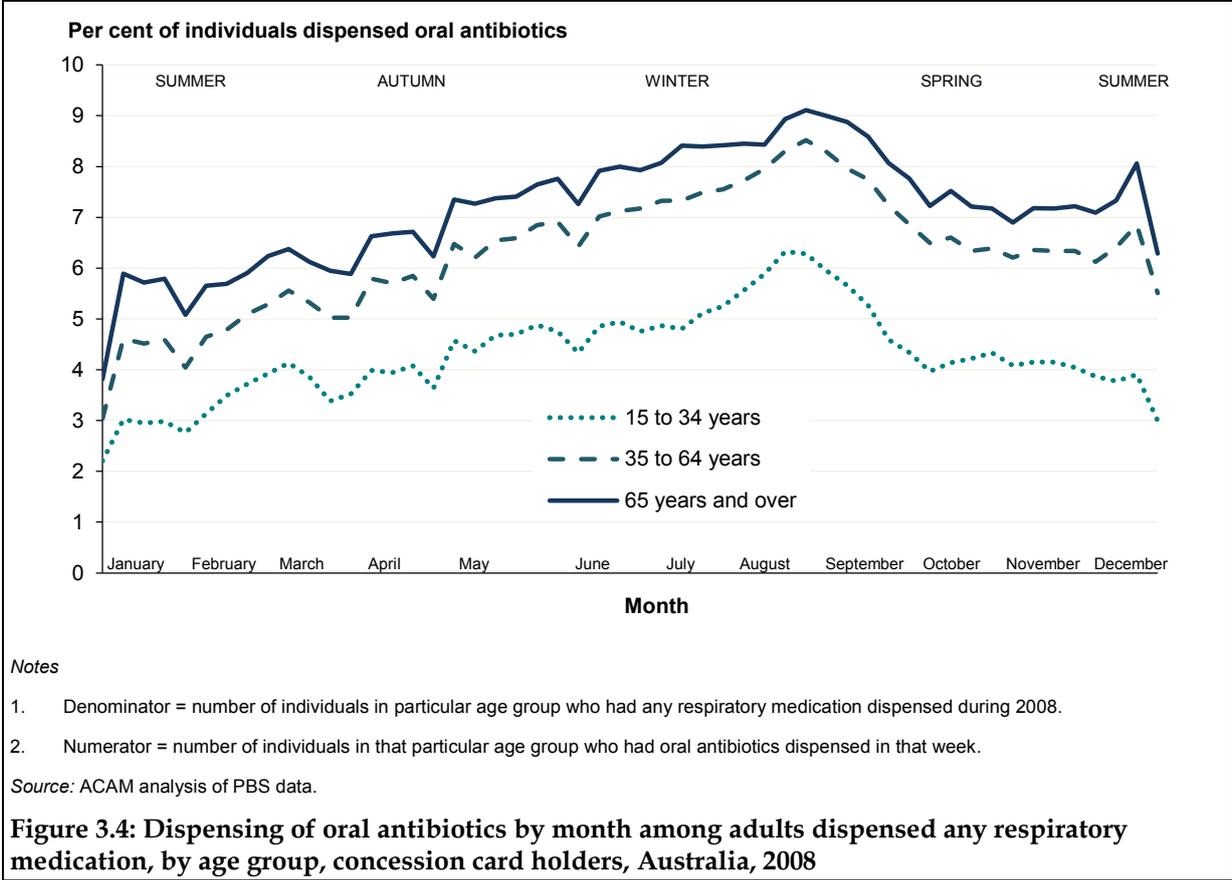
The timing of the peaks in antibiotic dispensing in children mirror those in hospital admissions for asthma in this age group (AIHW: ACAM 2008), although the magnitude of the February peak in oral antibiotic dispensing is less marked than that for asthma admissions.

The small peak in February coincides with the return to school after the summer holidays and is a well-documented time of year for respiratory infections in children, particularly those with asthma (Lister et al. 2001).

Interestingly, a dip in oral antibiotic dispensing occurred in July before the largest peak in August/September. This was apparent in both younger and older children.



In 2008, among adults receiving respiratory medication, there was a gradual rise in oral antibiotic dispensing from January to late winter before a decline in spring (Figure 3.4). The relative magnitude of the seasonal change in prescribing antibiotics to people taking respiratory medications is larger for children than adults. This may be due to the seasonality in children of specific bacterial infections showing as acute otitis media and pharyngitis, and the higher overall dispensing of antibiotics in older adults.



The rise in respiratory medications dispensed at the end of the calendar year and the corresponding reduction in the first week of the calendar year, shown in figures 3.3 and 3.4, probably reflects patients reaching the safety net threshold and stockpiling prescriptions at the cheaper rate.

4 Pattern of use of antibiotics among adults most likely to have COPD

There is no diagnostic information available in the PBS data set and, since many medications are used for the treatment of both asthma and COPD, it is difficult to investigate the use of medications for one condition or the other. However, tiotropium bromide is an inhaled long-acting anticholinergic medication that is only approved for use in Australia for treatment of COPD. COPD is also most common among people aged 55 and over. Thus, limiting the cohort to those in this age group who were dispensed this medication once or more during 2008 increases the likelihood that the cohort comprised people with COPD.

This section examines the use of antibiotics in this cohort of adult concession card holders who are most likely to have COPD.

Frequency of dispensing of oral antibiotics among adults most likely to have COPD

Among people dispensed any respiratory medication in 2008, 178,903 concession card holders were aged 55 and over and were dispensed tiotropium at least once throughout the year. These individuals represent a cohort who are assumed to have COPD. Within this cohort, 138,796 (77.6%) were also dispensed oral antibiotics in the same year.

Antibiotics are recommended for treatment of exacerbations of COPD (McKenzie et al. 2010). Despite this recommendation, we cannot detect any increased use of antibiotics in the COPD cohort compared with patients receiving any respiratory medications who were dispensed antibiotics. The proportion of individuals with COPD who were dispensed oral antibiotics in 2008 (77.6%) is only slightly higher than the overall proportion of patients receiving any respiratory medications who were dispensed antibiotics (75%, see Chapter 3).

The most common type of oral antibiotic dispensed among this population was amoxicillin with clavulanic acid (21.4%), followed by roxithromycin (17.4%) (Table 4.1).

Table 4.1: Number of prescriptions for oral antibiotics among concession card holders who were dispensed tiotropium, by type of antibiotic (ATC level), 2008

Antibiotic group (ATC level 3/4)	Number of scripts	Percentage of scripts (n=789,810)
Tetracycline	52,113	6.60
Beta-lactam antibacterials, penicillins	268,958	34.05
Other beta-lactam antibacterials	168,881	21.38
Sulfonamides and trimethoprim	39,382	4.99
Macrolides, lincosamides and streptogramins	208,350	26.38
Quinolone antibacterials	32,661	4.14
Other antibacterials	19,465	2.46

Notes

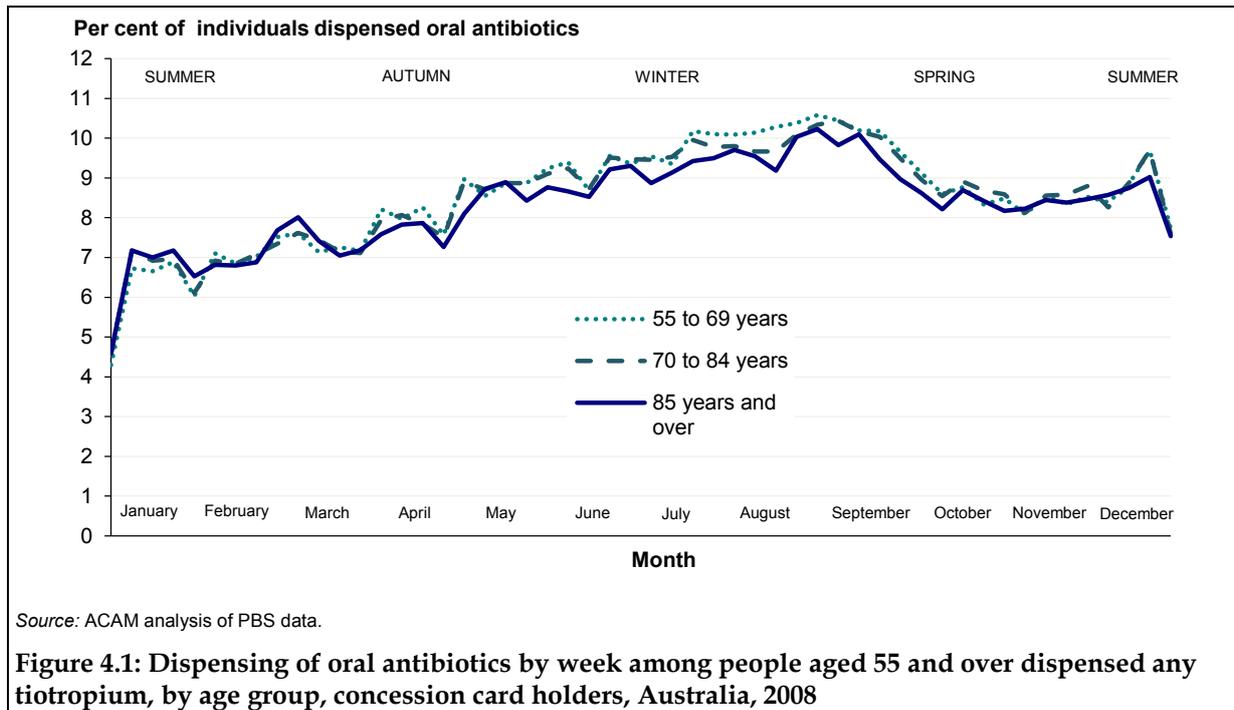
1. Some individuals had more than one antibiotic dispensed, therefore, the number of scripts for antibiotics (n=789,810) is greater than the number of individuals most likely to have COPD who were dispensed oral antibiotics (n=138,796).
2. Refer to Appendix A for a more detailed analysis.

