MEDICINEINSIGHT

Post-market Surveillance Report 11: COPD

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Contents

1. EXECUTIVE SUMMARY

1.1. Purpose

The purpose of this report is to inform post-market review and medicines policy on the use of medicines for chronic obstructive pulmonary disease (COPD).

1.2. Data and focus

For this second report on COPD for the Department of Health, data are drawn from 423 clinically relevant practice sites, 3,835 active GPs and 2,230,658 active patients, to 31 December 2016 inclusive.

The subset of regular patients (who attended a clinically relevant practice 3 or more times in the past 2 years), marked as 'active' in the clinical information system (CIS) who were 35 years and over were included in the main analysis population (n=1,283,107).

The report presents data addressing specific questions on the following topics: patient profile, patterns of drug utilisation, coprescribing, initial therapy, associated care and adverse events.

1.3. Results

1.3.1. COPD patient profile

A patient was defined as having a history of COPD if they had ever had a recorded diagnosis of COPD, chronic obstructive airways disease (COAD), chronic airflow/airways limitation (CAL), emphysema or chronic bronchitis in any designated text or code field in relevant diagnosis tables (history, reason for prescription or reason for visit). Patients were identified with a history of asthma similarly. If a patient had a record of both asthma and COPD, they were categorised as having COPD plus asthma.

Of the1.28 million regular MedicineInsight patients aged 35 years and over included in this report, 4.6% were ever diagnosed with COPD with or without asthma (**COPD (all)**; n=59,196). 3.0% of MedicineInsight patients had a COPD diagnosis without mention of asthma (**COPD only**; n=38,650), and 1.6% had both **COPD plus asthma** diagnoses (n=20,546). Just over one-third of patients with a diagnosis of COPD also had an asthma diagnosis.

The age-specific prevalence of patients diagnosed with COPD increased with patient age. The prevalence of COPD among MedicineInsight regular patients 45 years and over was 5.9%, compared with 5.1% reported by the 2014–15 ABS National Health Survey.

There was a significantly higher prevalence of COPD in men compared to women, those living in inner regional areas and outer/remote areas and patients residing in more socioeconomic disadvantaged areas.

As might be expected, MedicineInsight patients who were ex-smokers and current smokers were more likely to have a diagnosis of COPD compared to non-smokers. Patients who were underweight (BMI < 18.5) had a higher prevalence of COPD than those in the healthy or overweight ranges.

1.3.2. Drug utilisation

In MedicineInsight in 2016, 51,903 original prescriptions for the medicines of interest were ordered for regular patients with **COPD only**. The most commonly ordered medicines (by class) for patients with **COPD only** were the fixed-dose combination (FDC) of long-acting $beta_2$ agonists and inhaled corticosteroids (ICS + LABA) (31.8%), followed by short-acting $beta_2$ agonists (SABA) (27.1%) and long-acting muscarinic antagonists (LAMA) (26.2%). Less

common medicines (by class) were the FDC of LAMA + LABA (4.3%), followed by ICS (4.1%) and LABA (2.9%).The most commonly prescribed medicines for patients with **COPD only** were salbutamol (26.0%), tiotropium (21.8%) and fluticasone + salmeterol (18.4%).

In 2016, 54,197 original prescriptions for the medicines of interest were ordered for patients with **COPD plus asthma**. The most commonly prescribed medicines (by class) for patients with **COPD plus asthma** were ICS + LABA (36.3%), SABA (31.4%) and LAMA (19.2%). The most commonly prescribed medicines for patients with **COPD plus asthma** were salbutamol (30.1%), fluticasone + salmeterol (20.9%) and tiotropium (15.8%).

From 2012 to 2016 the annual rate of all COPD prescriptions for **COPD only** patients increased from 9.0 to 11.2 scripts per 100 GP visits. The annual rate of all COPD prescriptions for **COPD plus asthma** patients was higher than for COPD-only patients, and remained relatively stable with a mean average between 2012 and 2016 of 18.6 scripts per 100 GP visits.

The ICS + LABA combination products had the highest annual rate of prescribing, increasing from 2012 to 2016 from 31.7 to 35.5 scripts per 1,000 GP visits with **COPD only** patients and increasing from 2012 to 2016 from 64.9 to 67.4 scripts per 1,000 GP visits with **COPD plus asthma** patients. LABA/LAMA combination products were introduced onto the PBS in 2014/15, and by 2016 were prescribed at the same rate (6.1 scripts per 1,000 GP visits) for **COPD only** and **COPD plus asthma** patients. There was a moderate increase in the annual LAMA script rate for all COPD patients.

For patients with **COPD only**, tiotropium had the highest annual rate of prescribing in 2012 at 26.6 scripts per 1,000 GP visits, dropping to second highest in 2016 with 24.4 scripts per 1,000 visits – the introduction of newer LAMAs (aclidinium, glycopyrronium, umeclidinium) onto the PBS in 2014 may explain this. Salbutamol had the highest rate of prescribing by 2016 and fluticasone + salmeterol FDC had the third highest rate of prescribing across all years. The rate of prescribing for fluticasone + salmeterol FDC increased moderately from 2012 to 2014 and then decreased until 2016, possibly due to the introduction of fluticasone + vilanterol FDC on the PBS in 2014 and the steady increase in budesonide + formoterol FDC from 2012 to 2016 with the fourth highest prescribing rate across all years.

For patients with **COPD plus asthma**, the top four medicines by prescribing rate were consistent from 2012 to 2016. Salbutamol had the highest annual rate of prescribing followed by fluticasone + salmeterol FDC, tiotropium and budesonide + formoterol FDC. The rate of prescribing for fluticasone + salmeterol FDC and tiotropium decreased after 2014.

1.3.3. Coprescribing in 2016

Overall 15.7% (9,319) of patients with **COPD (all)** had one original prescription for the medicines of interest ordered in 2016; 14.5% (8,588) had two; 11.1% (6,558) had 5 to 10 and 41.6% (24,611) had no original prescriptions ordered in 2016.

The average (mean) number of original prescriptions ordered in 2016 per patient with **COPD (all)** was 3.1. Patients with **COPD plus asthma** had on average 3.5 original prescriptions over the 12-month period, followed by **COPD only** patients with 2.7 original prescriptions.

According to patients' current medicines, 52.7% (n=20,352) of the patients with **COPD only** and 80.8% (n=16,558) of the patients with **COPD plus asthma** were currently on at least one maintenance therapy (ie, all medicines for COPD except for the short-acting beta$_2$ agonists (SABA) or short acting muscarinic antagonists (SAMA) (see TABLE 1). Of the patients with **COPD only** currently on maintenance therapy 38.0% were currently on dual therapy with ICS + LABA, 24.1% were on triple therapy with ICS + LABA + LAMA, 18.3% were on monotherapy with a LAMA and 8% were on LAMA + LABA dual therapy. Of the patients with **COPD plus asthma** currently on maintenance therapy, 47.2% were currently on dual therapy with ICS + LABA, 30.3% were on triple therapy with ICS + LABA + LAMA, 5.7% were on monotherapy with a LAMA and 3.9% were on LAMA + LABA dual therapy.

With regard to medicine combinations associated with safety concerns, these analyses suggest that around 3.9% of patients with **COPD only** on maintenance therapy may be at risk of having duplicated therapy and 1.6% had concomitant use of a SAMA and a LAMA. Of

patients with **COPD plus asthma** on maintenance therapy, 6.1% may be at risk of having duplicated therapy and 3.2% had concomitant use of a SAMA and a LAMA.

1.3.4. Initial therapy for COPD

Of the 3,043 patients with **COPD only** who started therapy for COPD between 1 July 2015 and 31 December 2016, 48.6% were prescribed only one medicine of interest as initial therapy, 46.3% were prescribed dual therapy and 5.1% triple therapy. The most common choice of initial therapy by class was dual therapy with ICS + LABA (38.5%; almost all were FDC), followed by LAMA monotherapy (35.9%) and LAMA + LABA dual therapy (7.4%). The most common choice of initial therapy by individual medicine(s) was tiotropium (23.5%) followed by fluticasone + salmeterol (17.5%) and budesonide + formoterol (16.4%).

When comparing initial therapy for **COPD only** in the earlier period (July 2013 to June 2015) with the current period (July 2015 to December 2016) we found initial therapy with: LAMA increased from 27.3% in 2013/15 to 35.9% in 15/16; LAMA + LABA increased from 1.9% to 7.4%; ICS + LABA decreased from 47.1% to 38.5%; and ICS + LABA + LAMA decreased slightly from 5.5% to 4.3%.

1.3.5. Associated care for COPD patients

Among patients with **COPD (all)**, 38.1% (n=22,524) ever had a record of one or more spirometry tests. This was lower than results reported in a 2012 survey of general practitioners which found 64% of COPD patients had undertaken a spirometry test for diagnosis, of which 60% were performed in the general practice.

Overall, among patients with **COPD (all)**, 26.3% (n=15,584) had ever been prescribed smoking cessation therapies. Among the 17,082 current smokers with COPD, 54.5% (n=9,313) had ever been prescribed smoking cessation therapy and of the 29,140 ex-smokers, 20.1% (n=5,865) had ever been prescribed smoking cessation therapy.

1.3.6. Adverse events

There were 1,528 adverse events recorded for LAMA of which 318 were not specified. For LABA, we found 598 adverse events recorded, of which 138 were not specified. For LAMA + LABA combination therapies, we found 38 adverse events recorded, of which 7 were not specified. For ICS + LABA combination therapies, we found 2,275 adverse events recorded, of which 499 were not specified. Note these records are presented, regardless of the indication for therapy.

The most common adverse events were:

- LAMAs: cough, dry mouth, laryngeal discomfort, rash, nausea, dyspnoea, pruritus, dizziness, vision blurred and headache.
- LABAs: tremor, cough, rash, palpitations, muscle spasms, headache, nausea, laryngeal discomfort, tachycardia and dyspnoea.
- LAMA + LABA combined medicines: constipation, cough, dysphonia, headache, nausea, tachycardia, anxiety, diarrhoea, epistaxis and malaise.
- ICS + LABA combined medicines: dysphonia, rash, tremor, laryngeal discomfort, nausea, cough, palpitations, oral candidiasis, headache and muscle spasms.

1.4. Discussion

This is the second report from MedicineInsight to provide a comprehensive view into the prevalence, drug utilisation and management of COPD patients in general practice and the prescribing of medicines related to their care.

In this second report, almost 60,000 regular patients aged 35 years and over attending the MedicineInsight practices had a diagnosis of COPD recorded (with or without asthma). Of

patients 45 years and over, 5.9% (95% CI:5.6 to 6.2) had a diagnosis of COPD recorded, compared with 5.1% (95% CI:4.6 to 5.7) reported by the 2014–15 ABS National Health Survey. This somewhat higher prevalence estimate in the MedicineInsight data may be partially explained by the restriction in our report to the patient population that regularly visits GP practices (3 visits in the past 2 years). These patients are more likely to have chronic conditions than the general population from the Australian Health Survey who might visit the GP less regularly.

Our patient profile is similar to that reported elsewhere, with higher COPD prevalence rates among patients who were older, male, residing in regional and remote areas and in areas of higher disadvantage.

In 2016, the most commonly ordered medicines (by class) for patients with **COPD only** were ICS + LABA (31.8%), SABA (27.1%) and LAMA (26.2%). The most commonly prescribed medicines for patients with COPD only were salbutamol (26.0%), tiotropium (21.8%) and fluticasone + salmeterol (18.4%).

In 2016, the most commonly prescribed medicines (by class) for patients with **COPD plus asthma** were ICS + LABA (36.3%), SABA (31.4%) and LAMA (19.2%). The most commonly prescribed medicines for patients with **COPD plus asthma** were salbutamol (30.1%), fluticasone + salmeterol (20.9%) and tiotropium (15.8%).

Between 2012 and 2016 the annual rate of all COPD prescriptions for **COPD only** patients increased from 9.0 to 11.2 scripts per 100 GP visits (with COPD only patients). For patients with **COPD plus asthma** the annual prescribing rate was higher than for COPD only patients, with a mean average between 2012 and 2016 of 18.6 scripts per 100 GP visits (with COPD plus asthma patients). A relatively high proportion (41.6%) of patients with COPD (with or without asthma) had no original prescriptions ordered in 2016. There are a number of potential explanations for this somewhat surprising result including: a proportion of patients with mild COPD treated with over-the-counter salbutamol, patients being prescribed medicines for COPD elsewhere (eg, another practice or specialist), patients having enough prescriptions ordered at the end of 2015 to last all of 2016, poor adherence, true management (undertreatment gap), or patients who left the practice in 2016 but were included in the report because they had 3 visits in the last 2 years.

Overall while prescribing for patients with COPD appeared to conform to guidelines in many cases, there was good evidence of inappropriate prescribing. It was not possible to provide definitive evidence of inappropriate prescribing without an understanding of the severity and stage of the disease.

Guidelines recommend a stepwise approach to the initiation of COPD therapy, irrespective of treatment severity, until adequate control has been reached. We found that 46% of patients with **COPD (only)** (without asthma) were prescribed dual therapy at initiation and 4% triple therapy. The most common choice of initial therapy by class was dual therapy with ICS + LABA (38.5%; almost all were FDC), followed by LAMA monotherapy (35.9%) and LAMA + LABA dual therapy (7.4%; almost all were FDC).

We identified a number of patients who may be at risk of adverse effects. These include newly diagnosed patients prescribed FDC of ICS + LABA as first-line therapy, and patients with combinations of medicine formulations in their current medication list that may pose safety concerns. This suggests that there may be some confusion among practitioners about the most appropriate first-line therapy, the composition of the different formulations and the possibility of adverse events when certain formulations are combined.

1.4.1. Interpreting the data

When reading this report it is important to keep in mind some of the issues that arise when using data extracted from general practice clinical information systems (CIS).

- MedicineInsight data are dependent on the accuracy and completeness of data recorded in and available for extraction from the general practice CIS. It is likely that there is under-reporting of clinical information, such as diagnoses, reasons for the encounter or medical

history, as information may not be consistently recorded. Information entered in 'progress notes' is not currently collected by MedicineInsight.

- Our classification of COPD, asthma and other respiratory conditions is based on commonly accepted definitions, and has been reviewed by two GPs (see Appendix B). However, there is likely to be variability in GPs' actual diagnostic labelling practices.
- The prevalence of chronic conditions will be overestimated because this report includes patients who regularly visit the practice (3 or more times in the past 2 years) and these patients are more likely to have chronic conditions than those who visit less frequently.
- Practices are recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Comparisons between regions should be interpreted with caution.
- MedicineInsight collects data at a practice level. However, some practices share the same general practice database, either because they are operating with common administration or in the same geographical area. In these instances, data from several practices may be combined. MedicineInsight cannot currently break up the data into individual practices but this functionality is planned for the future.
- Patients in the MedicineInsight database are currently unable to be uniquely identified across the program, although this functionality will be available in the future. Patients are uniquely recorded within a practice, and are recorded as a different patient if they move between practices.
- Medicine use information from MedicineInsight relates to records of GP prescribing, and therefore differs in several important ways from national PBS dispensing data. Not all prescriptions and repeats will be dispensed ie, prescription counts are an overestimate of dispensed prescription counts; specialist and hospital prescriptions are not included; and there may be a delay of up to 12 months between prescribing and dispensing.
- We have no visibility of instructions to patients about the use of different regimens for exacerbations versus maintenance therapy and medicines may have been ceased without a record in the clinical system.
- A proportion of adverse reactions known to the GP may go unrecorded eg, when the reaction is unremarkable or symptoms are managed elsewhere, such as in hospital. Some adverse events may be recorded in the 'progress notes' which are not collected by MedicineInsight for confidentiality reasons.
- Coding of adverse reactions may differ slightly between MedicineInsight and TGA terms for some reactions.
- Further advice on interpreting the MedicineInsight data is included in each section.

2. INTRODUCTION

2.1. Current status of MedicineInsight program

At the end of December 2016:

- There were 591 general practices registered to participate in MedicineInsight from eight states and territories: NSW (185), Victoria (133), Queensland (112), Western Australia (72), Tasmania (45), South Australia (21), Northern Territory (12) and Australian Capital Territory (11).
- MedicineInsight software has been installed and is operational in 578 of these practices.