Source: ACAM analysis of PBS data.

In the cohort of people most likely to have COPD, the type of antibiotics prescribed reflects the nature of expected infections in people with COPD compared with people with other obstructive airways diseases. Amoxycillin with clavulanic acid (as opposed to amoxicillin alone) is the antibiotic of choice when amoxycillin-resistant infections, such as *Haemophilus influenzae*, are present or suspected. These organisms are more common in people with COPD than in the general population.

Seasonality

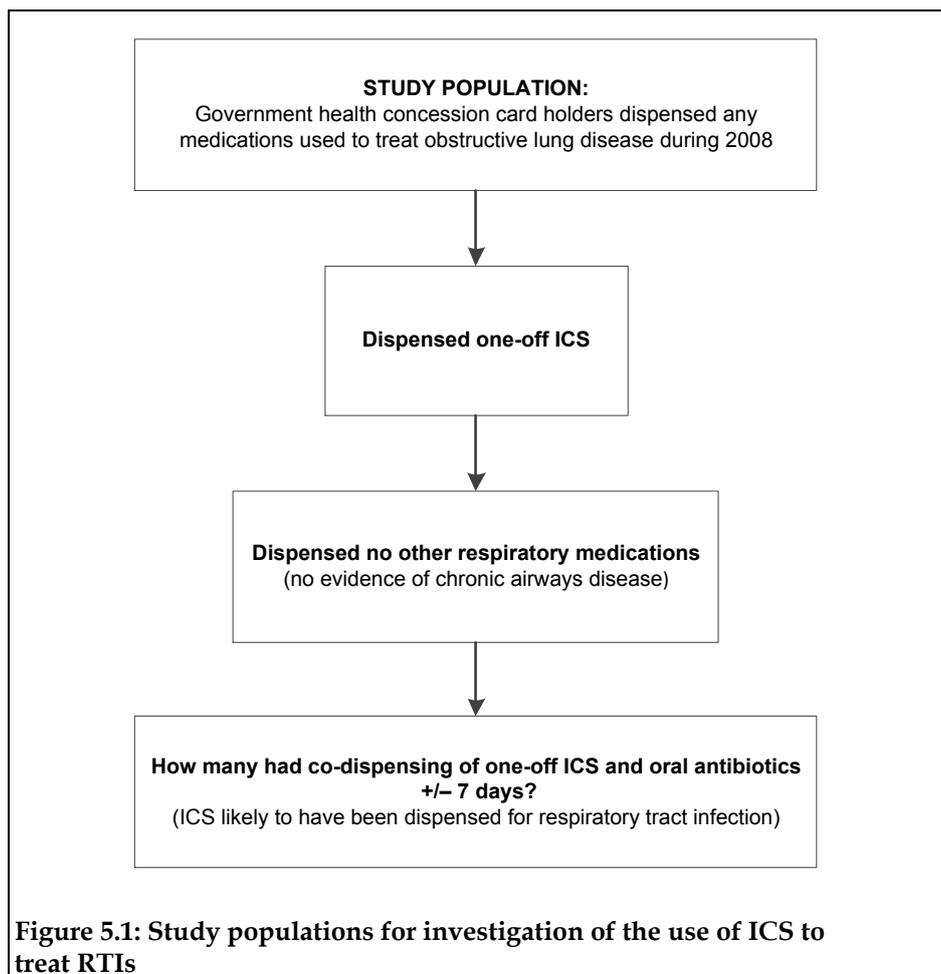
In 2008, within the cohort presumed to have COPD, dispensing of antibiotics increased from January to August, reaching a peak at the beginning of spring (Figure 4.1). Oral antibiotics were dispensed throughout the year, in contrast to the substantial winter peak in GP visits and hospitalisations (AIHW: ACAM 2011) observed in this age group. The seasonality of antibiotic dispensing in people with COPD (Figure 4.1) is similar to the seasonality in oral antibiotic dispensing in people with obstructive airways disease in general (Figure 3.4).



5 Are inhaled corticosteroids being used as treatment for respiratory tract infections?

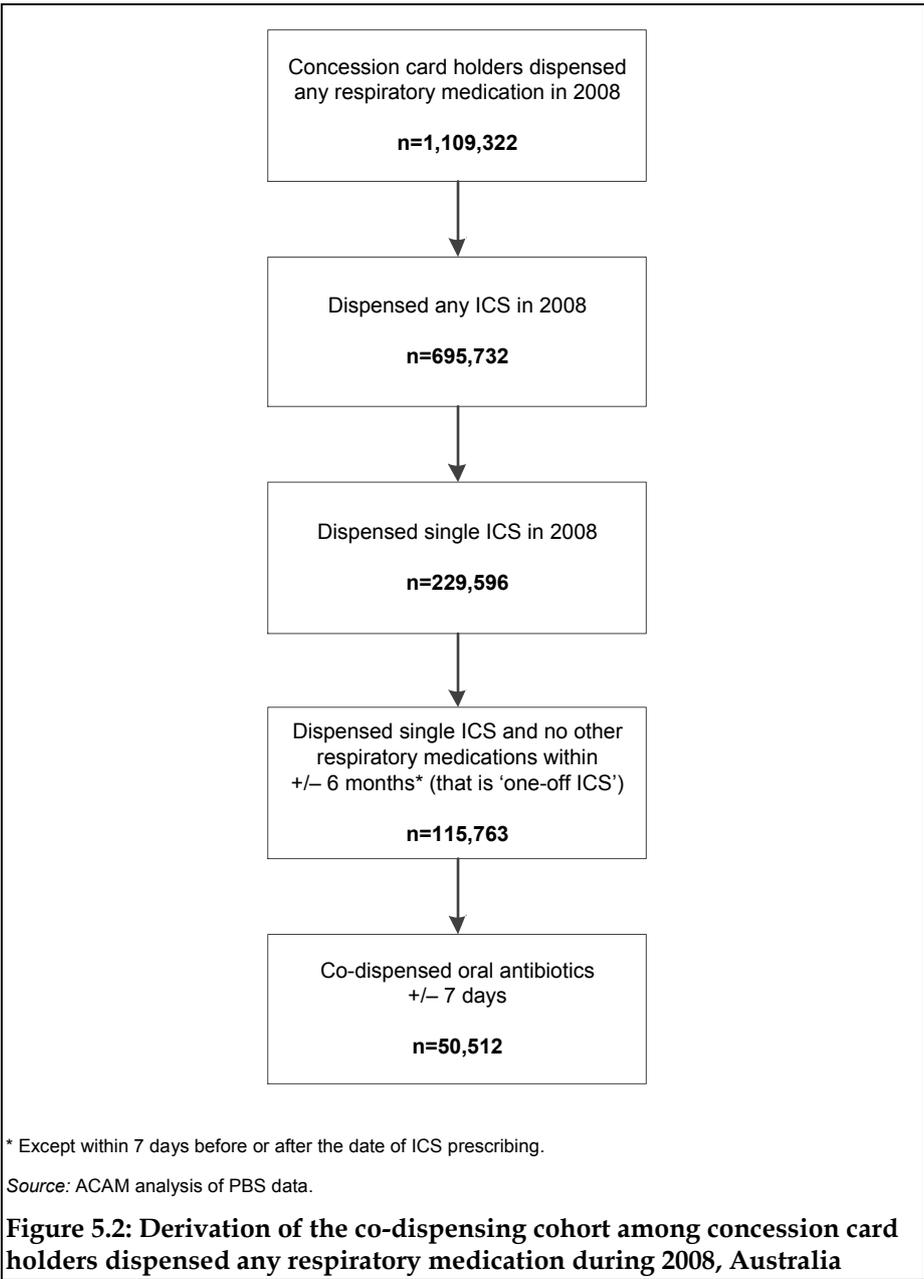
Inhaled corticosteroids are recommended for regular daily use in the management of obstructive airway disease such as asthma and moderate to severe COPD. However, as indicated in Chapter 2, 40% of concession card holders aged 15 to 64 who were dispensed any ICS in 2008 were only dispensed one ICS prescription during that year. If these patients received no other respiratory medications during the year, this would suggest that they did not have evidence of chronic airways disease warranting treatment with ICS. Further, if the one-off ICS was dispensed at the same time as an antibiotic, it would suggest that the ICS itself had been inappropriately prescribed for the management of an RTI. This is not supported by evidence, nor recommended in treatment guidelines.

This chapter examines the apparent use of ICS as treatment for RTIs in patients without any evidence of obstructive airways disease using the cohort described in Figure 5.1. See Chapter 2 for a description of the methods.



As shown in Figure 5.2, there were 695,732 patients with a concession card who were dispensed ICS-containing medication during 2008. Of these, 229,596 (33%) were dispensed a one-off prescription for ICS and 115,763 (50%) of these had no other ICS or other respiratory medications dispensed between 8 days and 6 months on either side of this event. Within this final cohort, who appeared to have no evidence of obstructive airways disease, 50,512 (44%) were co-dispensed oral antibiotics with their one-off dispensing of ICS.

As a further investigation, a sensitivity analysis was conducted to examine the effect of excluding those whose concessional status changed during 2008. The sensitivity analysis showed that change in concessional status during the course of the year had only minimal impact on the findings (see Appendix B).



Frequency of co-dispensing inhaled corticosteroids and oral antibiotics

Co-dispensing of medications containing ICS and oral antibiotics within this cohort was slightly more common in females, and in adults more than children. There was no difference in co-dispensing according to socioeconomic status. People living in *Major cities* of Australia were more likely to be co-dispensed ICS and antibiotics than people living in other areas (Table 5.1).

Table 5.1: Proportion of concession card holders dispensed medications containing ICS only once during 2008 (and no other respiratory medication) who were co-dispensed oral antibiotics (within 7 days before or after), by demographic variables, Australia

Demographic variable (%)	Proportion of total (n=115,763) co-dispensed oral antibiotics	Relative risk (95% CI)
Overall	50,512 (43.6%)	
Sex		
Males (38.9)	18,705 (41.5%)	1.0
Females (61.1)	31,781 (45.0%)	1.08 (1.07–1.10)
Age group (years)		
0 to 4 (4.3)	1,944 (39.0%)	1.03 (0.99–1.07)
5 to 14 (16.1)	7,032 (37.8%)	1.0
15 to 34 (19.4)	10,303 (46.0%)	1.22 (1.19–1.25)
35 to 64 (29.9)	16,003 (46.2%)	1.22 (1.20–1.25)
65 and over (30.4)	15,204 (43.3%)	1.15 (1.12–1.17)
Socioeconomic status (from SEIFA)		
SES 1 (low SES) (21.6)	10,876 (43.7%)	0.98 (0.96–1.00)
SES 2 (21.5)	10,569 (42.8%)	0.96 (0.94–0.98)
SES 3 (21.4)	10,610 (43.2%)	0.97 (0.95–0.99)
SES 4 (18.5)	9,428 (44.4%)	0.99 (0.97–1.02)
SES 5 (high SES) (17.0)	8,726 (44.6%)	1.0
Remoteness category (ASGC)		
Major cities (68.9)	35,875 (45.2%)	1.0
Inner regional areas (20.9)	9,757 (40.5%)	0.90 (0.88–0.91)
Outer regional areas (9.0)	4,139 (40.0%)	0.89 (0.86–0.91)
Remote/Very remote (0.3)	529 (36.3%)	0.80 (0.75–0.86)

Notes

1. In this table, relative risk describes the risk (or probability) of being co-dispensed one-off ICS and oral antibiotics according to each demographic variable.
2. For each demographic variable we have estimated the risk of being co-dispensed oral antibiotics compared with the reference group, which has a relative risk of 1.0 and is shown in bold.
3. Demographic variable percentages may not add up to 100% due to missing values.

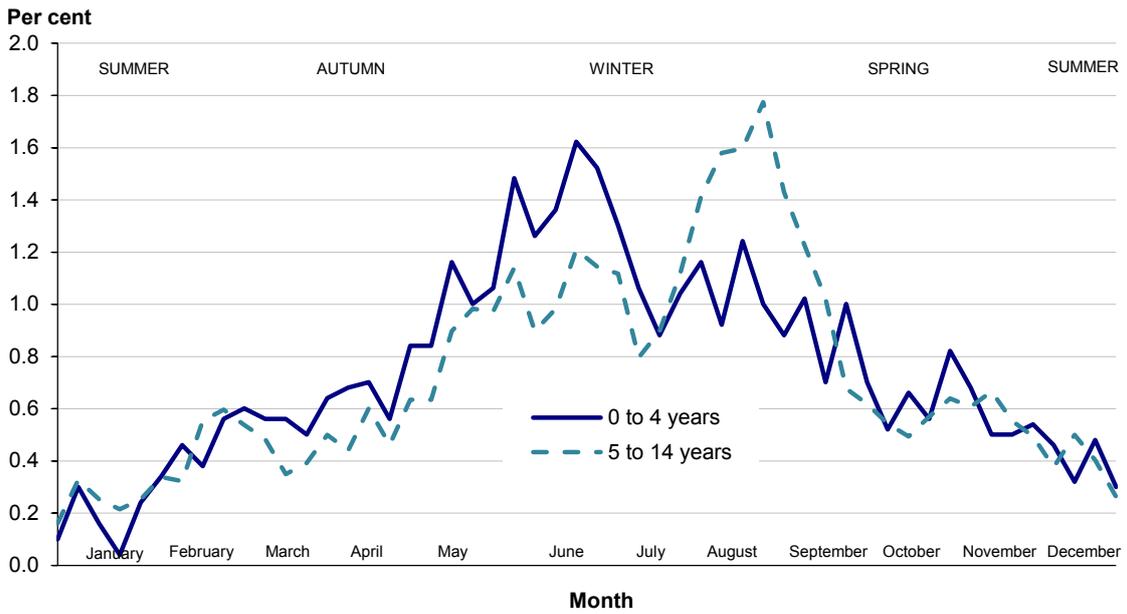
Source: ACAM analysis of PBS data.

The majority (70%) of co-dispensed ICS and oral antibiotics were dispensed on the same day; in 22.5% of cases the antibiotics were dispensed 1-7 days before the one-off ICS, and for the remaining 7.5% of cases they were dispensed 1-7 days after the one-off ICS (Table 5.2).

Table 5.2: Timing of co-dispensing of one-off ICS and oral antibiotics, concession card holders, Australia, 2008