For more information about the program see Appendix D – Section 5.4 About MedicineInsight.

2.2. About the report

This report is for the Australian Government Department of Health (DoH). The purpose of this report is to inform the post-market review of medicines for chronic obstructive pulmonary disease (COPD) recommended by the Pharmaceutical Benefits Advisory Committee (PBAC). It is the eleventh report in a series from MedicineInsight to describe medicine utilisation and uptake patterns in general practice.

This report investigates the use of medicines by patients with COPD with or without asthma in the MedicineInsight data. A list of medicines of interest was agreed with the Department of Health. (See TABLE 1).

The investigation focuses on these aspects.

- The profile of the patient cohort with COPD.
- The medicines used for COPD.
- The coprescribing of COPD medicines.
- Initial medicine use in COPD patients.
- Associated care for patients with COPD.
- Adverse events/allergies related to COPD medicines.

Section 3 presents a summary of the methods and Section 4 the results of the investigations.

2.3. Background

2.3.1. Chronic obstructive pulmonary disease (COPD)

COPD is a progressive and disabling long-term lung disease which limits airflow in the lungs. It can lead to mild or severe shortness of breath (dyspnoea), which unlike asthma, cannot be completely reversed even with treatment. COPD is an umbrella term for different lung conditions. People with COPD have emphysema, chronic bronchitis or both.

Smoking is the main risk factor for the development of COPD. However, other environmental factors such as exposure to smoke, air pollution, occupational fumes and dusts, or a history of tuberculosis, childhood respiratory infections or chronic asthma may also increase risk.

The prevalence of COPD reported by the 2014–15 ABS National Health Survey (NHS) in patients 45 years and over was 5.1% (95% CI:4.6 to 5.7)[1]

In 2013, COPD was the fifth largest cause of disease burden within Australia and was responsible for 207,700 years of healthy life lost in 2013.[2]

2.3.2. Treatment of COPD

COPD is a progressive condition. Once started, most people will need to be on medicines for the rest of their lives. Many of these medicines can be used to treat asthma or COPD. They include:

- short-acting beta$_2$ agonists (SABAs)
- short-acting muscarinic antagonists (SAMAs)
- long-acting beta$_2$ agonists (LABAs)
- long-acting muscarinic antagonists (LAMAs)
- fixed-dose combinations of inhaled corticosteroids (ICS) + LABA
- fixed-dose combinations of LAMA + LABA
- oral corticosteroids (OCS)
- theophylline
- antibiotics, and
- mucolytics.

2.3.3. Quality use of medicines issues

NPS MedicineWise recently completed a comprehensive formative research report on COPD to inform the direction and focus of an NPS MedicineWise program on COPD, launched in 2017. Various prescribing issues and evidence practice gaps were identified from interviews conducted by NPS MedicineWise and other data sources. They include:

- Australian studies suggest that the proportion of people with COPD who also have asthma could range from 17% to 50%.[3,4,5] This large variation may reflect a gap in practice around the accurate diagnosis of asthma and/or COPD. Differentiation is important as there are differences in the way asthma and COPD are managed.
- Guidelines recommend a stepwise approach to the initiation of COPD therapy, irrespective of treatment severity,[6] until adequate control has been reached, but this may not always be occurring in practice.
- From qualitative interviews conducted with physicians, pharmacists and nurses:
  - Keeping up to date with the 'huge avalanche' of new COPD medicines recently listed on the PBS was a commonly reported issue.
  - A small but potentially growing number of patients may be exposed to unsafe medicine use practices including double dosing and regimens that include concomitant use of a SAMA and a LAMA.
  - Medicines used to treat asthma and COPD may be being used to treat respiratory tract infections.
  - There may be a small number of people with asthma who are using tiotropium despite it only being PBS-subsidised for COPD.
  - Management of COPD may be suboptimal. Health professionals may not be checking inhaler technique. Advice on managing exacerbations may be inadequate and patients may be prescribed medicines that are not supported by guidelines.
  - Underuse of spirometry may be leading to misclassification of COPD, including in patients with normal lung function, with subsequent inappropriate use of respiratory medicines.

2.4. MedicineInsight data used in this report

The information presented in this report is based on general practice clinical data collected from volunteer practices recruited to the MedicineInsight program. For this second report, data is drawn from 423 clinically relevant practice sites, 3,835 active GPs and 2,230,658 active patients, to 31 December 2016 inclusive.

This report uses the following information from the clinical data.

- Patient demographics (including age, sex, Department of Veterans Affairs (DVA) status, rurality of residence, socioeconomic status).

- Medicines prescribed (including medicine generic name, trade name, ATC classification, reason for prescription).
- Encounters (including reason for encounters).
- Diagnosis/Condition.
- Test results, Observations and MBS service items (Spirometry tests).
- Allergy/Adverse event status.

For more information about MedicineInsight see:

- Appendix D – About MedicineInsight.

2.5. Guide to interpretation of MedicineInsight data

When reading this report it is important to keep in mind some of the issues that arise when using data extracted from general practice clinical information systems (CIS).

- MedicineInsight data are dependent on the accuracy and completeness of data recorded in and available for extraction from the general practice CIS. It is likely that there is under-reporting of clinical information, such as diagnoses, reasons for the encounter or medical history, as information may not be consistently recorded. Information entered in 'progress notes' is not currently collected by MedicineInsight.
- Our classification of COPD, asthma and other respiratory conditions is based on commonly accepted definitions, and has been reviewed by two GPs. However, there is likely to be variability in GPs' actual diagnostic labelling practices.
- Practices are recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Comparisons between regions should be interpreted with caution.
- MedicineInsight collects data at a practice level. However, some practices share the same general practice database, either because they are operating with common administration or in the same geographical area. In these instances, data from several practices may be combined. MedicineInsight cannot currently break up the data into individual practices but this functionality is planned for the future.
- Patients in the MedicineInsight database are currently unable to be uniquely identified across the program, although this functionality will be available in the future. Patients are uniquely recorded within a practice, and are recorded as a different patient if they move between practices.
- Medicine use information from MedicineInsight relates to records of GP prescribing, and therefore differs in several important ways from national PBS dispensing data. Not all prescriptions and repeats will be dispensed – prescription counts are an overestimate of dispensed prescription counts, specialist and hospital prescriptions are not included, and there may be a delay of up to 12 months between prescribing and dispensing.
- We have no visibility of instructions to patients about the use of different regimens for exacerbations versus maintenance therapy and medicines may have been ceased without a record in the clinical system.
- A proportion of adverse reactions known to the GP may go unrecorded, eg, when the reaction is unremarkable or symptoms are managed elsewhere, such as in hospital.
- Coding of adverse reactions may differ between MedicineInsight and TGA for some reactions.
- Further advice on interpreting the MedicineInsight data is included in each section.

3. METHODS

In this section, we present a summary of the methods used for this COPD report.

3.1. Report questions

Objectives	Questions
Patient cohort profile (Section 4.1)	▷ What is the prevalence in MedicineInsight of patients with 'COPD (all)' (with or without asthma), 'COPD only' (without asthma) and 'COPD plus asthma' including: – the age-specific prevalence – the gender-specific prevalence – the region-specific prevalence (rurality) – the socioeconomic-specific prevalence (SEIFA) – the DVA status-specific prevalence – the smoking status-specific prevalence – the BMI-specific prevalence.
Patterns of drug utilisation (Section 4.2)	For patients with COPD only and COPD plus asthma: ▷ What medicine classes and medicines of interest were prescribed in 2016? ▷ How has the utilisation of the medicines of interest changed in the last 5 years (2012 to 2016)?
Coprescribing of COPD medicines (Section 4.3)	For patients with COPD only and COPD plus asthma: ▷ How often over the 12-month period (2016) were patients prescribed medicines of interest? ▷ What combination of medicine formulations (by class) were recorded as their 'current medications' in 2016, highlighting the combinations with safety concerns?
Initial pharmacotherapy (Section 4.4)	For all patients with COPD only and COPD plus asthma who started therapy for the first time between 1 July 2015 and 31 December 2016: ▷ How many medicines were used for initial therapy? ▷ What medicines were used for initial therapy? ▷ Has the distribution of initial therapies changed in this period compared with the period 1 July 2013 to 30 June 2015?
Associated care for patients with COPD (Section 4.5)	For all patients with COPD (with or without asthma): ▷ How many had a record of a spirometry test (ever)? ▷ How many had smoking cessation medicines coprescribed (ever)? ▷ How many were current smokers in 2016? ▷ How many had smoking cessation medicines coprescribed (ever), by smoking status?
Adverse events/Allergies (Section 4.6)	Of all adverse events/allergies recorded in the Allergy table: ▷ What adverse reactions/allergies are recorded for specific COPD medicines (LAMA, LABA, LABA + LAMA, ICS + LABA)?

3.2. Methods

3.2.1. Study type/design

- This was a descriptive analysis of electronic Australian national general practice data. All analyses were cross-sectional.

3.2.2. Study time period

- 1 January 2016 to 31 December 2016 inclusive, unless otherwise specified.

3.2.3. Study population

- Patients were included if they met the following criteria ('regular patients'):
  - ≥ 35 years of age (although some patients < 35 years of age have a diagnosis of COPD, there is more certainty that the condition is COPD and not another respiratory condition for this age group)
  - visited a GP at a clinically representative practice (namely those practices that have been established for two years with no significant interruptions to practice data, and are typical, rather than specialised)
  - had 3 or more visits to the clinically relevant practice in the past 2 years prior to 31 December 2016 (the definition recommended by the RACGP to encompass patients who are regularly cared for by the practice)
  - not deceased
  - marked as active by the practice clinical information system (CIS).
- Where additional restrictions were applied for specific objectives, these are described under the relevant sub-sections in Section 4.

3.2.4. Defining COPD and asthma

- A patient was defined as having a **history of COPD** if they had ever had a recorded diagnosis of COPD, chronic obstructive airways disease (COAD), chronic airflow/airways limitation (CAL), emphysema or chronic bronchitis in any designated text or code field in relevant diagnosis tables (history (active), reason for prescription or reason for visit).
- Patients were identified with a **history of asthma** similarly.
- If a patient had a record of both asthma and COPD, they were categorised as having **COPD plus asthma**. Patients with **asthma only** and **COPD only** were also identified.
- Condition-related terms and codes are listed in Appendix D.
- Patients with α-1-antitrypsin deficiency (A1ATD) – *an underrecognised hereditary disorder associated with the premature onset of chronic obstructive pulmonary disease* – made up a small proportion of the total COPD population. As management may differ for these patients, they were excluded from the definition of COPD.

3.2.5. Medicines and medicine classes

- TABLE 1 lists the medicines of interest commonly used for COPD, asthma and other respiratory conditions and their PBS restrictions.
- Prescriptions for the medicines of interest were identified by an Anatomical Therapeutic Chemical (ATC) code, generic name and/or trade name (as assigned by the clinical system). Appendix D lists the ATC, generic names and trade names of the medicines investigated.
- All PBS/RPBS prescriptions for COPD medicines were extracted for the period from 1 January 2012 up to and including 31 December 2016.
- Data was extracted BOTH from the prescription transaction file (which contains all information about each prescription ordered) and the prescription history table (which contains information about current medications and ceased medications).

- TABLE 2 list the medicines of interest commonly used for smoking cessation therapy.
- All PBS/RPBS prescriptions for the smoking cessation therapies were extracted up to 31 December 2016.

TABLE 1 MEDICINES USED IN COPD

Class	Generic name	PBS Restriction
SABA	Salbutamol	COPD / Asthma
SABA	Terbutaline	COPD / Asthma
SAMA	Ipratropium	COPD / Asthma
LAMA	Aclidinium	COPD only
LAMA	Glycopyrronium	COPD only
LAMA	Tiotropium	COPD only
LAMA	Umeclidinium	COPD only
LABA	Formoterol	Asthma only
LABA	Indacaterol	COPD only
LABA	Salmeterol	Asthma only
ICS	Beclometasone	Asthma only
ICS	Budesonide	Asthma only
ICS	Ciclesonide	Asthma only
ICS	Fluticasone	Asthma only
LABA + LAMA	Aclidinium + formoterol	COPD only
LABA + LAMA	Indacaterol + glycopyrronium	COPD only
LABA + LAMA	Umeclidinium + vilanterol	COPD only
LABA + LAMA	Tiotropium + olodaterol	COPD only
ICS + LABA	Budesonide + formoterol	COPD / Asthma
ICS + LABA	Fluticasone + formoterol	Asthma only
ICS + LABA	Fluticasone + salmeterol	COPD / Asthma
ICS + LABA	Fluticasone + vilanterol	COPD / Asthma

TABLE 2 MEDICINES USED IN SMOKING CESSATION

Class	Generic name
Nicotine replacement therapy (NRT)	Nicotine
Non-nicotine therapy	Bupropion
Nicotinic receptor partial agonist	Varenicline

3.2.6. Defining a ‘current medication’

To investigate the use of combinations of medicine formulations (Section 4.3; Coprescribing of COPD medicines) we identified all ‘current medications’ for patients according to the Prescription History table and removed records marked as ceased or deleted. Note, this methodology is new and replaces methods used in previous reports for defining coprescribing. Previously we analysed the Prescription table (the transactional record of scripts printed at the practice) to report on combinations of products prescribed during a certain time period and prescribed on the same day, as proxies for coprescribing. This new methodology should provide improved estimates of coprescribing by reflecting the ‘current medication list’ from the clinical software system. Please note, some medicines may have been ceased without a record in the clinical system which could lead to some misclassification of current medications.

3.2.7. Analysis plan

Analysis of the data was conducted using SAS version 9.3 (SAS Institute In., Cary, NC, USA). Definitions of the measures (proportions and rates) calculated for this report are detailed in Section 4.

To indicate the reliability of the estimated prevalences and proportions, 95% confidence intervals were calculated (a range of values that should contain the actual proportion 95% of the time). Comparisons within categories were made by comparing the degree of the overlap of the corresponding 95% confidence intervals. The MedicineInsight data shows variability between patients in different practices that is larger than the variability between patients within a practice. Failing to account for practice- as well as patient-level variability could result in a falsely optimistic estimate in the precision of our estimated proportions. To account for this, cluster-corrected 95% confidence intervals were calculated using the practice as the unit of clustering. The analyses used SAS PROC SURVEYFREQ procedure to calculate confidence intervals.

4. RESULTS

In this section, we present a summary of results found from our investigations with additional notes on the methods used, where required. This section contains the following sub-sections.

4.1. Patient cohort profile

4.2. Patterns of drug utilisation

4.3. Coprescribing of medicines

4.4. Initial pharmacotherapy

4.5. Associated care for patients with COPD

4.6. Adverse events/allergies

4.1. Patient cohort profile

4.1.1. Questions

- What is the prevalence in MedicineInsight of patients with COPD (all), COPD only and COPD plus asthma?
- What is the prevalence in MedicineInsight of patients with COPD (all), COPD only and COPD plus asthma, according to sociodemographic and risk factor profiles?

4.1.2. Methods

Rurality and socioeconomic status (SEIFA) were assigned based on a mapping of each patient's postcode of residence. The mapping of rurality was provided by the Australian Bureau of Statistics (ABS) mapping of Postcode 2012 to ASGS Remoteness Areas 2011.[7] Socioeconomic status was calculated in accordance to the ABS Index of Relative Socioeconomic Advantage and Disadvantage (IRSAD).[8]

We calculated the following for the study population diagnosed with COPD (all), COPD only and COPD plus asthma:

- Number and proportion of patients with the diagnosis of interest.
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by age group (**age-specific prevalence**).
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by region (rurality) (**region-specific prevalence**).
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by socioeconomic status (**SEIFA-specific prevalence**).
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by Department of Veterans Affairs (DVA) status (**DVA status-specific prevalence**).
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by smoking status (**smoking-specific prevalence**).
- Number of patients with the diagnosis of interest per 100 regular MedicineInsight patients by BMI status (**BMI-specific prevalence**).

4.1.3. Data interpretation

Practices were recruited to MedicineInsight using non-random sampling, and systematic sampling differences between regions cannot be ruled out. Comparisons between regions should be interpreted with caution.

4.1.4. Results

All COPD patients, COPD only, and COPD plus asthma

Prevalence

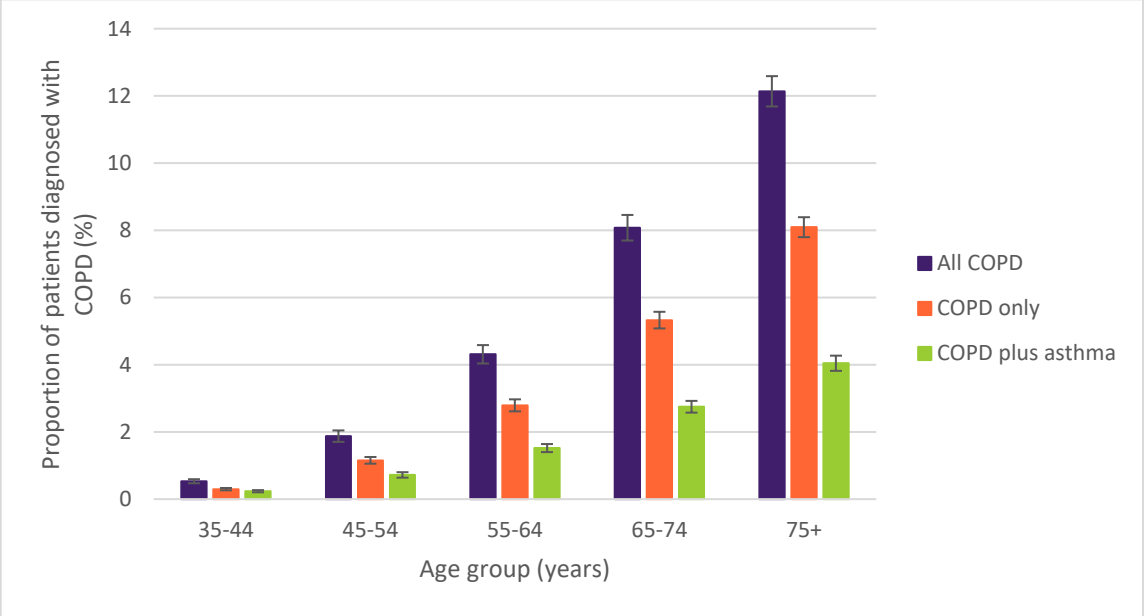
Of all 1.28 million regular MedicineInsight patients 35 years and over, 4.6% (1 in 22 patients) were ever diagnosed with COPD, with or without asthma (COPD (all): n=59,196; 4.6%; 95% CI:4.4 to 4.9), 3.0% had a COPD diagnosis without mention of asthma (COPD only, n=38,650), and 1.6% had both COPD plus asthma diagnoses (n=20,546). Of the patients with a history of COPD included in this study (ie, active patients who regularly attend the practice) just over one-third also had a history of asthma.

The prevalence of COPD in regular MedicineInsight patients 45 years and over was 5.9% (95% CI:5.6 to 6.2), compared with 5.1% (95% CI:4.6 to 5.7) reported by the 2014–15 ABS National Health Survey (NHS).[1]

Prevalence according to sociodemographic factors

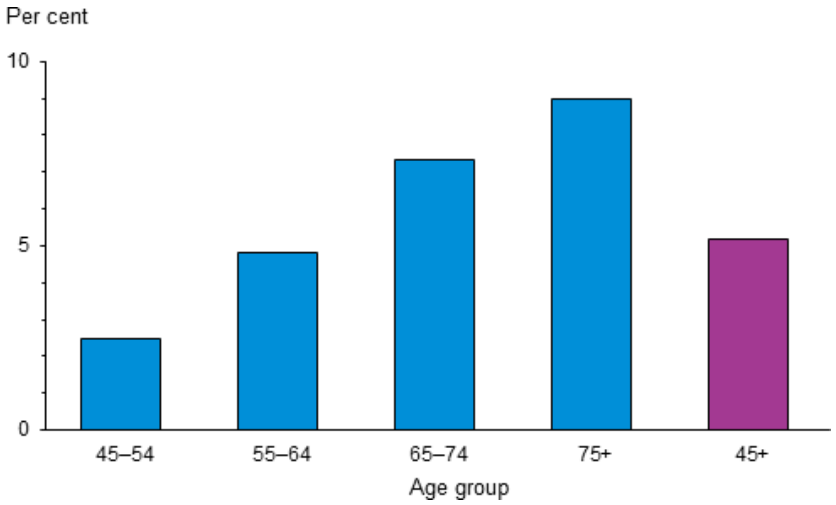
The prevalence of patients diagnosed with COPD according to sociodemographic factors is presented in TABLE 3. There was a significantly higher prevalence of COPD in males (5.2 %; 95% CI:4.9 to 5.5.) compared to females (4.2 %; 95% CI:3.9 to 4.4). The age-specific prevalence of patients diagnosed with COPD increased with age (FIGURE 1). The lowest prevalence was among younger patients aged 35–44 years (0.53%) and 45–54 years (1.9%) and highest among patients aged 75 years and older (12.1 per 100 patients). (FIGURE 1). These figures are largely comparable to the age-specific prevalences reported by the by the 2014–15 ABS National Health Survey (NHS) (FIGURE 2): prevalence was 2.5% (95% CI:1.8 to 3.2) in those aged 45–54 years and 9.0 (95% CI:7.0 to 10.9) among people 75 years and older.[1] Age-specific prevalence in MedicineInsight is presented separately for patients with COPD only and COPD plus asthma (FIGURE 1).

FIGURE 1 PREVALENCE OF COPD BY AGE, MEDICINEINSIGHT, 31 DECEMBER 2016.



Patients were less likely to have a COPD diagnosis if they lived in major cities (3.9 per 100) compared those living in inner regional areas (5.7 per 100) and outer regional /remote areas. There was higher prevalence of COPD in the more socioeconomically disadvantaged areas (7.0 per 100 patients in areas of 1–2 SEIFA and 5.7 per 100 patients in areas of 3–4 SEIFA) compared to more advantaged areas. (TABLE 3)

FIGURE 2 PREVALENCE OF COPD, AGES 45+, BY AGE, REPORTED BY THE 2014–15 ABS NATIONAL HEALTH SURVEY (NHS)[1]



Notes: COPD here refers to self-reported doctor-diagnosed current and long-term bronchitis and/or emphysema.

TABLE 3 PREVALENCE OF COPD, BY SOCIODEMOGRAPHIC FACTORS, MEDICINEINSIGHT, 31 DECEMBER 2016

	COPD (all)		COPD only		COPD plus asthma	
Sociodemographic factors	**%**	**(95% CI)**	**%**	**(95% CI)**	**%**	**(95% CI)**
Gender						
Male	5.2	(4.87-5.46)	3.7	(3.47-3.88)	1.5	(1.39-1.6)
Female	4.2	(3.93-4.43)	2.5	(2.35-2.63)	1.7	(1.56-1.81)
Rurality						
Major cities	3.9	(3.64-4.24)	2.6	(2.4-2.78)	3.9	(3.64-4.24)
Inner regional	5.7	(5.22-6.23)	3.7	(3.35-4.02)	5.7	(5.22-6.23)
Outer regional	5.9	(5.2-6.65)	3.8	(3.41-4.23)	5.9	(5.2-6.65)
Remote	4.9	(3.77-5.98)	4.9	(3.77-5.98)	4.9	(3.77-5.98)
Very remote	3.9	(2.51-5.24)	3.9	(2.51-5.24)	3.9	(2.51-5.24)
Socioeconomic status						
1–2 (most disadvantaged)	7.0	(6.43-7.61)	4.5	(4.1-4.84)	2.6	(2.26-2.84)
3–4	5.7	(5.35-6.07)	3.8	(3.54-4.04)	1.9	(1.76-2.07)
5–6	5.0	(4.58-5.43)	3.2	(2.95-3.52)	1.8	(1.59-1.94)
7–8	3.8	(3.45-4.05)	2.5	(2.31-2.68)	1.3	(1.11-1.4)
9–10 (most advantaged)	2.7	(2.52-2.97)	1.8	(1.67-1.97)	0.9	(0.82-1.03)
Indigenous status						
Aboriginal	9.5	(8.76-10.23)	5.5	(4.97-5.98)	4.0	(3.63-4.42)
Torres Strait Islander	6.0	(4.43-7.56)	2.9	(1.62-4.21)	3.1	(1.97-4.18)
Aboriginal and Torres Strait Islander	8.2	(6.75-9.58)	5.2	(4.21-6.16)	3.0	(2.2-3.77)
Not Aboriginal or Torres Strait Islander	5.0	(4.7-5.27)	3.2	(3.05-3.41)	1.8	(1.63-1.88)
Not stated (missing)	3.4	(3.07-3.68)	2.3	(2.1-2.5)	1.1	(0.95-1.19)
DVA						
Yes	12.9	(12.28-13.59)	9.0	(8.51-9.56)	3.9	(3.57-4.24)
No	4.5	(4.22-4.74)	2.9	(2.76-3.08)	1.6	(1.45-1.68)

Prevalence according to risk factors

The prevalence of patients diagnosed with COPD according to risk factors is presented in TABLE 4. There was a significantly higher prevalence of COPD in smokers (10.1 per 100 patients) and ex-smokers (9.4 per 100 patients) compared to non-smokers (1.6 per 100 patients). Patients were much more likely to have a COPD diagnosis if they were underweight (BMI < 18.5) (18.3 per 100), compared to normal weight (7.7 per 100) and overweight/obese.

TABLE 4 PREVALENCE OF COPD, BY RISK FACTORS, MEDICINEINSIGHT, 31 DECEMBER 2016

	COPD (all)		COPD only		COPD plus asthma	
Sociodemographic/ Risk factors	**%**	**(95% CI)**	**%**	**(95% CI)**	**%**	**(95% CI)**
Smoking status						
Smoker	10.1	(9.64-10.65)	7.1	(6.77-7.49)	3.0	(2.81-3.23)
Ex-smoker	9.4	(9.01-9.87)	6.2	(5.89-6.46)	3.3	(3.08-3.46)
Non-smoker	1.6	(1.5-1.73)	0.9	(0.8-0.92)	0.8	(0.69-0.81)
Unknown	1.6	(1.42-1.78)	1.2	(1.1-1.36)	0.4	(0.3-0.44)
BMI category						
Underweight (< 18.5)	18.3	(17.03-19.56)	13.3	(12.32-14.28)	5.0	(4.38-5.6)
Healthy weight range (18.5–< 25)	7.7	(7.22-8.25)	5.2	(4.86-5.56)	2.5	(2.32-2.73)
Overweight (25–< 30)	6.2	(5.84-6.55)	4.0	(3.73-4.19)	2.2	(2.08-2.39)
Obese (30+)	6.7	(6.37-7.1)	3.9	(3.71-4.13)	2.8	(2.62-3.01)
Not recorded	2.9	(2.74-3.14)	2.0	(1.9-2.16)	0.9	(0.82-1)

4.2. Patterns of drug utilisation

4.2.1. Questions

For patients with COPD only (no asthma) and COPD plus asthma:

1. What medicine classes and medicines of interest were prescribed in 2016?
2. How has the utilisation of the medicines of interest changed in the last 5 years (2012 to 2016)?

4.2.2. Methods

For the 5-year analysis of prescribing trends (Question 2) patients were included if they had 3 or more visits to the clinically relevant practice in the **past 5 years** prior to 31 December 2016 (rather than 3 visits in the past 2 years which was applied to the main study population).

All PBS/RPBS prescriptions for medicine classes and medicines of interest (TABLE 1) were extracted for the period from 1 January 2016 to 31 December 2016 (Question 1) and for the period from 1 January 2012 to 31 December 2016 (Question 2). Multiple prescriptions for the same medication prescribed on the same day were counted as a single prescription and only the last prescription recorded that day was used to count repeats. Private scripts made up less than 1% of the total number of prescriptions and were excluded from analyses.

When calculating the count of originals and repeats, if the medication was ceased during therapy, we included only the number of repeats that would have been filled before the cease date, assuming repeats are filled every 30 days.

For each medicine and medicine class of interest, we calculated:

- The total count of prescriptions (originals/originals + repeats) ordered in 2016 for patients with COPD only or COPD plus asthma
- The yearly rate of prescriptions (originals + repeats) per 1000 GP visits for patients with COPD only or COPD plus asthma from 2012 to 2016. We calculated the rate as the sum of the number of prescriptions ordered per year divided by the number of GP encounters for patients with COPD only or COPD plus asthma per year (multiplied by 1,000).
- The yearly proportion of prescriptions (originals + repeats) written in 2012 to 2016 for patients with COPD only or COPD plus asthma by class. We calculated the proportion as the total count of prescriptions ordered per class per year for patients with COPD only or COPD plus asthma divided by the total count of prescriptions ordered for all COPD medicines per year for patients with COPD only or COPD plus asthma.

4.2.3. Results

All prescriptions for patients with COPD (all)

In 2016, 106,100 original prescriptions for these medicines were ordered for regular MedicineInsight patients 35 years and over with COPD (with or without asthma).

The fixed-dose combination of inhaled corticosteroids and long-acting beta$_2$ agonists (ICS + LABA) was the most common class of medicines ordered for patients with COPD (34.1%), followed by short-acting beta$_2$ agonists (SABA) (29.3%) and long-acting muscarinic antagonists (LAMA) (22.6%). (TABLE 5)

TABLE 5 MEDICINE CLASSES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD (ALL) (ORIGINALS AND ORIGINAL + REPEATS), MEDICINEINSIGHT, 2016

	Number of prescriptions ordered in 2016 (originals)		Number of prescriptions ordered in 2016 (originals + repeats)	
Medicine class	**N**	**%**	**N**	**%**
ICS + LABA	36,168	34.09	198,240	34.95
SABA	31,106	29.32	164,389	28.98
LAMA	24,001	22.62	132,521	23.36
LABA + LAMA	4,606	4.34	23,837	4.20
ICS	4,316	4.07	17,483	3.08
LABA	3,127	2.95	16,753	2.95
SAMA	2,776	2.62	13,643	2.40
Total	**106,100**	**100.00**	**566,866**	**100.00**

The most commonly prescribed medicines for patients with COPD (originals; originals + repeats) were salbutamol (28.1%; 27.8%), fluticasone + salmeterol (FDC) (19.7%; 20.3%), tiotropium (18.7%; 19.6%) and budesonide + formoterol (FDC) (11.5%; 11.8%). (TABLE 6)

TABLE 6 MEDICINES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD (ALL) (ORIGINALS AND ORIGINAL AND REPEATS), MEDICINEINSIGHT, 2016

	Number of prescriptions ordered in 2016 (originals)		Number of prescriptions ordered in 2016 (originals + repeats)	
Medicine	**N**	**%**	**N**	**%**
Salbutamol	29,809	28.10	157,691	27.82
Fluticasone + salmeterol	20,861	19.66	115,210	20.32
Tiotropium	19,900	18.76	110,931	19.57
Budesonide + formoterol	12,253	11.55	66,844	11.79
Ipratropium	2,776	2.62	13,643	2.41
Fluticasone + vilanterol	2,625	2.47	13,929	2.46

Indacaterol	2,551	2.40	13,632	2.40
Fluticasone	2,068	1.95	5,961	1.05
Aclidinium	2,011	1.90	10,657	1.88
Indacaterol + glycopyrronium	1,471	1.39	7,613	1.34
Umeclidinium + vilanterol	1,332	1.26	7,014	1.24
Terbutaline	1,297	1.22	6,698	1.18
Ciclesonide	1,209	1.14	6,331	1.12
Tiotropium + olodaterol	1,209	1.14	6,278	1.11
Umeclidinium	1,149	1.08	6,193	1.09
Glycopyrronium	941	0.89	4,740	0.84
Budesonide	816	0.77	4,030	0.71
Aclidinium + formoterol	594	0.56	2,932	0.52
Fluticasone + formoterol	429	0.40	2,257	0.40
Formoterol	338	0.32	1,821	0.32
Salmeterol	238	0.22	1,300	0.23
Beclometasone	223	0.21	1,161	0.20
Total	**106,100**	**100.00**	**566,866**	**100.00**