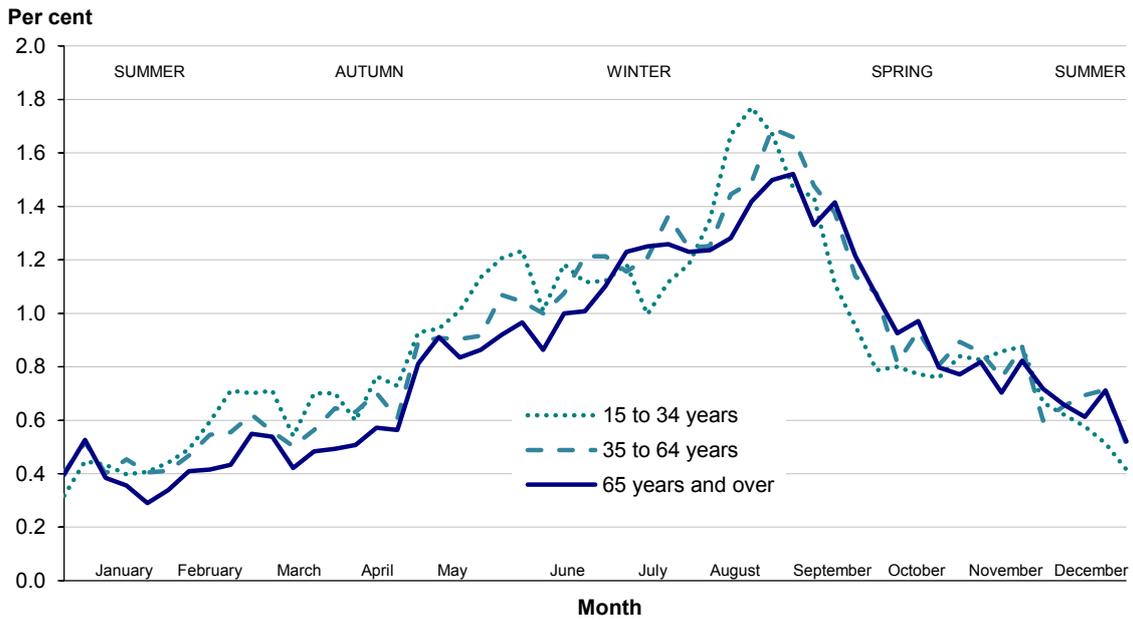
Antibiotics dispensed on	Frequency (%) n=50,512
-5-7 days	6,005 (11.9)
-3-4 days	3,280 (6.5)
-1-2 days	2,090 (4.1)
Same day as ICS	35,359 (70.0)
+1-2 days	1,118 (2.2)
+3-4 days	1,084 (2.2)
+5-7 days	1,576 (3.1)

Source: ACAM analysis of PBS data.



Source: ACAM analysis of PBS data.

Figure 5.3a: Co-dispensing of oral antibiotics by week among children dispensed one prescription of any ICS, by age group, concession card holders, Australia, 2008



Source: ACAM analysis of PBS data.

Figure 5.3b: Co-dispensing of oral antibiotics by week among adults dispensed one prescription of any ICS, by age group, concession card holders, Australia, 2008

Seasonality of co-dispensing of one-off inhaled corticosteroid and oral antibiotics

By contrast with the seasonality of general dispensing of antibiotics in patients receiving respiratory medications (Figures 3 and 4), co-dispensing of one-off ICS with oral antibiotics was primarily a late winter/early spring phenomenon in children aged 5 to 14 (Figure 5.3a) and adults (Figure 5.3b). Among younger children aged 0 to 4, co-dispensing rose steadily from the start of the calendar year to a peak in mid-winter. The highly seasonal nature of the co-prescribing supports the hypothesis that ICS are being prescribed inappropriately for the treatment of RTIs.

Type of antibiotic co-dispensed with one-off inhaled corticosteroid

Among concession card holders with one-off dispensing of ICS during 2008, the most common type of oral antibiotics co-dispensed were amoxicillin (25.7%) and roxithromycin (21.8%; Table 5.3).

These antibiotics are commonly used for treatment of respiratory infections – further evidence that these medications were being co-prescribed for the treatment of such events.

Table 5.3: Co-dispensing of one-off ICS (and no other respiratory medications) and oral antibiotics within 7 days before or after the ICS, concession card holders, Australia, 2008

Antibiotic group (ATC level 3/4)	Number of scripts	Percentage of scripts (n=52,786)
Tetracycline	2,356	4.50
Beta-lactam antibacterials, penicillins	23,250	44.05
Other beta-lactam antibacterials	7,750	14.68
Sulfonamides and trimethoprim	794	1.50
Macrolides, lincosamides and streptogramins	18,026	34.15
Quinolone antibacterials	198	0.38
Other antibacterials	412	0.78

Notes

1. Some patients were dispensed more than one prescription of oral antibiotics, therefore, the total number of prescriptions for oral antibiotics (n=52,786) exceeds the number of patients who were co-dispensed one-off ICS and oral antibiotics (n=50,512).
2. Refer to Appendix A for a more detailed analysis.

Source: ACAM analysis of PBS data.

Other types of medication dispensed within the co-dispensing period

Data about other types of respiratory medications prescribed during the time of the co-dispensing of one-off ICS and oral antibiotics may provide additional insight into the clinical problem that was being managed, or its severity.

In this section, other types of respiratory medications that were dispensed within 7 days before or after the one-off ICS, in patients also co-dispensed oral antibiotics, are reported. Of the 50,512 concession card holders who were co-dispensed one-off ICS and oral antibiotics, 30% were also co-dispensed a SABA, 10% were co-dispensed OCS, and 1% were co-dispensed a SAAC (Table 5.4).

The large majority of these other respiratory medications were dispensed on the same day as the antibiotic and ICS, suggesting that the prescribing of multiple medications during this period was largely proactive rather than due to failure of the clinician's initial therapeutic strategy.

Table 5.4: Other types of respiratory medication dispensed within 7 days of the one-off ICS and the timing of dispensing in relation to the one-off ICS

Timing of dispensing	Number of SABA prescriptions (%)	Number of SAAC prescriptions (%)	Number of OCS prescriptions (%)
-5-7 days	730 (4.6)	26 (4.8)	383 (7.2)
-3-4 days	516 (3.2)	25 (4.6)	312 (5.9)
-1-2 days	388 (2.4)	26 (4.8)	218 (4.1)
Same day as ICS	13,569 (85.0)	346 (63.7)	3,329 (62.8)
+1-2 days	239 (1.5)	42 (7.7)	288 (5.4)
+3-4 days	235 (1.5)	36 (6.6)	357 (6.7)
+5-7 days	280 (1.8)	42 (7.7)	413 (7.8)
Total prescriptions	15,957 (100)	543 (100)	5,300 (100)

Notes

1. SABA—short-acting beta-agonists.
2. SAAC—short-acting anti-cholinergics.
3. OCS—oral corticosteroids.
4. Some patients were dispensed more than one prescription of the same class of drug.
5. The total number of individuals dispensed each of the respiratory drugs were: SABA—15,333 persons, SAAC—526 persons, OCS—5,102 persons.

Source: ACAM analysis of PBS data.

Cost of one-off inhaled corticosteroid dispensing to Government

In 2008, the cost to the Australian Government of one-off ICS co-dispensed with oral antibiotics to concession card holders was about \$2.7 million (Table 5.5). Overall, the majority (77%) of one-off ICS prescriptions co-dispensed with oral antibiotics were dispensed as combination therapy (ICS with LABA) and most of these (82.3%, about \$2.2 million) were the moderate- to high-dose formulations (Table 5.5).

Table 5.5: Nature, dose and cost of ICS dispensed as one-off prescriptions with co-dispensing of oral antibiotics, concession card holders, Australia, 2008

Nature of ICS (% of one-off ICS scripts in that age group)	Dose	Number (%) of scripts dispensed	Total cost to Government (\$)
ICS alone (23%)	Low	3,221 (27%)	\$41,912
	Moderate	4,885 (41%)	\$135,972
	High	3,717 (31%)	\$158,249
	Total ICS alone	11,823 (100%)	\$336,132
ICS/LABA combination (77%)	Low	3,187(8%)	\$139,846
	Moderate	21,290 (55%)	\$1,139,549
	High	14,212 (37%)	\$1,069,451
	Total ICS/LABA combination	38,689 (100%)	\$2,348,846
Total ICS dispensed		50,512	\$2,684,979

Note: Refer to Appendix A for a more detailed analysis.

Source: ACAM analysis of PBS data.

Children were most commonly dispensed the lower doses of ICS and were most commonly dispensed ICS alone (that is, not in combination with a long-acting beta-agonist), particularly at age 0–4. One-off ICS dispensed as ICS alone accounted for 69% of prescriptions dispensed in children aged 0–4 (of which 88% were the lowest dose) and 38% of those in children aged 5–14 (of which 60% were the lowest dose). These results are similar to those reported for dispensing of ICS to children in general (AIHW: ACAM 2008).

For adults, one-off ICS were most commonly prescribed as combination therapy, at moderate/high doses. In 2008, 97% of one-off ICS prescribed as combination therapy were dispensed at moderate/high doses (Table 5.5). These formulations are the most expensive and the most likely to cause side effects (NAC 2006). A similar pattern is seen for dispensing of ICS overall (AIHW: ACAM 2008).

In addition to the costs to Government, there are also costs to the patient. The cost of the one-off ICS scripts paid by the patient at the concessional rate (\$5 per script in 2008) amounted to \$252,560 in total. Therefore, the total cost of one-off prescriptions of ICS co-dispensed with oral antibiotics among concession card holders of the Australian community in 2008 was \$2,937,539.