All prescriptions for patients with COPD only (without asthma)

In 2016, 51,903 original prescriptions for the medicines of interest were ordered for patients with **COPD only** (276,004 original + repeat prescriptions). The most commonly prescribed medicine classes for patients with **COPD only** were ICS + LABA (31.8%), SABA (27.1%) and LAMA (26.2%) (TABLE 7)

TABLE 7 MEDICINE CLASSES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD ONLY (ORIGINALS AND ORIGINAL + REPEATS), MEDICINEINSIGHT, 2016

	No of prescriptions ordered in 2016 (originals)		No of prescriptions ordered in 2016 (originals + repeats)	
Medicine class	**N**	**%**	**N**	**%**
ICS + LABA	16,499	31.79	89,950	32.53
SABA	14,091	27.15	73,111	26.44
LAMA	13,587	26.18	75,093	27.16
LABA + LAMA	2,839	5.47	14,821	5.36
LABA	1,924	3.71	10,330	3.74
ICS*	1,841	3.55	7,289	2.64
SAMA	1,122	2.16	5,410	1.96
Total	**51,903**	**100.00**	**276,004**	**100.00**

The most commonly prescribed medicines (originals; original + repeats) for patients with **COPD only** were salbutamol (26.0%; 25.4%), tiotropium (21.8%; 22.8%) and fluticasone + salmeterol (18.4%; 19.0%). (TABLE 8)

TABLE 8 MEDICINES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD ONLY (ORIGINALS AND ORIGINAL + REPEATS), MEDICINEINSIGHT, 2016

	No of prescriptions ordered in 2016 (originals)		No of prescriptions ordered in 2016 (originals + repeats)	
Medicine	**N**	**%**	**N**	**%**
Salbutamol	13,507	26.02	70,144	25.37
Tiotropium	11,315	21.8	63,145	22.84
Fluticasone + salmeterol	9,537	18.37	52,460	18.97
Budesonide + formoterol	5,652	10.89	30,612	11.07
Indacaterol	1,698	3.27	9,107	3.29
Fluticasone + vilanterol	1,179	2.27	6,215	2.25
Ipratropium	1,122	2.16	5,410	1.96
Aclidinium	1,093	2.11	5,843	2.11
Fluticasone*	925	1.78	2,654	0.96
Umeclidinium + vilanterol	854	1.65	4,576	1.66
Indacaterol + glycopyrronium	846	1.63	4,395	1.59
Tiotropium + olodaterol	766	1.48	4,022	1.45
Umeclidinium	649	1.25	3,471	1.26
Terbutaline	584	1.13	2,967	1.07
Glycopyrronium	530	1.02	2,634	0.95
Ciclesonide*	447	0.86	2,326	0.84
Budesonide*	378	0.73	1,867	0.68
Aclidinium + formoterol	373	0.72	1,828	0.66
Fluticasone + formoterol*	131	0.25	663	0.24
Formoterol*	115	0.22	635	0.23
Salmeterol*	111	0.21	588	0.21
Beclometasone*	91	0.18	442	0.16
Total	**51,903**	**100.00**	**276,004**	**100.00**

All prescriptions for patients with COPD plus asthma

In 2016, 54,197 originals prescriptions for the medicines of interest were ordered for patients with **COPD plus asthma** (290,862 original + repeat prescriptions). The most commonly prescribed medicine classes for patients with **COPD plus asthma** were ICS + LABA (36.3%), SABA (31.4%) and LAMA (19.2%). (TABLE 9)

TABLE 9 MEDICINE CLASSES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD PLUS ASTHMA (ORIGINALS AND ORIGINAL + REPEATS), MEDICINEINSIGHT, 2016

	No of prescriptions ordered in 2016 (originals)		No of prescriptions ordered in 2016 (originals + repeats)	
Medicine class	**N**	**%**	**N**	**%**
ICS + LABA	19,669	36.29	108,290	36.93
SABA	17,015	31.39	91,278	31.13
LAMA	10,414	19.22	57,428	19.59
ICS	2,475	4.57	10,194	3.48
LABA + LAMA	1,767	3.26	9,016	3.07
SAMA	1,654	3.05	8,233	2.81
LABA	1,203	2.22	6,423	2.19
Total	**54,197**	**100**	**290,862**	**100.00**

The most commonly prescribed medicines (originals; original + repeats) for patients with **COPD plus asthma** were salbutamol (30.1%; 29.9%), fluticasone + salmeterol (20.9%; 21.4%) and tiotropium, (15.8%; 16.3%). (TABLE 10)

TABLE 10 MEDICINES OF INTEREST PRESCRIBED FOR PATIENTS WITH COPD PLUS ASTHMA (ORIGINALS AND ORIGINAL + REPEATS), MEDICINEINSIGHT, 2016

	No of prescriptions ordered in 2016 (originals)		No of prescriptions ordered in 2016 (originals + repeats)	
Medicine	**N**	**%**	**N**	**%**
Salbutamol	16,302	30.08	87,547	29.86
Fluticasone + salmeterol	11,324	20.89	62,750	21.40
Tiotropium	8,585	15.84	47,786	16.30
Budesonide + formoterol	6,601	12.18	36,232	12.36
Ipratropium	1,654	3.05	8,233	2.81
Fluticasone + vilanterol	1,446	2.67	7,714	2.63
Fluticasone	1,143	2.11	3,307	1.13
Aclidinium	918	1.69	4,814	1.64
Indacaterol	853	1.57	4,525	1.54
Ciclesonide	762	1.41	4,005	1.37
Terbutaline	713	1.32	3,731	1.27
Indacaterol + glycopyrronium	625	1.15	3,218	1.10
Umeclidinium	500	0.92	2,722	0.93
Umeclidinium + vilanterol	478	0.88	2,438	0.83
Tiotropium + olodaterol	443	0.82	2,256	0.77
Budesonide	438	0.81	2,163	0.74
Glycopyrronium	411	0.76	2,106	0.72

	No of prescriptions ordered in 2016 (originals)		No of prescriptions ordered in 2016 (originals + repeats)	
Medicine	**N**	**%**	**N**	**%**
Fluticasone + formoterol	298	0.55	1,594	0.54
Aclidinium + formoterol	221	0.41	1,104	0.38
Formoterol	223	0.41	1,186	0.40
Beclometasone	132	0.24	719	0.25
Salmeterol	127	0.23	712	0.24
Total	**54,197**	**100.00**	**290,862**	**100.00**

All prescriptions in the last 5 years (2012 to 2016) for patients with COPD only or COPD plus asthma

For the period between 1 January 2012 and 31 December 2016, we extracted a total of 198,118 and 243,354 prescriptions (originals) for COPD medicines for patients with COPD only and COPD plus asthma, respectively.

Annual prescribing rates

The annual rate of all COPD prescriptions for COPD only patients increased from 9.0 to 11.2 scripts per 100 GP visits (with COPD only patients) between 2012 and 2016. The annual rate of all COPD prescriptions for COPD plus asthma patients was higher than for COPD only patients, and remained relatively stable with a mean average between 2012 and 2016 of 18.6 scripts per 100 GP visits (with COPD plus asthma patients).

FIGURE 3 shows the rate of COPD medicine prescriptions (originals) by class per 1,000 GP visits with COPD only or COPD plus asthma patients, by year. The ICS + LABA combination products had the highest annual rate of prescribing, increasing from 2012 to 2016 for COPD only patients from 31.7 to 35.6 scripts per 1,000 GP visits with COPD only patients and for COPD plus asthma patients from 64.9 to 67.4 scripts per 1,000 GP visits with COPD plus asthma patients. LABA + LAMA combination products were introduced onto the PBS in 2014/15, and by 2016 were prescribed at the same rate (6.1 scripts per 1,000 GP visits) for COPD only and COPD plus asthma patients. There was a moderate increase in the annual LAMA script rate for all COPD patients.

FIGURE 4 shows the rate of individual COPD medicine prescriptions (originals) per 1,000 GP visits with COPD only or COPD plus asthma patients, by year. For patients with COPD only, tiotropium had the highest annual rate of prescribing in 2012 at 26.6 scripts per 1,000 GP visits, dropping to second highest in 2016 with 24.4 scripts per 1,000 visits – the introduction of newer LAMAs (aclidinium, glycopyrronium, umeclidinium) on the PBS in 2014 may explain this. Salbutamol had the highest rate of prescribing by 2016 and fluticasone + salmeterol FDC had the third highest rate of prescribing across all years. The rate of prescribing for fluticasone + salmeterol FDC increased moderately from 2012 to 2014 and then decreased until 2016, possibly due to the introduction of fluticasone + vilanterol FDC on the PBS in 2014 and the steady increase in budesonide + formoterol FDC from 2012 to 2016 (10.8 to 12.2 scripts per 1,000 GP visits), with the fourth highest prescribing rate across all years. (FIGURE 4)

For patients with COPD plus asthma (FIGURE 4), the top four medicines by prescribing rate were consistent from 2012 to 2016. Salbutamol had the highest annual rate of prescribing followed by fluticasone + salmeterol FDC, tiotropium and budesonide + formoterol FDC. The rate of prescribing for fluticasone + salmeterol FDC and tiotropium decreased after 2014, possibly due to the introduction of the new ICS + LABA FDC product (fluticasone + vilanterol) and the new LAMA products on the PBS in 2014.

Annual distribution of prescriptions

TABLE 11 shows the yearly trends in the proportions of COPD medicine classes prescribed for patients with COPD only. There were small variations in the distribution of classes across the 5 years, with ICS + LABAs consistently making up just over a third of the total COPD medicines prescribed each year, until 2016 when their share decreased to 31.8%. The proportion of LAMAs decreased from 29.4% of the total COPD medicines prescribed in 2012 to 26.2% by 2016. LABA + LAMA combination products increased from 0.1% of prescriptions in 2014 to 5.5% in 2016. The yearly trends in the proportions of individual COPD medicines prescribed for patients with COPD only are detailed in TABLE 12.

FIGURE 3 **RATE OF COPD PRESCRIPTIONS (ORIGINALS) BY CLASS PER 1,000 GP VISITS FOR PATIENTS WITH COPD ONLY AND COPD PLUS ASTHMA, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016**

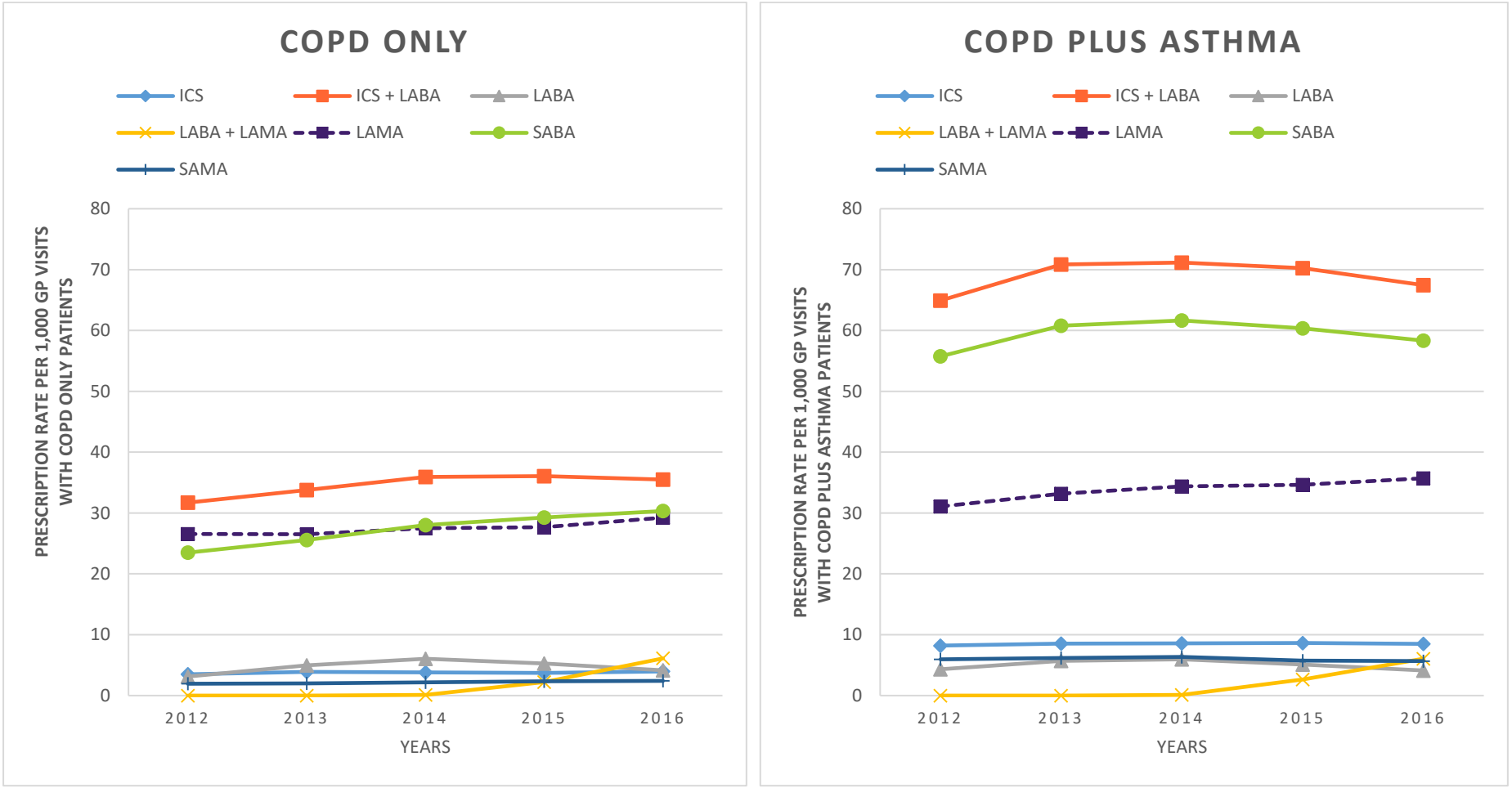
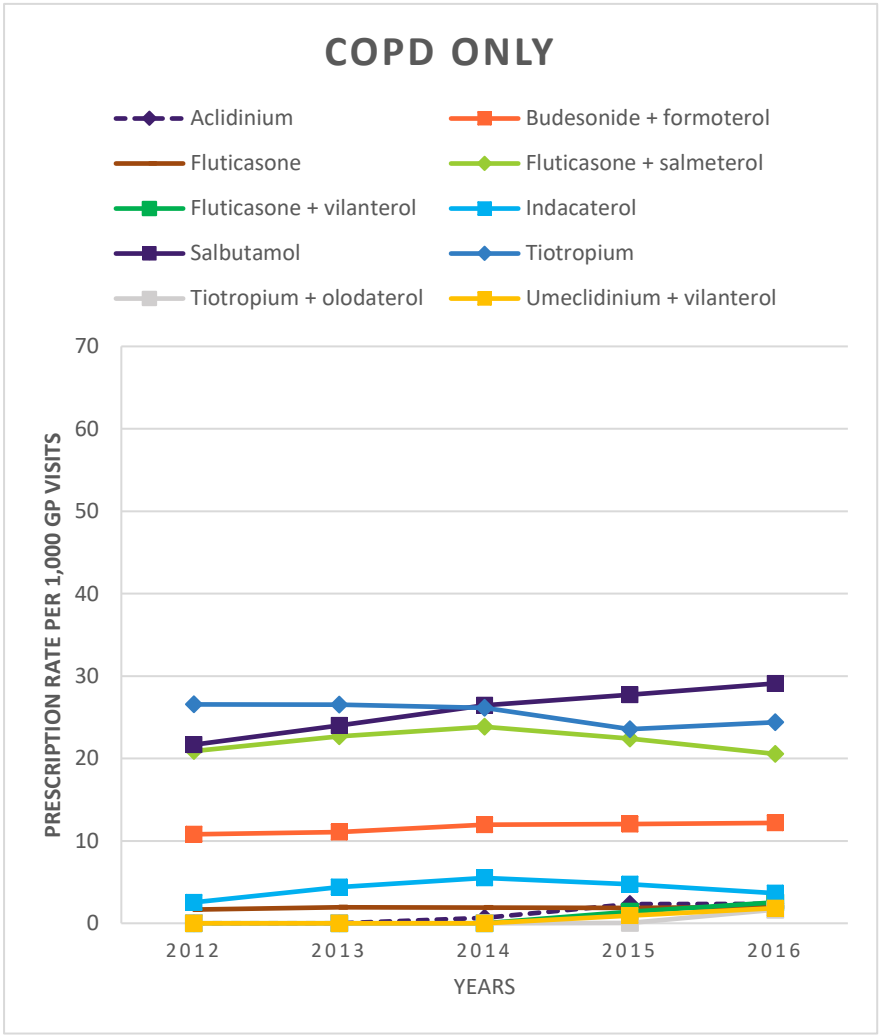