6 Conclusions

Limitations of the data used in this study

The extent of co-dispensing of one-off ICS in conjunction with oral antibiotics will have been underestimated in this report. Firstly, our study population was limited to concession card holders. The prevalence of this co-dispensing in the population without a health concession card could not be ascertained from this study since oral antibiotics and some medications used to treat obstructive airways disease fall below the general threshold and are not captured in the PBS data set. Concessional card holders are older, live in more socioeconomically disadvantaged areas, and have a higher prevalence of asthma and COPD than general beneficiaries (Ampon et al. 2009). Future collection of PBS data for medications under the co-payment threshold will allow a more comprehensive assessment of medication use in Australia.

Further, we chose 7 days as the cut-off for the identification of one-off ICS and oral antibiotics that were co-dispensed. This is substantially shorter than the typical duration of LRTIs (median 18 days, mean 24 days) (Ward et al. 2005). It is likely, therefore, that the extent of co-prescribing of one-off ICS with antibiotics would have been underestimated.

On the other hand, it is possible that some patients who may have been newly diagnosed with obstructive airways disease and prescribed ICS did not return for follow-up. In this case, the extent of prescribing/dispensing one-off ICS in people we have assumed do not have a history of obstructive disease may be a slight overestimation. However, it is unlikely that such patients, if they truly had asthma or COPD, would not be dispensed any SABA in the following 6 months.

Alternatively, it is possible that some people may have filled prescriptions that had been issued on a previous date on the same day as receiving their additional prescription of oral antibiotics or inhaled corticosteroids. If this were the case, the effect would be a slight overestimation of co-dispensing of ICS with antibiotics.

Use of antibiotics in people with obstructive airways disease

It is well known that antibiotics are used commonly in the Australian community and this report provides evidence that people with obstructive airways disease are no exception. In 2008, 75% of people dispensed any respiratory medication at the concessional rate were also dispensed oral antibiotics.

In the cohort of people most likely to have COPD, for whom antibiotics are indicated for the treatment of acute exacerbations, 77% of concession card holders aged 55 and over who were dispensed tiotropium in 2008 were also dispensed oral antibiotics.

Adults and children who are frequent users of ICS are also dispensed more antibiotics than less frequent users. However, no information is available to assess the appropriateness of the prescribing of antibiotics in these populations, and no published data are available for the proportion of the general Australian population who are prescribed antibiotics for comparison with these results.

A complex relationship exists between medication use, disease severity, and health-care use. People with more severe obstructive airways disease are more likely to suffer from respiratory infections. They may also visit the GP more often and, as a result, are more likely to leave the GP's office with a prescription. Given this complex relationship it is difficult to draw inferences from these data. However, monitoring of medication use is the first step towards assessing the appropriateness of prescribing and evaluating the health benefits or risks of the medications.

Co-prescribing of one-off ICS and antibiotics

In the past, intermittent use of ICS has been mainly attributed to poor adherence by patients (Andrade et al. 2006). This report provides evidence that low rates of dispensing ICS in Australia may be due, in part, to prescribing practices in primary care.

This report investigated the co-dispensing of oral antibiotics in patients who were dispensed ICS only once during the year and no other respiratory medications. In 2008, 44% of these individuals, whose prescription record did not include any evidence that they had obstructive airways disease, were co-dispensed one-off ICS with oral antibiotics.

This is of particular concern among the adult population, where treatment guidelines for use of ICS indicate that they should be used as regular long-term treatment for patients who have been diagnosed with asthma or moderate to severe COPD, and whose symptoms are not controlled by short-acting beta-agonist medications alone.

A short-term course of ICS may be considered as a therapeutic trial in a patient presenting with symptoms consistent with asthma or COPD, in conjunction with diagnostic evaluation including spirometry; however, spirometry is rarely performed in general practice in Australia (AIHW: ACAM 2011), and for asthma, clinical practice guidelines indicate that treatment should start with low-dose ICS alone rather than the high-dose combination ICS-LABA that was mostly observed in this study.

In children, intermittent asthma is common and, therefore, intermittent use of medications containing ICS may be appropriate treatment.

Several factors lead the authors to the conclusion that co-dispensing of one-off ICS with oral antibiotics is likely to represent prescribing patterns for the treatment of RTIs:

- The co-prescribing was highly seasonal, with large peaks during times when RTIs are most common, namely late winter.
- The majority of the co-dispensing episodes occurred on the same date, strongly indicating that the one-off ICS and antibiotics were most likely prescribed for the same clinical event.
- The antibiotics most commonly co-dispensed were those normally used for the treatment of RTIs.

The present data do not allow us to conclude whether the one-off ICS and oral antibiotics were being co-prescribed for treatment of an acute respiratory infection or for chronic non-specific symptoms such as prolonged post-viral cough.

The use of short-term courses of ICS as treatment of RTIs in patients without any evidence of obstructive airways disease is neither supported by evidence nor recommended in treatment guidelines.

Prescribing of ICS for purposes beyond which they are intended comes at a cost. Financially, these data suggest the cost to the Australian Government and to patients amounted to about \$2.9 million in 2008. Clinically, inappropriate prescribing of ICS also increases the risk of adverse events, thereby further increasing the cost.

Further research in this area is needed, firstly to confirm the findings from this study by incorporating clinical data from other sources and, secondly, to understand the reasons for such prescribing patterns in primary care.

Currently, the National Prescribing Services Better Choices, Better Health (NPS) activities are targeted at reducing the use of antibiotics for the treatment of RTIs, most of which are treated in primary care (NPS 2009). See also: <www.nps.org.au/health_professionals/activities> for current and planned NPS activities. However, these new findings suggest that strategies are needed to assist in the diagnosis of patients presenting with respiratory symptoms in the primary care setting. Improved diagnostic accuracy may avoid the need to give empirical therapy to cover a number of possible diagnoses.

Ongoing monitoring of the use of antibiotics and one-off dispensing of ICS is needed to assess the impact of any interventions.

Appendix A: Additional tables

Table A.1: Number of scripts for oral antibiotic dispensing among concession card holders who were dispensed any respiratory medication, by type of antibiotic (ATC level), 2008

Antibiotic group (ATC level 3/4)	Specific antibiotic (ATC level 5)	Number of scripts	Percentage of scripts (n=3,545,506)
Tetracycline		170,144	4.80
	Minocycline	601	0.02
	Doxycycline	169,543	4.78
Beta-lactam antibacterials, penicillins		1,360,696	38.38
Penicillin with extended spectrum	Amoxicillin	682,296	19.24
Beta-lactamase sensitive penicillins	Phenoxyethylpenicillin	26,432	0.75
Combinations of penicillins, including beta-lactamase inhibitors	Amoxicillin with clavulanic acid	651,968	18.39
Other beta-lactam antibacterials		796,060	22.50
First-generation cephalosporins	Cephalexin	607,262	17.13
Second-generation cephalosporins	Cefaclor	162,029	4.57
	Cefuroxime axetil	26,769	0.75
Sulfonamides and trimethoprim		175,085	4.94
Trimethoprim and derivatives	Trimethoprim	106,226	3.00
Combinations of sulphonamides and trimethoprim, including derivatives	Trimethoprim with sulfamethoxazole	68,859	1.94
Macrolides, lincosamides and streptogramins		850,758	24.00
Macrolides	Erythromycin	24,016	0.68
	Roxithromycin	536,195	15.12
	Erythromycin ethyl succinate	97,710	2.76
	Azithromycin	9,577	0.27
	Clarithromycin	158,443	4.47
Lincosamides	Clindamycin	24,817	0.70
Quinolone antibacterials		87,304	2.46
Fluoroquinolones	Ciprofloxacin	56,685	1.60
	Norfloxacin	30,508	0.86
	Moxifloxacin hydrochloride	111	0.003
Other antibacterials		105,459	2.97

Source: ACAM analysis of PBS data.