FIGURE 4 **PRESCRIBING RATE OF TOP 10 COPD MEDICINE PRESCRIPTIONS (ORIGINALS) PER 1,000 GP VISITS WITH COPD ONLY AND COPD PLUS ASTHMA, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016**



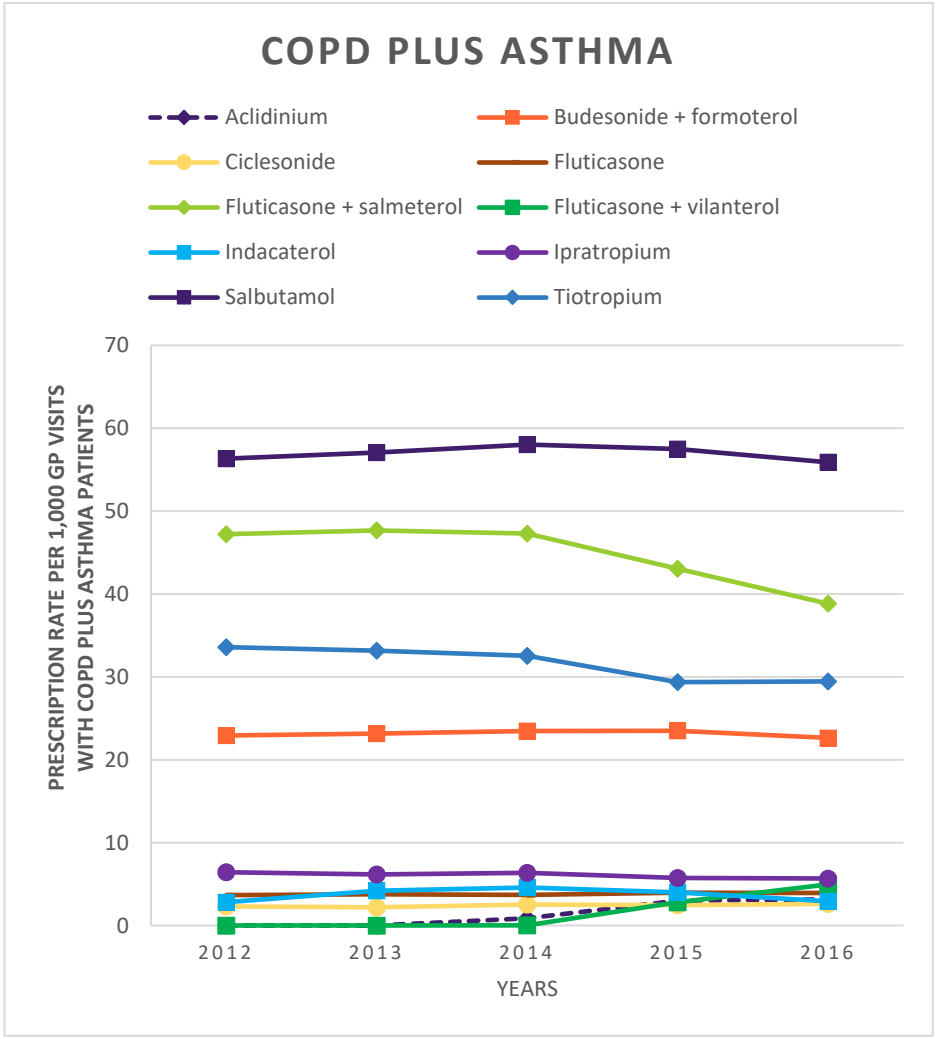


TABLE 11 YEARLY TRENDS IN PROPORTION OF COPD MEDICINE CLASSES PRESCRIBED FOR PATIENTS WITH COPD ONLY, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016

	COPD ONLY						
	2012	2013	2014	2015	2016	Direction of change	Test for trend (p-value)
Medicine	%	%	%	%	%		
ICS + LABA	35.10	34.91	34.70	33.84	31.79	↓	<0.0001
LAMA	29.40	27.41	26.56	25.95	26.18	↓	<0.0001
SABA	26.01	26.44	27.03	27.46	27.15	↑	<0.0001
ICS	3.87	4.01	3.68	3.51	3.55	↓	0.0002
LABA	3.46	5.15	5.84	4.94	3.71	↑	0.004
SAMA	2.15	2.07	2.10	2.21	2.16	–	0.4416
LABA + LAMA	0	0	0.09	2.10	5.47	↑	<0.0001
Total number of scripts (n)	26552	32440	40206	47017	51903		

TABLE 12 YEARLY TRENDS IN PROPORTION OF COPD MEDICINES PRESCRIBED FOR PATIENTS WITH COPD ONLY, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016

	2012	2013	2014	2015	2016	Direction of change	Test for trend (p-value)
Medicine	%	%	%	%	%		
Tiotropium	29.40	27.41	25.24	22.10	21.80	↓	<0.0001
Salbutamol	23.99	24.81	25.55	26.02	26.02	↑	<0.0001
Fluticasone + salmeterol	23.15	23.47	23.02	21.02	18.37	↓	<0.0001
Budesonide + formoterol	11.95	11.44	11.55	11.31	10.89	↓	<0.0001
Indacaterol	2.81	4.54	5.31	4.45	3.27	–	0.1781
Ipratropium	2.15	2.07	2.10	2.21	2.16	–	0.4416
Terbutaline	2.01	1.64	1.49	1.44	1.13	↓	<0.0001
Fluticasone	1.84	2	1.84	1.76	1.78	–	0.0759
Budesonide	0.98	0.94	0.78	0.73	0.73	↓	<0.0001
Ciclesonide	0.78	0.80	0.88	0.88	0.86	–	0.1372
Salmeterol	0.37	0.33	0.28	0.26	0.21	↓	<0.0001
Beclometasone	0.28	0.27	0.18	0.14	0.18	↓	<0.0001
Formoterol	0.28	0.28	0.25	0.22	0.22	↓	0.0329
Aclidinium	0	0	0.65	2.18	2.11	↑	<0.0001
Aclidinium + formoterol	0	0	0	0.04	0.72	↑	<0.0001
Fluticasone + formoterol	0	0	0.11	0.19	0.25	↑	<0.0001
Fluticasone + vilanterol	0	0	0.01	1.32	2.27	↑	<0.0001
Glycopyrronium	0	0	0.65	1.07	1.02	↑	<0.0001
Indacaterol + glycopyrronium	0	0	0.09	1.18	1.63	↑	<0.0001
Tiotropium + olodaterol	0	0	0	0.02	1.48	↑	<0.0001
Umeclidinium	0	0	0.01	0.59	1.25	↑	<0.0001
Umeclidinium + vilanterol	0	0	0	0.86	1.65	↑	<0.0001
Total number of scripts (n)	26552	32440	40206	47017	51903		

TABLE 13 shows the yearly trends in the proportions (distribution) of COPD medicine classes prescribed for patients with COPD plus asthma. ICS + LABAs consistently made up around 38% of the total COPD medicines prescribed each year, until 2016 when their share decreased to 36.3%. Compared with COPD only patients, LAMAs made up a smaller proportion of the total COPD medicines prescribed for patients with COPD plus asthma (between 18 and 19%) and SABAs made up a higher proportion of the total (decreasing form 32.8% and 31.4%) across the 5-year period. LABA + LAMA combination products increased from 0.1% of prescriptions in 2014 to 3.3% in 2016. The yearly trends in the proportions of individual COPD medicines prescribed for patients with COPD plus asthma are detailed in TABLE 14.

TABLE 13 YEARLY TRENDS IN PROPORTION OF COPD MEDICINE CLASSES PRESCRIBED FOR PATIENTS WITH COPD PLUS ASTHMA, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016

	COPD PLUS ASTHMA						
	2012	2013	2014	2015	2016	Direction of change	Test for trend (p-value)
Medicine	%	%	%	%	%		
ICS + LABA	38.14	38.24	37.81	37.49	36.29	↓	<0.0001
SABA	32.75	32.82	32.75	32.21	31.39	↓	<0.0001
LAMA	18.26	17.92	18.26	18.5	19.22	↑	<0.0001
ICS	4.83	4.62	4.57	4.62	4.57	–	0.107
SAMA	3.49	3.33	3.38	3.06	3.05	↓	<0.0001
LABA	2.54	3.07	3.17	2.72	2.22	↓	<0.0001
LABA + LAMA	0	0	0.07	1.4	3.26	↑	<0.0001
Total number of scripts (n)	40399	44720	50238	53802	54195		

TABLE 14 YEARLY TRENDS IN PROPORTION OF COPD MEDICINES PRESCRIBED FOR PATIENTS WITH COPD PLUS ASTHMA, MEDICINEINSIGHT, JANUARY 2012 TO DECEMBER 2016

	2012	2013	2014	2015	2016	Direction of change	Test for trend (p-value)
Medicine	%	%	%	%	%		
Salbutamol	30.62	30.83	30.84	30.69	30.08	–	0.0459
Fluticasone + salmeterol	25.68	25.74	25.14	22.99	20.89	↓	<.0001
Tiotropium	18.26	17.92	17.29	15.68	15.84	↓	<.0001
Budesonide + formoterol	12.46	12.5	12.46	12.54	12.18	–	0.2452
Ipratropium	3.49	3.33	3.38	3.06	3.05	↓	<.0001
Terbutaline	2.13	1.99	1.92	1.52	1.32	↓	<.0001
Fluticasone	1.99	2.04	1.97	2.11	2.11	–	0.1175
Indacaterol	1.53	2.26	2.43	2.13	1.57	–	0.1909
Ciclesonide	1.24	1.19	1.35	1.32	1.41	↑	0.0043
Budesonide	1.17	1.02	0.91	0.85	0.81	↓	<.0001
Formoterol	0.65	0.55	0.46	0.36	0.41	↓	<.0001
Beclometasone	0.43	0.38	0.34	0.33	0.24	↓	<.0001
Salmeterol	0.36	0.27	0.27	0.23	0.23	↓	0.0003
Aclidinium	0	0	0.47	1.60	1.69	↑	<.0001
Aclidinium + formoterol	0	0	0	0.02	0.41	↑	<.0001
Fluticasone + formoterol	0	0	0.19	0.47	0.55	↑	<.0001
Fluticasone + vilanterol	0	0	0.02	1.49	2.67	↑	<.0001
Glycopyrronium	0	0	0.50	0.74	0.76	↑	<.0001

Medicine	2012 %	2013 %	2014 %	2015 %	2016 %	Direction of change	Test for trend (p-value)
Indacaterol + glycopyrronium	0	0	0.06	0.85	1.15	↑	<.0001
Tiotropium + olodaterol	0	0	0	0	0.82	↑	<.0001
Umeclidinium	0	0	0	0.48	0.92	↑	<.0001
Umeclidinium + vilanterol	0	0	0.01	0.54	0.88	↑	<.0001
Total number of scripts (n)	40399	44720	50238	53802	54195		

4.3. Coprescribing of medicines

A small number of patients may be exposed to unsafe medicine use practices including double dosing and regimens that include concomitant use of a SAMA and a LAMA.

4.3.1. Questions

For patients with COPD only and COPD plus asthma:

- How often over the 12-month period (2016) were patients prescribed medicines of interest?
- What combination of medicine formulations (by class) were recorded as their 'current medications' in 2016, highlighting the combinations with safety concerns?

4.3.2. Methods

All prescriptions for medicine classes and medicines of interest (TABLE 1) were extracted for the period from 1 January 2016 to 31 December 2016. Multiple prescriptions for the same drug prescribed on the same day were counted as a single prescription.

To investigate the use of combinations of medicine formulations we identified all 'current medications' according to the Prescription History file and removed records marked as ceased or deleted. Medicine formulation combinations with potential safety concerns are identified as 'duplicated therapy' in TABLE 17 and specifically detailed under TABLE 18. We did not include the SABA class of medicines in this analysis as they can be used safely with all COPD medicines.

- For patients with COPD only and COPD plus asthma we calculated:
- The proportion of patients with 1,2,3,4, 5–10, or > 10 original prescriptions for COPD medicines ordered in 2016.
- The average (mean) number of original prescriptions for COPD medicines ordered in 2016 per patient.
- The proportion of patients on mono-, dual-, triple-therapy and the specific combinations of medicine formulations according to their latest 'current medications'.
- The proportion of patients on duplicated therapy.
- The proportion of patients on both LAMA maintenance therapy and SAMA reliever therapy.

4.3.3. Additional caveats

- Medicines may have been ceased without a record in the clinical system.
- SABA medicines are available over the counter, therefore SABA use may be underestimated in this report.

4.3.4. Results

Prescriptions ordered in 2016

Overall, 15.7% (9,319) of patients with COPD (all) had one original prescription for the medicines of interest; 14.5% (8,588) had two; 11.1% (6,558) had 5 to 10 and 41.6% (24,611) had no original prescriptions over 12 months (FIGURE 5).

The average (mean) number of original prescriptions ordered in 2016 per patient with COPD (all) was 3.1. Patients with COPD plus asthma had on average 3.5 original prescriptions over the 12-month period, followed by COPD only patients with 2.7 original prescriptions. (TABLE 15).

FIGURE 5 DISTRIBUTION OF PATIENTS BY TOTAL NUMBER OF ORIGINAL PRESCRIPTIONS FOR COPD MEDICINES ORDERED IN 2016, MEDICINEINSIGHT 2016: COPD (ALL) (N=59,196); COPD ONLY (N=38,650); COPD PLUS ASTHMA (N= 20,546)

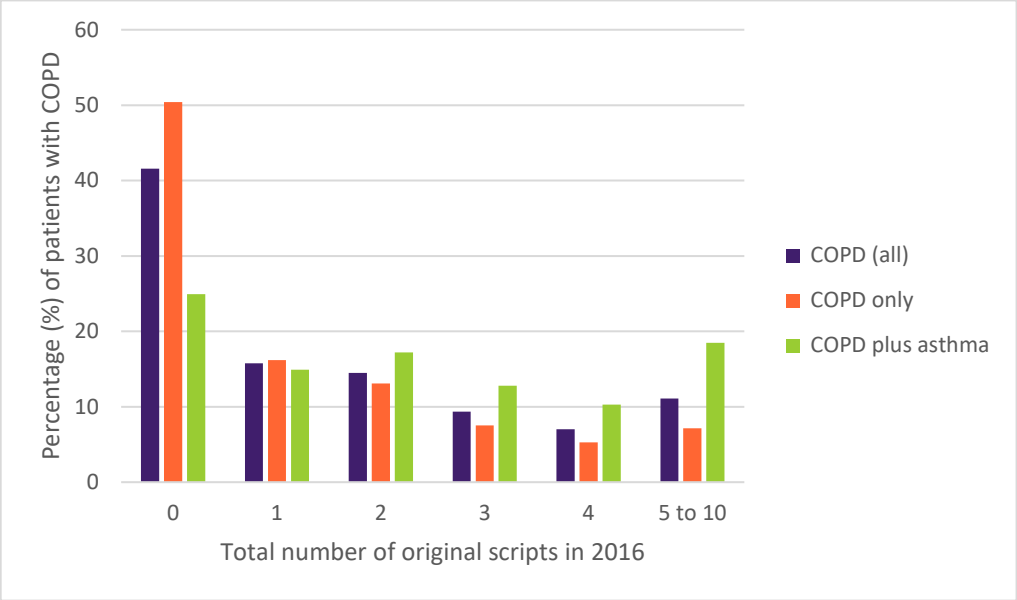


TABLE 15 AVERAGE NUMBER OF ORIGINAL PRESCRIPTIONS FOR COPD MEDICINES ORDERED IN 2016 PER PATIENT, MEDICINEINSIGHT 2016

	Mean	Median	Interquartile Range
COPD (all)	3.10	2	(1-4)
COPD only	2.74	2	(1-4)
COPD plus asthma	3.54	3	(2-5)

Current medications in 2016

Of the 38,650 patients with COPD only, 61% didn't have a reliever medication recorded according to their current medications, 36% were on a SABA, 0.7% SAMA and 2% SABA + SAMA. Of the 20,546 patients with COPD plus asthma, 28% had no reliever medication recorded, 65% were on a SABA, 0.7% SAMA and 6% SABA + SAMA (TABLE 16). The availability of reliever medications over the counter (without a prescription) means these medicines may not be on a patient's general practice record. Therefore this report underestimates the true use of reliever medications in patients with COPD.

TABLE 16 SUMMARY OF RELIEVER AND MAINTENANCE THERAPY ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	COPD ONLY		COPD PLUS ASTHMA	
Therapy	**N**	**%**	**N**	**%**
Relievers				
No current reliever	23,655	61.2	5,796	28.21
SAMA only	266	0.69	141	0.69
SABA only	13,912	35.99	13,368	65.06
SABA + SAMA	817	2.11	1,241	6.04
Total	38,650	100	20,546	100
Maintenance therapy				
No current maintenance therapy	18,298	47.37	3,988	19.45
At least one current maintenance therapy	20,352	52.69	16,558	80.77
Total	38,650	100	20,546	100

According to patients' current medication records, of the 20,352 patients with COPD only currently on at least one maintenance therapy, 38.0% were currently on dual therapy with ICS + LABA, 24.1% were on triple therapy with ICS + LABA + LAMA, 18.3% were on monotherapy with a LAMA and 8% were on LAMA + LABA dual therapy. Of the 16,558 patients with COPD plus asthma currently on at least one maintenance therapy, 47.2% were currently on dual therapy with ICS + LABA, 30.3% were on triple therapy with ICS + LABA + LAMA, 5.7% were on monotherapy with a LAMA and 3.9% were on LAMA + LABA dual therapy (TABLE 17).

TABLE 17 COPRESCRIBING OF COPD MEDICATIONS FOR MAINTENANCE THERAPY ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	COPD ONLY		COPD PLUS ASTHMA	
Combinations (Maintenance)	**N**	**%**	**N**	**%**
Monotherapy				
LAMA	3,723	18.3	944	5.7
LABA	677	3.3	210	1.3
ICS	678	3.3	688	4.2
Duplicated monotherapy				
LAMA x 2	45	0.2	12	0.1
LABA x 2	8	0.0	< 5	0.0
ICS x 2	5	0.0	7	0.0
Dual therapy				
LAMA + LABA	1,635	8.0	648	3.9
ICS + LABA	7,737	38.0	7,823	47.2
ICS & LAMA	182	0.9	186	1.1
Duplicated dual therapy				
ICS & (LAMA x 2)	< 5	0.0	< 5	0.0
ICS + LABA & LABA	117	0.6	89	0.5
(ICS x 2) & LAMA	59	0.3	155	0.9
ICS + LABA & ICS	0	0.0	< 5	0.0
LAMA + LABA & LABA	9	0.0	< 5	0.0
LAMA + LABA & LAMA	39	0.2	20	0.1
LAMA + LABA x 2	< 5	0.0	< 5	0.0
ICS + LABA x 2	98	0.5	186	1.1
Triple therapy				

	COPD ONLY		COPD PLUS ASTHMA	
Combinations (Maintenance)	**N**	**%**	**N**	**%**
ICS + LABA + LAMA	4,900	24.1	5,010	30.3
Duplicated triple therapy				
ICS + LABA & (LAMA x 2)	57	0.3	48	0.3
ICS + LABA & LAMA + LABA	215	1.1	210	1.3
ICS + LABA & LAMA & ICS	21	0.1	102	0.6
ICS + LABA & LAMA + LABA & LAMA	30	0.1	25	0.2
ICS + LABA + LAMA & ICS + LABA	81	0.4	124	0.7
(ICS + LABA + LAMA) x 2	5	0.0	15	0.1
Other	25	0.1	47	0.3
TOTAL	20,352	100.0	16,558	100.0

Current medications in 2016 – combinations with safety concerns

This analysis suggests that around 3.9% of patients with COPD only on maintenance therapy (795 out of 20,352) may be at risk of having duplicated therapy and 1.6% (333 out of 20,352) were currently on at least one LAMA product and at least one SAMA product. We found that 6.1% of patients with COPD plus asthma on maintenance therapy (1,002 out of 16,558) may be at risk of having duplicated therapy and 3.2% (531 out of 16,558) were currently on at least one LAMA product and at least one SAMA product (TABLE 18).

TABLE 18 COMBINATIONS WITH POTENTIAL SAFETY CONCERNS ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	COPD ONLY		COPD PLUS ASTHMA	
Combinations with potential safety concern	**N**	**%**	**N**	**%**
Concomitant LAMA and SAMA	333	1.64	531	3.21
Duplicated therapy (see TABLE 17)	795	3.91	1,002	6.05
Total patients on at least one maintenance therapy	20,352	100	16,558	100

4.4. Initial pharmacotherapy

4.4.1. Questions

For patients with COPD only and COPD plus asthma who started therapy for the first time between 1 July 2015 and 31 December 2016:

- How many medicines were used for initial therapy?
- What medicines were used for initial therapy?
- Has the distribution of initial therapies changed in this period compared with the period 1 July 2013 to 30 June 2015?

We also compared our results to those presented in the previous MedicineInsight COPD report for the period 1 July 2013 to 30 June 2015 – see Appendix C (section 5.3.2). To align with the previous report this analysis was on all patients with COPD (with or without asthma).

4.4.2. Methods

This was a cross-sectional analysis of data for all regular patients 35 years or older diagnosed with COPD only and COPD plus asthma who attended clinically representative sites and who started therapy for the first time between 1 July 2015 and 31 December 2016 or between 1 July 2013 and 30 June 2015:

We excluded patients:

- with a record of a COPD medication prior to 1 July 2013, or
- who started their first COPD medicine within 12 months of their first encounter at the practice (on the basis they may have been prescribed COPD medications from other sources before joining the practice (eg, another GP practice or specialist/hospital)

We identified the first medicine class(es) and medicine(s) of interest prescribed for each patient. Please note, the previous MedicineInsight COPD Report (1 July 2013 to 30 June 2015) excluded SABA medicines from the analysis of initial therapy; to produce comparable results for this report we also excluded SABA medicines when defining initial therapy.

All prescriptions for medicine classes and medicines of interest (TABLE 1 were extracted for these patients for the period from 1 July 2013 to 31 December 2016. Patients with more than one script for the same medicine class or medicine had the relevant class or medicine only counted once as an initial therapy.

We calculated:

- The proportion of patients with 1, 2, or 3 medicines prescribed as initial therapy.
- The number and proportion of patients prescribed each medicine of interest as initial therapy.

We compared:

- The number and proportion of patients prescribed each medicine of interest as initial therapy in 1 July 2013 to 30 June 2015 versus 1 July 2015 to 31 December 2016.

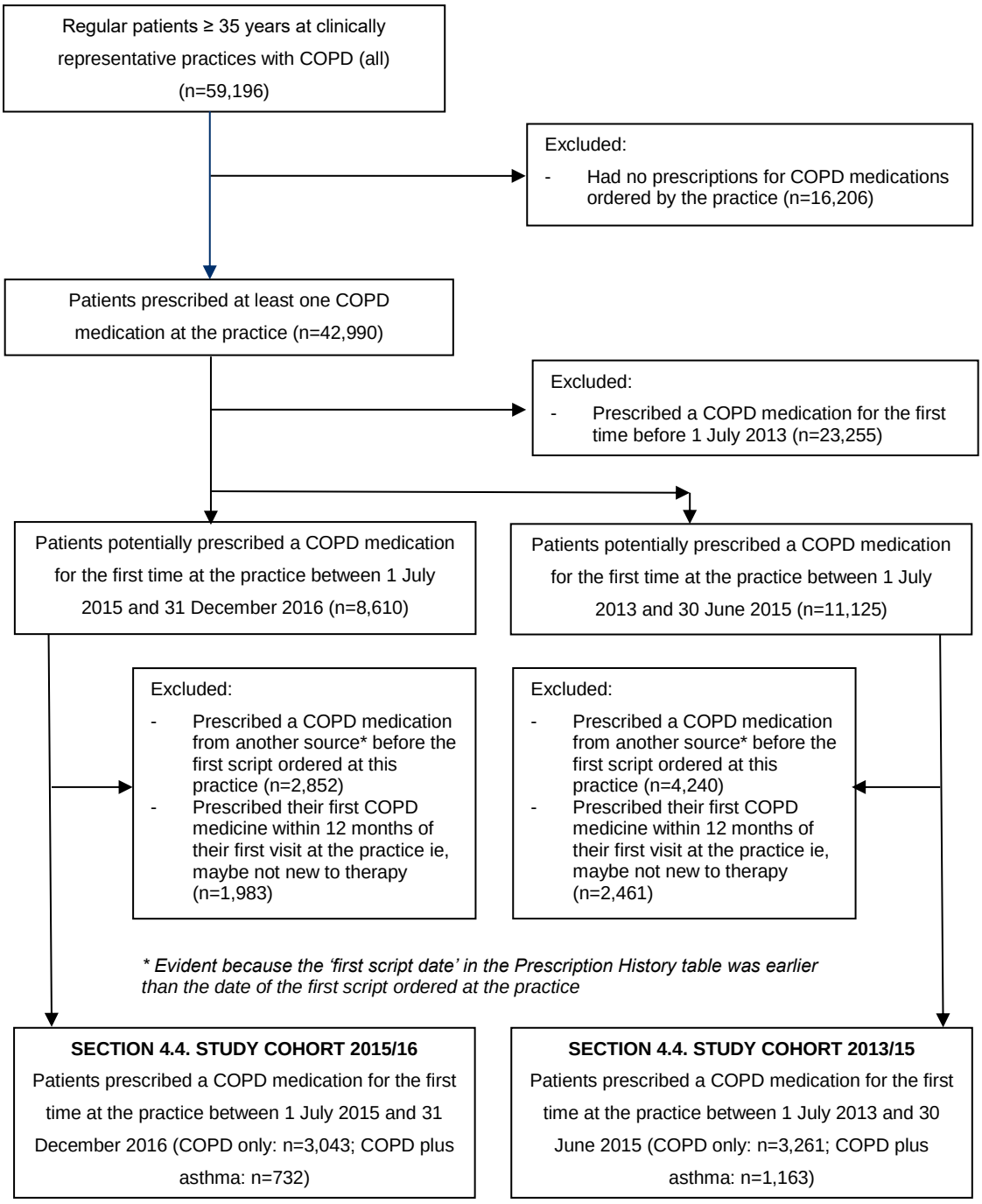
4.4.3. Additional caveats

- Specialist and hospital prescriptions are not included in MedicineInsight unless manually entered into the clinical information system by the practice staff. If the initial prescription was written by a specialist (in secondary care) the first prescription will be missing.
- Patients may have had their first diagnosis of COPD after their first COPD medication.

4.4.4. Defining the population who started therapy

Of the 59,196 regular patients 35 years and over with COPD only and COPD plus asthma, we identified 3,775 who started therapy with a COPD medication (not including SABA) between 1 July 2015 and 31 December 2016 (COPD only: n=3,043 / COPD plus asthma: n=732) and 4,424 who initiated therapy between 1 July 2013 and 30 June 2015 (COPD only: n=3,261 / COPD plus asthma: n=1,163). The flow diagram for selecting the patient cohort eligible for this section of the report is described in FIGURE 6.

FIGURE 6 FLOW DIAGRAM FOR THE SELECTION OF PATIENTS WHO STARTED THERAPY FOR COPD BETWEEN 1 JULY 2015 AND 31 DECEMBER 2016 AND BETWEEN 1 JULY 2013 AND 30 JUNE 2015



4.4.5. Results

Initial pharmacotherapy in patients with COPD only

Of the 3,043 patients with COPD only who started therapy for COPD between 1 July 2015 and 31 December 2016, 48.6% were prescribed only one medicine of interest as initial therapy, 46.3% were prescribed dual therapy and 5.1% triple therapy. The most common choice of initial therapy by class was dual therapy with ICS + LABA (38.5%; almost all were FDC), followed by LAMA monotherapy (35.9%) and LAMA + LABA dual therapy (7.4%) (TABLE 19). The most common choice of initial therapy by individual medicine(s) was tiotropium (23.5%) followed by fluticasone + salmeterol (17.5%) and budesonide + formoterol (16.4%) (TABLE 20).

When comparing initial therapy for patients with COPD only in the period July 2013 to June 2015 versus July 2015 to December 2016 we found the following:

- Initial therapy with LAMA increased from 27.3% in 2013/15 to 35.9% in 15/16
- Initial therapy with LAMA + LABA increased from 1.9% to 7.4%
- Initial therapy with ICS + LABA decreased from 47.1% to 38.5%
- Initial therapy with ICS + LABA + LAMA decreased slightly from 5.5% to 4.3%

TABLE 19 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD ONLY BY MEDICINE CLASS, MEDICINEINSIGHT JUL 2015–DEC 2016 AND JUL 2013–JUN 2015

	COPD ONLY			
	Jul 2015–Dec 2016		Jul 2013–Jun 2015	
Initial therapy	N	%	N	%
Monotherapy				
SAMA	97	3.19	101	3.10
LAMA	1094	35.95	892	27.35
LABA	146	4.80	237	7.27
ICS	141	4.63	197	6.04
Dual therapy				
LAMA + LABA	225	7.39	61	1.87
ICS + LABA	1172	38.51	1536	47.10
ICS & LAMA	6	0.20	5	0.15
ICS & SAMA	6	0.20	5	0.15
Triple therapy				0.00
ICS + LABA & LAMA	132	4.34	178	5.46
ICS + LABA & SAMA	8	0.26	18	0.55
Other	16	0.53	31	0.95
TOTAL	3043	100.00	3261	100.00

TABLE 20 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD ONLY BY INDIVIDUAL MEDICINE(S), MEDICINEINSIGHT JUL 2015-DEC 2016 AND JUL 2013 - JUN 2015

		COPD ONLY			
Class	Medicine	Jul 2015–Dec 2016		Jul 2013–Jun 2015	
Monotherapy		N	%	N	%
SAMA	*Ipratropium*	97	3.19	101	3.10
LAMA	*Aclidinium*	169	5.55	108	3.31
	Glycopyrronium	96	3.15	69	2.12
	Tiotropium	714	23.46	694	21.28