Table A.2: Number of prescriptions for oral antibiotics among concession card holders who were dispensed tiotropium, by type of antibiotic (ATC level), 2008

Antibiotic group (ATC level 3/4)	Specific antibiotic (ATC level 5)	Number of scripts	Percentage of scripts (n=789,810)
Tetracycline		52,113	6.60
	Minocycline	175	0.02
	Doxycycline	51,938	6.58
Beta-lactam antibacterials, penicillins		268,958	34.05
Penicillin with extended spectrum	Amoxicillin	97,734	12.37
Beta-lactamase sensitive penicillins	Phenoxyethylpenicillin	2,098	0.27
Combinations of penicillins, including beta-lactamase inhibitors	Amoxicillin with clavulanic acid	169,126	21.41
Other beta-lactam antibacterials		168,881	21.38
First-generation cephalosporins	Cephalexin	131,488	16.65
Second-generation cephalosporins	Cefaclor	28,894	3.66
	Cefuroxime axetil	8,499	1.08
Sulfonamides and trimethoprim		39,382	4.99
Trimethoprim and derivatives	Trimethoprim	24,438	3.09
Combinations of sulphonamides and trimethoprim, including derivatives	Trimethoprim with sulfamethoxazole	14,944	1.89
Macrolides, lincosamides and streptogramins		208,350	26.38
Macrolides	Erythromycin	5,171	0.65
	Roxithromycin	137,147	17.36
	Erythromycin ethyl succinate	11,979	1.52
	Azithromycin	2,705	0.34
	Clarithromycin	45,235	5.73
Lincosamides	Clindamycin	6,113	0.77
Quinolone antibacterials		32,661	4.14
Fluoroquinolones	Ciprofloxacin	24,652	3.12
	Norfloxacin	7,938	1.01
	Moxifloxacin hydrochloride	71	0.01
Other antibacterials		19,465	2.46

Note: Some individuals had more than one antibiotic dispensed, therefore, the number of scripts for antibiotics (n=789,810) is greater than the number of individuals most likely to have COPD who were dispensed oral antibiotics (n=138,796).

Source: ACAM analysis of PBS data.

Table A.3: Co-dispensing of one-off ICS (and no other respiratory medications) and oral antibiotics within 7 days before or after the ICS, concession card holders, Australia, 2008

Antibiotic group (ATC level 3/4)	Specific antibiotic (ATC level 5)	Number of scripts	Percentage of scripts (n=52,786)
Tetracycline		2,356	4.50
	Minocycline	5	0.01
	Doxycycline	2,351	4.49
Beta-lactam antibacterials, penicillins		23,250	44.05
Penicillin with extended spectrum	Amoxicillin	13,548	25.67
Beta-lactamase sensitive penicillins	Phenoxymethylpenicillin	342	0.65
Combinations of penicillins, including beta-lactamase inhibitors	Amoxicillin with clavulanic acid	9,360	17.73
Other beta-lactam antibacterials		7,750	14.68
First-generation cephalosporins	Cephalexin	4,462	8.45
Second-generation cephalosporins	Cefaclor	2,876	5.45
	Cefuroxime axetil	412	0.78
Sulfonamides and trimethoprim		794	1.50
Trimethoprim and derivatives	Trimethoprim	341	0.65
Combinations of sulphonamides and trimethoprim, including derivatives	Trimethoprim with Sulfamethoxazole	453	0.86
Macrolides, lincosamides and streptogramins		18,026	34.15
Macrolides	Erythromycin	344	0.65
	Roxithromycin	11,481	21.75
	Erythromycin ethyl succinate	2,250	4.26
	Azithromycin	97	0.18
	Clarithromycin	3,756	7.12
Lincosamides	Clindamycin	98	0.19
Quinolone antibacterials		198	0.38
Fluoroquinolones	Ciprofloxacin	109	0.21
	Norfloxacin	89	0.17
Other antibacterials		412	0.78

Note: Individuals were dispensed more than one prescription of oral antibiotics, therefore, the total number of prescriptions for oral antibiotics (n=52,786) exceeds the number of patients who were co-dispensed one-off ICS and oral antibiotics (n=50,512).

Source: ACAM analysis of PBS data.

Table A.4: Nature, dose and cost of ICS dispensed as one-off prescriptions with co-dispensing of oral antibiotics, concession card holders, Australia, 2008

Age group (years)	Nature of ICS (% of one-off ICS scripts in that age group)	Dose	Number (%) of scripts dispensed	Total cost to Government (\$)
0–4	ICS alone (69%)	Low	1,172 (88%)	13,939
		Moderate	156 (12%)	4,257
		High	4 (<0.5%)	173
	ICS/LABA combination (31%)	Low	491 (80%)	20,618
		Moderate	106 (17%)	5,705
		High	15 (2%)	1,107
5–14	ICS alone (38%)	Low	1,580 (60%)	19,698
		Moderate	916 (35%)	23,934
		High	158 (6%)	6,901
	ICS/LABA combination (62%)	Low	1,680 (38%)	72,405
		Moderate	2,185 (50%)	117,330
		High	513 (12%)	38,008
15–34	ICS alone (20%)	Low	141 (7%)	2,336
		Moderate	1,025 (51%)	28,354
		High	861 (42%)	36,916
	ICS/LABA combination (80%)	Low	286 (3%)	13,080
		Moderate	4,556 (55%)	243,883
		High	3,434 (41%)	256,825
35–64	ICS alone (18%)	Low	168 (6%)	3,026
		Moderate	1,377 (47%)	39,343
		High	1,369 (47%)	58,322
	ICS/LABA combination (82%)	Low	334 (3%)	15,391
		Moderate	7,178 (55%)	384,063
		High	5,577 (43%)	419,844
65 and over	ICS alone (19%)	Low	160 (6%)	2,912
		Moderate	1,408 (49%)	40,000
		High	1,322 (46%)	55,807
	ICS/LABA combination (81%)	Low	394 (3%)	18,268
		Moderate	7,254 (59%)	387,980
		High	4,666 (38%)	353,155

Notes

- 26 individuals had a missing age group, therefore were not included in the break down by age group. The cost to Government does not include the cost of the script paid by the patient (\$5 in 2008).
- Least potent includes Qvar 50, Qvar 50 Autohaler, Pulmicort Turbuhaler 100, Alvesco 80, Flixotide Jnr Accuhaler 100, Flixotide Jnr Oral pressurised inhalation 50 micrograms per dose (120 doses) CFC-free formulation, Seretide Accuhaler 100/50, Seretide MDI 50/25, Symbicort Turbuhaler 100/6.
- Intermediate level includes Qvar 100, Qvar 100 Autohaler, Pulmicort Respules 500 mcg, Pulmicort Turbuhaler 200, Alvesco 160, Flixotide Accuhaler 250, Flixotide 125, Seretide Accuhaler 250/50, Seretide MDI 125/25, Symbicort Turbuhaler 200/6.
- Most potent includes Pulmicort Respules 1 g, Pulmicort Turbuhaler 400, Flixotide Accuhaler 500, Flixotide MDI 250, Seretide Accuhaler 500/50, Seretide MDI 250/25, Symbicort Turbuhaler 400/12. ICS = inhaled corticosteroids; LABA = long-acting beta-agonists (see Table 2.1 for a description of the medications).

Source: ACAM analysis of PBS data.

Table A.5: ICS prescriptions with at least one AB prescription, all ages

Age (years)		Number of ICS prescriptions				
		1	2–3	3–6	7–12	13+
0–4	Number	12,310	6,188	2,341	832	84
	% of all ICS prescriptions	82.78	82.43	84.53	85.10	91.66
5–14	Number	33,041	18,573	8,198	3,723	355
	% of all ICS prescriptions	68.37	68.92	67.84	71.55	79.71
15–34	Number	39,038	18,693	9,469	4,986	961
	% of all ICS prescriptions	71.34	67.84	66.35	71.25	81.16
35–64	Number	68,517	49,665	37,430	31,716	8,364
	% of all ICS prescriptions	74.57	72.13	72.08	76.74	83.82
65+	Number	76,505	78,550	81,551	84,938	19,023
	% of all ICS prescriptions	76.87	74.79	75.20	84.36	84.36

Source: ACAM analysis of PBS data.

Table A.6: ICS and AB prescriptions, 0–4 years

	Number of ICS prescriptions				
	1	2–3	3–6	7–12	13+
Number of AB prescriptions	Per cent in AB prescriptions group				
0	17.21	14.78	15.46	14.90	8.30
1	18.82	16.44	15.24	13.70	8.30
2	17.21	15.89	14.69	12.62	5.95
3–4	22.80	22.83	21.91	21.63	17.85
5–8	18.24	22.16	21.91	23.56	33.33
9+	5.71	7.90	10.76	13.58	26.19
All AB prescriptions (%)	100	100	100	100	100
All AB prescriptions (n)	12,310	6,188	2,341	832	84

Source: ACAM analysis of PBS data.

Table A.7: ICS and AB prescriptions, 5–14 years

	Number of ICS prescriptions				
	1	2–3	4–6	7–12	13+
Number of AB prescriptions	Per cent in AB prescriptions group				
0	31.61	31.08	32.15	28.44	20.28
1	24.51	20.84	20.18	18.27	14.08
2	16.95	16.38	15.03	14.35	15.21
3–4	16.55	17.60	16.85	16.83	18.59
5–8	8.58	11.08	11.23	14.60	19.15
9+	1.77	3.02	4.56	7.45	12.68
All AB prescriptions (%)	100	100	100	100	100
All AB prescriptions (n)	33,041	18,573	8,198	3,723	355

Source: ACAM analysis of PBS data.