		COPD ONLY			
Class	**Medicine**	**Jul 2015–Dec 2016**		**Jul 2013–Jun 2015**	
	Umeclidinium	115	3.78	21	0.64
LABA	*Formoterol*	5	0.16	<5	
	Indacaterol	132	4.34	224	6.87
	Salmeterol	9	0.30	9	0.28
ICS	*Beclometasone*	9	0.30	10	0.31
	Budesonide	39	1.28	64	1.96
	Ciclesonide	17	0.56	22	0.67
	Fluticasone	76	2.50	101	3.10
Dual therapy					
LAMA + LABA (FDC)	*Aclidinium + formoterol*	35	1.15	0	0.00
	Glycopyrronium + indacaterol	51	1.68	16	0.49
	Umeclidinium + vilanterol	85	2.79	15	0.46
	Tiotropium + olodaterol	46	1.51	0	0.00
LAMA & LABA	*Aclidinium & indacaterol*	0	0.00	0	0.00
	Aclidinium & salmeterol	0	0.00	0	0.00
	Glycopyrronium & indacaterol	5	0.16	0	0.00
	Tiotropium & formoterol	0	0.00	0	0.00
	Tiotropium & indacaterol	<5		20	0.61
	Tiotropium & salmeterol	0	0.00	<5	
ICS + LABA (FDC)	*Budesonide + formoterol*	500	16.43	631	19.35
	Fluticasone + formoterol	9	0.30	10	0.31
	Fluticasone + salmeterol	531	17.45	859	26.34
	Fluticasone + vilanterol	132	4.34	36	1.10
Triple therapy					
ICS + LABA & LAMA	*Budesonide + formoterol & aclidinium*	<5		<5	
	Budesonide + formoterol & glycopyrronium	<5		<5	
	Budesonide + formoterol & tiotropium	35	1.15	44	1.35
	Budesonide + formoterol & umeclidinium	<5		0	0.00
	Fluticasone + formoterol & tiotropium	<5		<5	
	Fluticasone + salmeterol & aclidinium	8	0.26	<5	
	Fluticasone + salmeterol & glycopyrronium	<5		<5	
	Fluticasone + salmeterol & tiotropium	63	2.07	124	3.80
	Fluticasone + salmeterol & umeclidinium	<5		0	0.00
	Fluticasone + vilanterol & tiotropium	5	0.16	<5	
	Fluticasone + vilanterol & umeclidinium	8	0.26	0	0.00
ICS + LABA & SAMA	*Budesonide + formoterol & ipratropium*	6	0.20	6	0.18
Other		30	0.99	60	1.84
TOTAL		3,043	100.00	3,261	100.00

Initial pharmacotherapy in patients with COPD plus asthma

Of the 732 patients with COPD plus asthma who started therapy for COPD between 1 July 2015 and 31 December 2016, 60.2% were prescribed two medicines of interest as initial therapy, 35.1% were prescribed monotherapy and 4.6% triple therapy. The most common choice of initial therapy by class was dual therapy with ICS + LABA (54.5%; almost all were FDC), followed by LAMA monotherapy (18.8%) and ICS monotherapy (10.8%) (TABLE 21). The most common choice of initial therapy by individual medicine(s) was budesonide + formoterol (24.7%), followed by fluticasone + salmeterol (24.0%) and tiotropium (13.0%) (TABLE 22).

When comparing initial therapy for patients with COPD plus asthma in the period July 2013 to June 2015 versus July 2015 to December 2016 we found the following:

- Initial therapy with LAMA increased from 13.3% in 2013/15 to 18.9% in 15/16
- Initial therapy with LAMA + LABA increased from 0.5% to 5.6%
- Initial therapy with ICS + LABA decreased from 64.1% to 54.5%
- Initial therapy with ICS + LABA + LAMA decreased slightly from 4.6% to 4.0%

TABLE 21 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD PLUS ASTHMA BY MEDICINE CLASS, MEDICINEINSIGHT JUL 2015–DEC 2016 AND JUL 2013–JUN 2015

	COPD PLUS ASTHMA			
	Jul 2015–Dec 2016		Jul 2013–Jun 2015	
Initial therapy	**N**	**%**	**N**	**%**
Monotherapy				
SAMA	17	2.32	26	2.24
LAMA	138	18.85	155	13.33
LABA	23	3.14	34	2.92
ICS	79	10.79	130	11.18
Dual therapy				
LAMA + LABA	41	5.60	6	0.52
ICS + LABA	399	54.51	746	64.14
ICS & LAMA	<5		<5	
ICS & SAMA	0	0.00	0	0.00
Triple therapy				
ICS + LABA & LAMA	29	3.96	54	4.64
ICS + LABA & SAMA	<5		<5	
Other	<5		6	0.52
TOTAL	732	100.00	1163	100.00

TABLE 22 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD PLUS ASTHMA BY INDIVIDUAL MEDICINE(S), MEDICINEINSIGHT JUL 2015-DEC 2016 AND JUL 2013 - JUN 2015

		COPD PLUS ASTHMA			
Class	**Medicine**	**Jul 2015–Dec 2016**		**Jul 2013–Jun 2015**	
Monotherapy		**N**	**%**	**N**	**%**
SAMA	*Ipratropium*	17	2.32	26	2.24
LAMA	*Aclidinium*	24	3.28	17	1.46
	Glycopyrronium	6	0.82	12	1.03
	Tiotropium	95	12.98	120	10.32
	Umeclidinium	13	1.78	6	0.52

		COPD PLUS ASTHMA			
Class	**Medicine**	**Jul 2015–Dec 2016**		**Jul 2013–Jun 2015**	
LABA	*Formoterol*	<5		0	0.00
	Indacaterol	20	2.73	30	2.58
	Salmeterol	<5		<5	
ICS	*Beclometasone*	5	0.68	9	0.77
	Budesonide	21	2.87	31	2.67
	Ciclesonide	11	1.50	15	1.29
	Fluticasone	42	5.74	75	6.45
Dual therapy					
LAMA + LABA (FDC)	*Aclidinium + formoterol*	5	0.68	0	0.00
	Glycopyrronium + indacaterol	11	1.50	<5	
	Umeclidinium + vilanterol	12	1.64	<5	
	Tiotropium + olodaterol	9	1.23	0	0.00
LAMA & LABA	*Aclidinium & indacaterol*	0	0.00	0	0.00
	Aclidinium & salmeterol	0	0.00	0	0.00
	Glycopyrronium & indacaterol	<5		0	0.00
	Tiotropium & formoterol	0	0.00	0	0.00
	Tiotropium & indacaterol	0	0.00	<5	
	Tiotropium & salmeterol	<5		<5	
ICS + LABA (FDC)	*Budesonide + formoterol*	181	24.73	295	25.37
	Fluticasone + formoterol	10	1.37	12	1.03
	Fluticasone + salmeterol	176	24.04	430	36.97
	Fluticasone + vilanterol	32	4.37	9	0.77
Triple therapy					
ICS + LABA & LAMA	*Budesonide + formoterol & aclidinium*	<5		0	0.00
	Budesonide + formoterol & glycopyrronium	0	0.00	0	0.00
	Budesonide + formoterol & tiotropium	8	1.09	22	1.89
	Budesonide + formoterol & umeclidinium	0	0.00	0	0.00
	Fluticasone + formoterol & tiotropium	<5		0	0.00
	Fluticasone + salmeterol & aclidinium	<5		<5	
	Fluticasone + salmeterol & glycopyrronium	<5		<5	
	Fluticasone + salmeterol & tiotropium	13	1.78	28	2.41
	Fluticasone + salmeterol & umeclidinium	0	0.00	0	0.00
	Fluticasone + vilanterol & tiotropium	0	0.00	0	0.00
	Fluticasone + vilanterol & umeclidinium	<5		0	0.00
ICS + LABA & SAMA	*Budesonide + formoterol & ipratropium*	<5		0	0.00
Other		5	0.68	12	1.03
TOTAL		732	100.00	1163	100.00

4.5. Associated care

4.5.1. Questions

For all patients with COPD (with or without asthma)

- How many had a record of a spirometry test (ever)?
- How many had smoking cessation medicines coprescribed (ever)?
- How many were current smokers in 2016?
- How many had smoking cessation medicines coprescribed (ever), by smoking status?

4.5.2. Methods

This was a cross-sectional analysis of data for regular patients ≥ 35 years diagnosed with COPD (with or without asthma) at clinically representative sites.

All spirometry test records were extracted from observations, tests ordered, test results, MBS service items and encounters (reason for visit), up to 31 December 2016. All prescriptions for medicines for smoking cessation (TABLE 2) were extracted up to 31 December 2016. Current smoking status was extracted.

We calculated:

- Number and proportion of patients with a diagnosis of COPD who EVER had a record of a spirometry test recorded.
- Number and proportion of patients with a diagnosis of COPD who were EVER prescribed smoking cessation medications.
- Number and proportion of patients with a diagnosis of COPD who were current smokers in 2016 who were EVER prescribed smoking cessation medications.
- Number and proportion of patients with a diagnosis of COPD who were ex-smokers in 2016 who were EVER prescribed smoking cessation medications.

4.5.3. Results

Among regular patients with COPD (all) (n=59,196), 38.1% (n=22,524) ever had a record of one or more spirometry tests. This was lower than results reported in a 2012 survey of general practitioners[9] which found 64% of COPD patients had undertaken a spirometry test for diagnosis, of which 60% were performed in the general practice (TABLE 23).

Overall, 26.3% of all patients with COPD (all) (n=15,584) had ever been prescribed smoking cessation therapies. Of the 17,082 current smokers with COPD, 54.5% (n=9,313) had ever been prescribed smoking cessation therapy and of the 29,140 ex-smokers, 20.1% (n=5,865) had ever been prescribed smoking cessation therapy. Interestingly, 17.2% of patients whose current smoking status was ‘non-smoker’ had smoking cessation therapy recorded, indicating some misclassification of smoking status in the clinical information system (TABLE 23).

TABLE 23 ASSOCIATED CARE (EVER) PROVIDED TO PATIENTS WITH COPD (ALL), MEDICINEINSIGHT 2016

Measure	Number	%
Spirometry		
Recorded (ever)	22,524	38.05
Not recorded	36,672	61.95
Smoking cessation therapy		
Recorded (ever)	15,584	26.33
Not recorded	43,612	73.67
Smoking status		
Not recorded	2,821	4.77
Non-smoker	10,153	17.15
Ex-smoker	29,140	49.23
Smoking cessation therapy recorded	*5,865*	*20.13*
Smoker	17,082	28.86
Smoking cessation therapy recorded	*9,313*	*54.52*

4.6. Adverse events/allergies

4.6.1. Questions

- What adverse reactions/allergies are recorded for specific COPD medicines?

4.6.2. Methods

This was a cross-sectional analysis of recorded adverse events related to the following medicine classes, regardless of the indication for therapy:

- LAMA (tiotropium, aclidinium, glycopyrronium, umeclidinium)
- LABA (salmeterol, indacaterol, formoterol)
- LAMA + LABA (indacaterol + glycopyrronium combination), (tiotropium + olodaterol combination), (umeclidinium + vilanterol combination), (aclidinium + formoterol combination),
- ICS + LABA (fluticasone propionate + salmeterol), (fluticasone furoate + vilanterol) and (budesonide + formoterol).

We extracted all drug reaction records where LAMA, LABA, LAMA + LABA or ICS + LABA combination were recorded as the 'substance name' in the Allergy/Adverse event table for the period from the start of recording up to and including 31 December 2016, regardless of the indication for therapy. Drug reaction records for the COPD medicines of interest were identified by the active medicinal ingredient and using any of the generic or trade names for the COPD medicine.

We compiled a merged list of adverse reactions to the aforementioned COPD medicines, categorising the reactions manually to MedDRA categories. Where multiple reactions were recorded, we noted each separately.

For comparison, we compared our results from MedicineInsight with the TGA Database of Adverse Events Notifications (DAEN) for all adverse events reports with COPD medicines to 16 November 2016 (last available date).

We calculated the following:

- Total number of adverse events/allergies records and types of adverse events for LAMA medicines
- Total number of adverse events/allergies records and types of adverse events for LABA medicines
- Total number of adverse events/allergies records and types of adverse events for LAMA + LABA combination medicines
- Total number of adverse events/allergies records and types of adverse events for ICS + LABA combination medicines
- Number of adverse events/allergies for LAMA medicines according to MedDRA classification recorded
- Number of adverse events/allergies for LABA medicines according to MedDRA classification recorded
- Number of adverse events/allergies for LAMA + LABA combination medicines according to MedDRA classification recorded
- Number of adverse events/allergies for ICS + LABA combination medicines according to MedDRA classification recorded
- Number of adverse events/allergies for LAMA medicines according to MedDRA classification recorded by the TGA DAEN
- Number of adverse events/allergies for LABA medicines according to MedDRA classification recorded by the TGA DAEN
- Number of adverse events/allergies for LAMA + LABA combination medicines according to MedDRA classification recorded by the TGA DAEN
- Number of adverse events/allergies for ICS + LABA combination medicines according to MedDRA classification recorded by the TGA DAEN

4.6.3. Additional caveats

- A proportion of adverse reactions known to the GP may go unrecorded, eg, when the reaction is unremarkable or symptoms are managed elsewhere, such as in hospital. Some adverse events may be recorded in the 'progress notes' which are not collected by MedicineInsight for confidentiality reasons.
- Coding of reactions may differ between MedicineInsight and TGA for some reactions.
- This analysis was not restricted to patients with COPD and may include patients prescribed these medicines for other indications.

4.6.4. Results

There were 1,528 adverse events recorded for LAMA of which 318 were not specified. For LABA, we found 598 adverse events recorded, of which 138 were not specified. For LAMA + LABA combination therapies, we found 38 adverse events recorded, of which 7 were not specified. For ICS + LABA combination therapies, we found 2,275 adverse events recorded, of which 499 were not specified. Note these records are presented, regardless of the indication for therapy.

The most common adverse events were:

- LAMAs: cough, dry mouth, laryngeal discomfort, rash, nausea, dyspnoea, pruritus, dizziness, vision blurred and headache. (TABLE 24)
- LABAs: tremor, cough, rash, palpitations, muscle spasms, headache, nausea, laryngeal discomfort, tachycardia and dyspnoea. (TABLE 25)
- LAMA + LABA combined medicines: constipation, cough, dysphonia, headache, nausea, tachycardia, anxiety, diarrhoea, epistaxis and malaise. (TABLE 26)
- ICS + LABA combined medicines: dysphonia, rash, tremor, laryngeal discomfort, nausea, cough, palpitations, oral candidiasis, headache and muscle spasms. (TABLE 27)

Adverse reactions reported for MedicineInsight patients which were not reported in the TGA DAEN database are described in TABLE 28.