Table A.8: ICS prescription and antibiotic prescriptions, 15-34 years

	Number of ICS prescriptions				
	1	2-3	4-6	7-12	13+
Number of AB prescriptions	Per cent in AB prescriptions group				
0	28.66	32.02	33.65	28.74	18.83
1	22.78	19.39	18.99	17.60	14.05
2	16.93	15.72	14.47	14.24	13.42
3-4	17.66	17.11	16.71	17.27	18.63
5-8	10.82	11.75	11.07	14.16	17.90
9+	2.92	4.00	5.11	7.98	17.17
All AB prescriptions (%)	100	100	100	100	100
All AB prescriptions (n)	39,038	18,693	9,469	4,986	961

Source: ACAM analysis of PBS data.

Table A.9: ICS prescription and antibiotic prescription, 35-64 years

	Number of ICS prescriptions				
	1	2-3	4-6	7-12	13+
Number of AB prescriptions	Per cent in AB prescriptions group				
0	25.42	27.86	27.92	23.25	15.25
1	17.30	14.52	13.68	11.78	9.31
2	16.33	14.52	14.28	13.30	11.00
3-4	19.22	18.09	16.97	17.10	15.75
5-8	15.14	15.91	16.09	18.44	20.81
9+	6.59	9.10	11.06	16.12	26.94
All AB prescriptions (%)	100	100	100	100	100
All AB prescriptions (n)	68,517	49,665	37,430	31,716	8,364

Source: ACAM analysis of PBS data.

Table A.10: ICS prescription and antibiotic prescription, 65 years and over

	Number of ICS prescriptions				
	1	2-3	4-6	7-12	13+
Number of AB prescriptions	Per cent in AB prescriptions group				
0	23.13	25.21	24.79	20.96	15.64
1	14.76	13.36	12.80	10.76	8.37
2	16.24	14.52	14.31	13.30	11.14
3-4	19.99	18.87	17.79	17.59	16.31
5-8	17.42	17.70	18.04	20.06	21.66
9+	8.46	10.34	12.25	17.32	26.86
All AB prescriptions (%)	100	100	100	100	100
All AB prescriptions (n)	76,505	78,550	81,551	84,938	19,023

Source: ACAM analysis of PBS data.

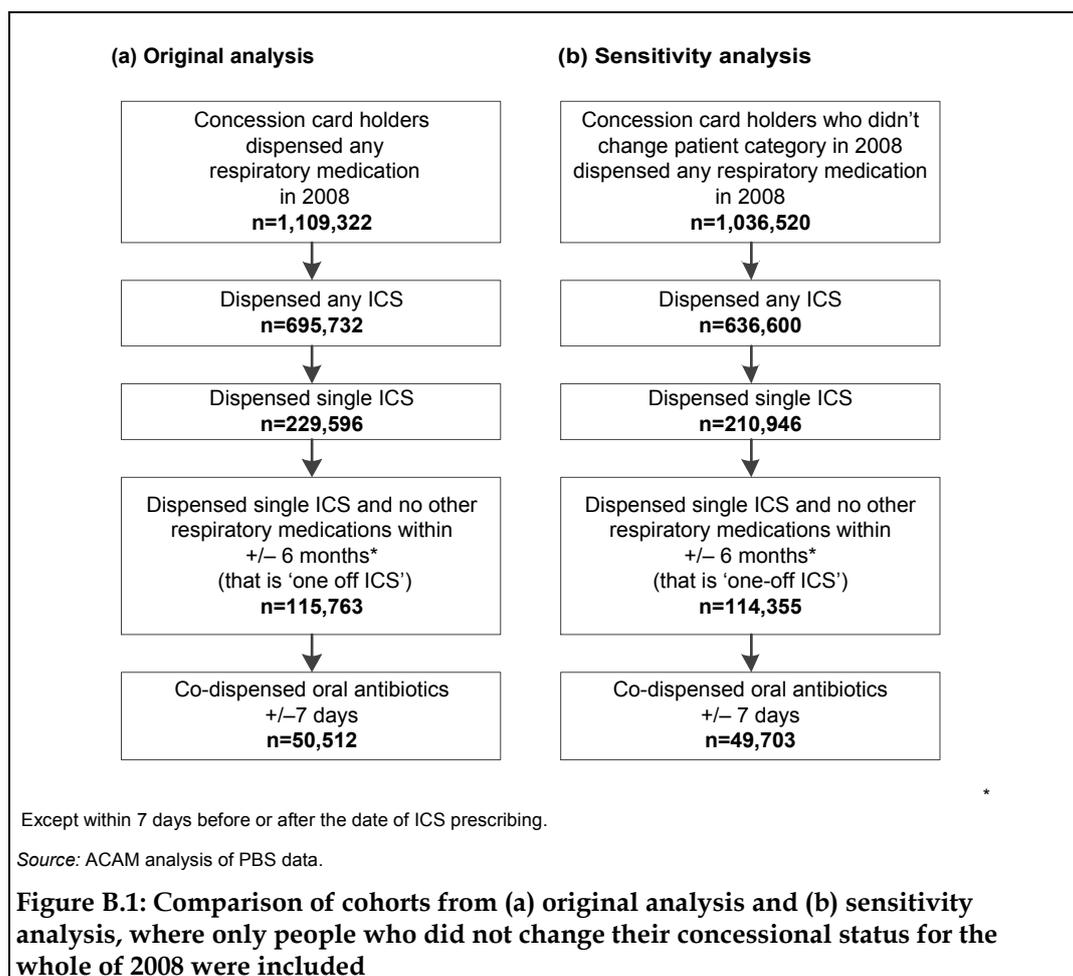
Appendix B: Sensitivity analysis

In the main analysis presented here we included all patients who received any respiratory medication at the concessional rate during 2008. This may have included some people who were general beneficiaries for a portion of the calendar year. For these people, complete dispensing data would not have been available for medications that cost less than the co-payment amount (\$31.30 in 2008). This would include some respiratory medications and most oral antibiotics which cost less than this amount and which would not have been included in the PBS data set.

We conducted a sensitivity analysis of the use of ICS to treat RTIs in people without any evidence of obstructive airways disease by only including patients whose concessional status did not change during 2008. The comparison of the numbers included in this sensitivity analysis and the original analysis is in Figure B.1.

Exclusion of people who changed their concessional status during 2008 (72,802 people) had little effect on the main analysis. Of those dispensed any ICS (636,600 people), 33.1% were dispensed only one ICS in the calendar year, compared with 33% from the main analysis.

Of those dispensed one-off ICS (that is, one ICS and no other respiratory medications within a year), 43.4% of people from the sensitivity analysis were co-dispensed oral antibiotics within 7 days (before or after), compared with 39.4% of individuals in the main analysis.



References

- AIHW (Australian Institute of Health and Welfare): Australian Centre for Asthma Monitoring 2008. Asthma in Australia 2008. Asthma series no. 3. Cat. no. ACM 14. Canberra: AIHW.
- AIHW: Australian Centre for Asthma Monitoring 2011. Asthma in Australia 2011: with a focus chapter on chronic obstructive pulmonary disease. Asthma series no. 4. Cat. no. ACM 22. Canberra: AIHW.
- AIHW: Britt H, Miller GC, Charles J, Henderson J, Bayram C, Pan Y et al. 2009. General practice activity in Australia, 2008–09. General practice series no. 25. Cat. no. GEP 25. Canberra: AIHW. Canberra: AIHW.
- AIHW: Britt H, Miller GC, Charles J, Henderson J, Bayram C, Pan Y et al. 2010. General practice activity in Australia 2009–10. General practice series no. 27. Cat. no. GEP 27. Canberra: AIHW.
- Albert RK, Connett J, Bailey WC, Casaburi R, Cooper JAD, Criner GJ et al. 2011. Azithromycin for prevention of exacerbations of COPD. *The New England Journal of Medicine* 365:689–98.
- Ampon RD, Reddel HK, Correll PK, Poulos LM & Marks GB 2009. Cost is a major barrier to the use of inhaled corticosteroids for obstructive lung disease. *Medical Journal of Australia* 191:319–23.
- Andrade SE, Kahler KH, Frech F & Chan KA 2006. Methods for evaluation of medication adherence and persistence using automated databases. *Pharmacoepidemiology and Drug Safety* 15:565–74. Britt H, Miller GC, Charles J, Henderson J, Bayram C, Pan Y et al. 2011. General practice activity in Australia 2010–11. General practice series no. 29. Sydney: Sydney University Press.
- Celli BR & Barnes PJ 2007. Exacerbations of chronic obstructive pulmonary disease. *European Respiratory Journal* 29:1224–38.
- Corne JM, Marshall C, Smith S, Schreiber J, Sanderson G, Holgate ST et al. 2002. Frequency, severity, and duration of rhinovirus infections in asthmatic and non-asthmatic individuals: a longitudinal cohort study. *The Lancet* 359:831–4.
- Crim C, Calverley PMA, Anderson JA, Celli B, Ferguson GT, Jenkins C et al. 2009. Pneumonia risk in COPD patients receiving inhaled corticosteroids alone or in combination: TORCH study results. *European Respiratory Journal* 34:641–7.
- DoHA (Australian Government Department of Health and Ageing) 2009. Australian Statistics on Medicines 2008. Canberra: Commonwealth of Australia.
- DoHA 2010. About the PBS. Canberra: Australian Government Department of Health and Ageing. Viewed 10 June 2010, <<http://www.health.gov.au/internet/wcms/publishing.nsf/Content/health-pbs-general-aboutus.htm-copy2>>.
- Douglass JA, Goeman DP, McCarthy EA, Sawyer SM, Aroni RA, Stewart K et al. 2012. Over-the-counter β_2 -agonist purchase versus script: A cross-sectional study. *Respiratory Medicine* 106:223–9.

- Ernst P, Gonzalez AV, Brassard P & Suissa S 2007. Inhaled corticosteroid use in chronic obstructive pulmonary disease and the risk of hospitalisation for pneumonia. *American Journal of Respiratory & Critical Care Medicine* 176:162–6.
- GINA (Global Initiative for Asthma) 2009. Global strategy for asthma management and prevention 2009 (update). Bethesda, Maryland: National Institutes of Health, National Heart, Lung and Blood Institute. Viewed 17 May 2010, <<http://www.ginasthma.com/Guidelineitem.asp?i1=2&i2=1&intId=1561>>.
- Glauber JH, Fuhlbrigge AL, Finkelstein JA, Homer CJ & Weiss ST 2001. Relationship between asthma medication and antibiotic use. *Chest* 120:1485–92.
- Hoban DJ, Doern GV, FLuit AC, ROussel-Delvallez M & Jones RN 2001. Worldwide prevalence of antimicrobial resistance in *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* in the SENTRY Antimicrobial Surveillance Program, 1997–1999. *Clinical Infectious Diseases* 32:S81–93.
- Johnston SL, Pattemore PK, Sanderson G, Smith S, Lampe F & Josephs L 1995. Community study of the role of viral infections in exacerbations of asthma in 9–11 year old children. *British Medical Journal* 310:1225–8.
- Laforest L, Ganse EV, Devouassoux G, Hasnaoui AE, Osman LM, Bauguil G et al. 2008. Dispensing of antibiotics, antitussives and mucolytics to asthma patients: a pharmacy-based observational survey. *Respiratory Medicine* 102:57–63.
- Levy SB & Marshall B 2004. Antibacterial resistance worldwide: causes challenges and responses. *Nature Medicine Supplement* 10:S122–9.
- Lister S, Sheppeard V, Morgan G, Corbett S, Kaldor J & Henry R 2001. February asthma outbreaks in NSW: a case control study. *Australian & New Zealand Journal of Public Health* 25:514–9.
- McKenzie DK, Abramson M, Crockett AJ, Glasgow N, Jenkins S, McDonald C et al. 2010. The COPD-X Plan: Australian and New Zealand Guidelines for the management of Chronic Obstructive Pulmonary Disease 2010.
- Moudgil H, Marshall T & Honeybourne D 2000. Asthma education and quality of life in the community: a randomised controlled study to evaluate the impact on white European and Indian subcontinent ethnic groups from socioeconomically deprived areas in Birmingham, UK. *Thorax* 55:177–83.
- NAC (National Asthma Council Australia) 2006. Asthma management handbook 2006. South Melbourne: NAC. Viewed 12 March 2009, <www.nationalasthma.org.au/>.
- Neu HC 1992. The Crisis in Antibiotic Resistance. *Science* 257:1064–73.
- NPS (National Prescribing Services BC, Better Health) 2009. NPS Prescribing Practice Review 46: Judicious antibiotics use. Sydney: NPS.
- NPS 2012. Antibiotics-medicine information. Viewed 24 August 2012, <<http://www.nps.org.au/medicines/antibiotics>>. O'Byrne PM, Pedersen S, Carlsson L-G, Radner F, Thoren A, Peterson S et al. 2011. Risks of pneumonia in patients with asthma taking inhaled corticosteroids. *American Journal of Respiratory & Critical Care Medicine* 183:589–95.
- Pan Y, Henderson J & Britt H 2006. Antibiotic prescribing in Australian general practice: How has it changed from 1990–91 to 2002–03? *Respiratory Medicine* 100:2004–11.

- Ram FSF, Rodriguez-Roisin R, Granados-Navarrete A, Garcia-Aymerich J & Barnes NC 2009. Antibiotics for exacerbations of chronic obstructive pulmonary disease (Review). Cochrane Database of Systematic Reviews 2006, Issue 2. Art. No. CD004403. DOI:10.1002/14651858.CD004403.pub2.
- Reddel H, Ware SI, Marks G, Salome C, Jenkins C & Woolcock A 1999. Differences between asthma exacerbations and poor asthma control. *The Lancet* 353:364–9.
- Roede BM, Bresser P, Prins JM, Schellevis F, Verheij TJM & Bindels PJE 2009. Reduced risk of next exacerbation and mortality associated with antibiotic use in COPD. *European Respiratory Journal* 33:282–8.
- Seemungal TAR, Wilkinson TMA, Hurst JR, Perara WR, Sapsford RJ & Wedzicha JA 2008. Long-term erythromycin therapy is associated with decreased chronic obstructive pulmonary disease exacerbations. *American Journal of Respiratory & Critical Care Medicine* 178:1139–47.
- Sin DD, Taskin D, Zhang X, Radner F, Sjobring U, Thoren A et al. 2009. Budesonide and the risk of pneumonia: a meta-analysis of individual patient data. *Lancet* 374:712–19.
- Thurlbeck WM 1990. Pathophysiology of chronic obstructive pulmonary disease. *Clinics in Chest Medicine* 11:389–403.
- Ward JL, Cherry JD, Chang S-J, Partridge S, Lee H, Treanor J et al. 2005. Efficacy of an acellular pertussis vaccine among adolescents and adults. *New England Journal of Medicine* 353:1555–63.
- Wark PAB, Johnston SL, Moric I, Simpson JL, Hensley MJ & Gibson PG 2002. Neutrophil degranulation and cell lysis is associated with clinical severity in virus-induced asthma. *European Respiratory Journal* 19:68–75.
- WHO (World Health Organization) 2012. Antimicrobial Resistance. Viewed 24 August 2012, <<http://www.who.int/mediacentre/factsheets/fs194/en/>>.

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Publications

This report, *Medications prescribed for people with obstructive airways disease: Antibiotics and inhaled corticosteroids*, is produced by the Australian Centre for Asthma Monitoring (ACAM) for the AIHW. Other AIHW-ACAM reports can be downloaded for free from the AIHW website <<http://www.aihw.gov.au/publications/index.cfm>>. The website also includes information on ordering printed copies, where available.

The following AIHW-ACAM publications relating to asthma and use of medications in people with asthma and other obstructive airways diseases might also be of interest:

- AIHW: Australian Centre for Asthma Monitoring 2007. Patterns of asthma medication use in Australia. Cat. no. ACM 11. Canberra: AIHW.
- AIHW: Australian Centre for Asthma Monitoring 2011. Asthma in Australia 2011: with a focus chapter on chronic obstructive pulmonary disease. Asthma series no. 4. Cat. no. ACM 22. Canberra: AIHW.

The NPS (National Prescribing Service BC, Better Health) Medicinewise website <<http://www.nps.org.au/>> may also be of interest to readers.

Appropriate use of medications is important in maximising health benefits for patients, minimising the negative effects of medications, and controlling health costs. This report focuses on the appropriate use of certain medications for the management of obstructive airways disease, including asthma and chronic obstructive pulmonary disease (COPD).

Data in this report suggest that antibiotics are commonly used among patients with asthma and COPD, and that supply patterns for inhaled corticosteroids are often not consistent with treatment guidelines for the management of these conditions.