TABLE 24 MOST FREQUENTLY REPORTED ADVERSE REACTIONS FOR LAMAS IN MEDICINEINSIGHT COMPARED WITH TGA DAEN, MEDICINEINSIGHT 2016

MedDRA system organ class	MedDRA reaction term	Number of cases (MedicineInsight)	Number of cases (TGA)	Number of cases with a single suspected medicine (TGA)
Not specified		318		
Respiratory, thoracic and mediastinal disorders	Cough	143	16	13
Gastrointestinal disorders	Dry mouth	108	23	18
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	82	1	1
Skin and subcutaneous tissue disorders	Rash	81	13	12
Gastrointestinal disorders	Nausea	54	9	8
Respiratory, thoracic and mediastinal disorders	Dyspnoea	48	29	24
Skin and subcutaneous tissue disorders	Pruritis	46	10	8
Nervous system disorders	Dizziness	45	7	5
Eye disorders	Vision blurred	44	11	11
Nervous system disorders	Headache	43	14	13
Respiratory, thoracic and mediastinal disorders	Dysphonia	37	8	6
Cardiac disorders	Palpitations	36	13	13
General disorders and administration site conditions	Malaise	27	8	8
Gastrointestinal disorders	Constipation	26	10	7
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	18	4	3
Respiratory, thoracic and mediastinal disorders	Bronchospasm	17	2	2
General disorders and administration site conditions	Oedema	17	0	0
Nervous system disorders	Tremor	17	6	6
Gastrointestinal disorders	Mouth ulceration	16	4	3

TABLE 25 MOST FREQUENTLY REPORTED ADVERSE REACTIONS FOR LABAS IN MEDICINEINSIGHT COMPARED WITH TGA DAEN, MEDICINEINSIGHT 2016

MedDRA system organ class	MedDRA reaction term	Number of cases (MedicineInsight)	Number of cases (TGA)	Number of cases with a single suspected medicine (TGA)
Not specified		138		
Nervous system disorders	Tremor	47	9	9
Respiratory, thoracic and mediastinal disorders	Cough	44	20	17
Skin and subcutaneous tissue disorders	Rash	42	7	4
Cardiac disorders	Palpitations	38	7	6
Musculoskeletal and connective tissue disorders	Muscle spasms	27	19	15
Nervous system disorders	Headache	24	18	15
Gastrointestinal disorders	Nausea	19	12	9
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	16	0	0
Cardiac disorders	Tachycardia	15	4	4
Respiratory, thoracic and mediastinal disorders	Dyspnoea	12	20	17
Skin and subcutaneous tissue disorders	Urticaria	11	13	10
Nervous system disorders	Dizziness	9	16	10
Respiratory, thoracic and mediastinal disorders	Bronchospasms	8	27	24
Respiratory, thoracic and mediastinal disorders	Dysphonia	8	5	3
Respiratory, thoracic and mediastinal disorders	Choking sensation	6	0	0
General disorders and administration site conditions	Malaise	5	6	4
Gastrointestinal disorders	Mouth ulceration	5	0	0
Gastrointestinal disorders	Swollen tongue	5	2	2

TABLE 26 MOST FREQUENTLY REPORTED ADVERSE REACTIONS FOR LAMA + LABA COMBINATION TREATMENTS IN MEDICINEINSIGHT COMPARED WITH TGA DAEN, MEDICINEINSIGHT 2016

MedDRA system organ class	MedDRA reaction term	Number of cases (MedicineInsight)	Number of cases (TGA)	Number of cases with a single suspected medicine (TGA)
Not specified		24		
Gastrointestinal disorders	Constipation	2	0	0
Nervous system disorders	Headache	2	0	0
Cardiac disorders	Palpitations	1	0	0
Respiratory, thoracic and mediastinal disorders	Epistaxis	1	0	0
Respiratory, thoracic and mediastinal disorders	Cough	1	2	2
Gastrointestinal disorders	Nausea	1	1	1
Respiratory, thoracic and mediastinal disorders	Dysphonia	1	0	0
Nervous system disorders	Tremor	1	0	0
Gastrointestinal disorders	Vomiting	1	0	0
Cardiac disorders	Tachycardia	1	1	0
Renal and urinary disorders	Pollakiuria	1	1	1
Respiratory, thoracic and mediastinal disorders	Dyspnoea	0	4	3
Renal and urinary disorders	Urinary retention	0	2	1
Gastrointestinal disorders	Dry mouth	0	1	1
Skin and subcutaneous tissue disorders	Rash	0	1	1
Eye disorders	Vision blurred	0	0	0
Skin and subcutaneous tissue disorders	Pruritis	0	0	0
Nervous system disorders	Dizziness	0	0	0
General disorders and administration site conditions	Malaise	0	0	0
Respiratory, thoracic and mediastinal disorders	Wheezing	0	0	0

TABLE 27 MOST FREQUENTLY REPORTED ADVERSE REACTIONS FOR ICS + LABA COMBINATION TREATMENTS IN MEDICINEINSIGHT COMPARED WITH TGA DAEN, MEDICINEINSIGHT 2016

MedDRA system organ class	MedDRA reaction term	Number of cases (MedicineInsight	Number of cases (TGA)	Number of cases with a single suspected medicine (TGA)
Not specified		1610		
Respiratory, thoracic and mediastinal disorders	Dysphonia	73	25	17
Skin and subcutaneous tissue disorders	Rash	45	20	16
Nervous system disorders	Tremor	44	15	12
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	36	0	0
Cardiac disorders	Palpitations	34	17	13
Nervous system disorders	Headache	31	19	13
Respiratory, thoracic and mediastinal disorders	Cough	30	21	16
Gastrointestinal disorders	Nausea	25	21	13
Musculoskeletal and connective tissue disorders	Muscle spasms	25	27	24
Gastrointestinal disorders	Oral candidiasis	23	4	1
Gastrointestinal disorders	Mouth ulceration	19	1	1
Skin and subcutaneous tissue disorders	Pruritis	14	15	10
General disorders and administration site conditions	Reaction NS	12	0	0
Nervous system disorders	Dizziness	12	13	7
General disorders and administration site conditions	Malaise	11	7	6
Gastrointestinal disorders	Swollen tongue	10	6	4
General disorders and administration site conditions	Oedema	10	1	1
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	9	9	7
Gastrointestinal disorders	Lip swelling	8	4	2
Respiratory, thoracic and mediastinal disorders	Dyspnoea	8	67	55

TABLE 28 ADVERSE REACTIONS FROM TOP 20 REACTIONS IN MEDICINEINSIGHT NOT MENTIONED IN THE TGA DAEN, NOVEMBER 2016 PER DRUG CLASS, MEDICINEINSIGHT 2016

MedDRA system organ class	MedDRA reaction term	Number of cases (MedicineInsight)	Number of cases (TGA)	Number of cases with a single suspected medicine (TGA)
LAMAs				
General disorders and administration site conditions	Oedema	17	0	0
LABAs				
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	16	0	0
Respiratory, thoracic and mediastinal disorders	Choking sensation	6	0	0
Gastrointestinal disorders	Mouth ulceration	5	0	0
LAMA + LABA combinations				
Gastrointestinal disorders	Constipation	2	0	0
Nervous system disorders	Headache	2	0	0
Cardiac disorders	Palpitations	1	0	0
Psychiatric disorders	Anxiety	1	0	0
Gastrointestinal disorders	Diarrhoea	1	0	0
Respiratory, thoracic and mediastinal disorders	Epistaxis	1	0	0
General disorders and administration site conditions	Malaise	1	0	0
Cardiac disorders	Palpitations	1	0	0
Renal and urinary disorders	Pollakiuria	1	0	0
Psychiatric disorders	Sleep Disorder	1	0	0
Nervous system disorders	Tremor	1	0	0
Gastrointestinal disorders	Vomiting	1	0	0
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	1	0	0
Respiratory, thoracic and mediastinal disorders	Oropharyngeal pain	1	0	0
Musculoskeletal and connective tissue disorders	Pain in extremity	1	0	0
ICS + LABA combinations				
Respiratory, thoracic and mediastinal disorders	Laryngeal discomfort	101	0	0

5. APPENDICES

5.1. Appendix A: Glossary and abbreviations

Term	Definition	Description
95% CI	95% confidence interval	A 95% confidence interval provides information about a range of values that should contain the actual rate 95% (95 times out of 100) of the time, as well as information on the direction and strength of the demonstrated effect. Wider confidence intervals reflect less certainty in the estimate of the rate. Confidence intervals enable conclusions to be drawn about the statistical plausibility and clinical relevance of findings.
ABS	Australian Bureau of Statistics	
ASGC	Australian Standard Geographical Classification	Used from 1984 to 2011 by the Australian Bureau of Statistics (ABS) to calculate geographical statistics. We use ASGC in this report to calculate rurality based on postcode (categorised as in major cities, inner regional, outer regional, remote and very remote areas).
ATC	Anatomical Therapeutic Chemical	System used to classify medicines into groups according to certain characteristics.
Average		Measurement of the 'central' value of a set of values.
BEACH	Bettering the Evaluation and Care of Health program	Cross-sectional program collecting information on GP activities in Australia.
Best Practice		Clinical management software for GPs.
Condition		An illness or abnormality that interferes with a person's usual activities or wellbeing.
CRM	Customer Relationship Management	A database used for storing details of customers etc. (eg, participating practices)
DoH	Australian Government Department of Health	Federal department overseeing Australia's health system.
DUSC	Drug Utilisation Sub-Committee (PBAC)	Collects and analyses data on actual drug use and provides advice to PBAC.
DVA	Department of Veterans' Affairs (Australia)	Federal department responsible for delivering government programs for war veterans, defence force and federal police members and their dependents.

Term	Definition	Description
Encounter		Any professional interchange between medical practitioner (GP or nurse) and patient.
FDC	Fixed-dose combination	
GP	General practitioner	
ICS	Inhaled corticosteroid	
LABA	Long-acting beta$_2$ agonist	
LAMA	Long-acting muscarinic antagonist	
Longitudinal database		A set of statistical data which observes the same analysis units over a substantial period of time.
Median		The number separating the upper and lower half of a sample of values.
Medical Director 3		Clinical management software for GPs.
MEDRA		Standardised medical terminology for regulatory information about medical products used by humans. Allows the consistent coding of adverse drugs reactions to medicines.
PBAC	Pharmaceutical Benefits Advisory Committee	Committee making recommendations to the Federal Minister of Health on which medicines should be available as pharmaceutical benefits.
PBS	Pharmaceutical Benefits Schedule	Program providing subsidised prescription medicines to Australians.
Practice		An organisation operating at one or more locations where GPs and other staff provide general practice consultations to the community, and which contributes data to MedicineInsight from a single clinical system database.
Prevalence		Proportion of the population with a particular condition at a given time.
Rate		Measure or ratio of how two factors are associated with one another, eg, a proportion of patients with a condition or the incidence of prescriptions per consultation.
RPBS	Repatriation Pharmaceutical Benefits Scheme	
SAS	Statistical Analysis System (SAS Institute)	Statistical software program.

Term	Definition	Description
SAMA	Short-acting muscarinic antagonist	
SAND	Supplementary Analysis of Nominated Data	Sub-studies of the BEACH program.
SEIFA	Socioeconomic Indices for Areas	Calculated by ABS Index of Relative Socio-Economic Advantage and Disadvantage.
Site		The unit of data collection corresponding to either one practice or to several practices that share the same clinical system database. Practices combined into one site are typically under common administration or operating in the same geographical area.
TGA	Therapeutic Goods Administration	Australia's regulatory agency for medical medicines and devices.
TGA DAEN	TGA Database of Adverse Event Notification	

5.2. Appendix B: Medicine and condition definitions

5.2.1. Medicine definitions

TABLE 29 MEDICINES OF INTEREST

Class	Generic name	ATC	Trade Names
SABA	Salbutamol	R03AC02	Airomir, Asmol, Butamol, Ventolin
SABA	Terbutaline	R03AC03	Bricanyl
SAMA	Ipratropium	R03BB01	Aeron, Apo-Ipratropium, Apoven, Atrovent, Ipratrin, Ipravent
LAMA	Aclidinium*	R03BB05	Bretaris
LAMA	Glycopyrronium*	R03BB06	Seebri, Tovanor
LAMA	Tiotropium*	R03BB04	Favint, Spiriva, Yanimo
LAMA	Umeclidinium*	R03BB07	Incruse
LABA	Indacaterol*	R03AC18	Arbeela, Onbrez
LABA	Formoterol**	R03AC13	Foradile, Oxis
LABA	Salmeterol	R03AC12	Serevent
ICS	Beclometasone**	R03BA01	Qvar
ICS	Budesonide**	R03BA02	Pulmicort
ICS	Ciclesonide**	R03BA08	Alvesco
ICS	Fluticasone**	R03BA09	Flixotide
LAMA + LABA	Indacaterol + glycopyrronium*	R03AL04	Ultibro, Xoterna
LAMA + LABA	Umeclidinium + vilanterol*	R03AL03	Anoro
LAMA + LABA	Aclidinium + formoterol	R03AL05	Brimica
LAMA + LABA	Tiotropium + olodaterol	R03AL06	Spiolto
ICS + LABA	Fluticasone + salmeterol	R03AK06	Airzate, Evocair, Pavtide, Seretide
ICS + LABA	Budesonide + formoterol**	R03AK07	Symbicort
ICS + LABA	Fluticasone + formoterol**	R03AK11	Flutiform
ICS + LABA	Fluticasone + vilanterol	R03AK10	Breo, Ellipta,

* Approved for COPD only **Approved for asthma only

5.2.2. Condition definitions

Asthma is defined as 'a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.'[10]

COPD is defined as 'a common preventable and treatable disease, characterized by persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways and the lungs to noxious particles or gases. Exacerbations and comorbidities contribute to the overall severity in individual patients'.[11]

Asthma plus COPD overlap syndrome (ACOS) is 'characterized by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD. ACOS is therefore identified in clinical practice by the features that it shares with both asthma and COPD.'

A patient was defined as *having a history* of a condition of interest if they:

- had ever had a recorded relevant term for that diagnosis in any designated text or code field in relevant diagnosis tables (history (currently active or inactive), reason for prescription and reason for visit).

TABLE 30 provides a summary of the terms included or excluded for each condition.

TABLE 30 DEFINITIONS FOR ASTHMA AND COPD CODED TO GROUPS

Condition	Source	Relevant terms
Asthma	DOCLE	ASTHMA
Asthma	DOCLE	INFECTIVE EXACERBATION OF ASTHMA
Asthma	DOCLE	ASTHMA - CHRONIC PERSISTENT
Asthma	DOCLE	ASTHMA - INFREQUENT EPISODIC
Asthma	DOCLE	ASTHMA - FREQUENT EPISODIC
Asthma	DOCLE	ALLERGIC ASTHMA
Asthma	DOCLE	ASTHMA, EXERCISE INDUCED
Asthma	DOCLE	ACUTE SEVERE ASTHMA
Asthma	DOCLE	ASTHMA ACTION PLAN PERFORMED
Asthma	DOCLE	ASTHMA ACTION PLAN PRINTED
Asthma	DOCLE	ASTHMA CYCLE OF CARE
Asthma	DOCLE	ASTHMA PRESCRIPTION
Asthma	DOCLE	ASTHMA REVIEW
Asthma	Pyefinch	ASTHMA
Asthma	Pyefinch	ASTHMA, INFECTIVE EXACERBATION
Asthma	Pyefinch	ALLERGIC ASTHMA
Asthma	Pyefinch	ASTHMA, EXERCISE INDUCED
Asthma	Pyefinch	ACUTE SEVERE ASTHMA
Asthma	Pyefinch	ASTHMA, FREQUENT EPISODIC
Asthma	Pyefinch	ASTHMA, INFREQUENT EPISODIC
Asthma	Pyefinch	ASTHMA, CHILDHOOD
Asthma	Pyefinch	ASTHMA, OCCUPATIONAL
Asthma	Pyefinch	ASTHMA REVIEW
Asthma	Pyefinch	ASTHMA ACTION PLAN
Asthma	Pyefinch	ASTHMA CARE PLAN REVIEW
Asthma	Text	ACUTE SEVERE ASTHMA
Asthma	Text	ALLERGIC ASTHMA
Asthma	Text	ALLERGY INDUCED ASTHMA
Asthma	Text	ASTHMA
Asthma	Text	ASTHMA - ALLERGY INDUCED
Asthma	Text	ASTHMA - CHRONIC PERSISTENT
Asthma	Text	ASTHMA - EXERCISE INDUCED
Asthma	Text	ASTHMA - FREQUENT EPISODIC
Asthma	Text	ASTHMA - INFREQUENT EPISODIC
Asthma	Text	ASTHMA, ALLERGY INDUCED

Condition	Source	Relevant terms
Asthma	Text	ASTHMA, CHILDHOOD
Asthma	Text	ASTHMA, EXERCISE INDUCED
Asthma	Text	ASTHMA, FREQUENT EPISODIC
Asthma	Text	ASTHMA, INFREQUENT EPISODIC
Asthma	Text	ASTHMA, OCCUPATIONAL
Asthma	Text	BRONCHIAL ASTHMA
Asthma	Text	EXERCISE INDUCED ASTHMA
Asthma	Text	EXERTIONAL ASTHMA
Asthma	Text	FREQUENT EPISODIC ASTHMA
Asthma	Text	INFREQUENT EPISODIC ASTHMA
Asthma	Text	OCCUPATIONAL ASTHMA
Asthma	Text	STATUS ASTHMATICUS
Asthma	Text	WHEEZY BRONCHITIS
Asthma	Text	ASTHMA - INFECTIVE EXACERBATION
Asthma	Text	ASTHMA, INFECTIVE EXACERBATION
Asthma	Text	INFECTIVE EXACERBATION OF ASTHMA
Asthma	Text	ASTHMA ACTION PLAN
Asthma	Text	ASTHMA CARE PLAN
Asthma	Text	ASTHMA CARE PLAN REVIEW
Asthma	Text	ASTHMA REVIEW
Asthma	Text	CARE PLAN, ASTHMA
Asthma	Text	CHECK UP, ASTHMA
Asthma	Text	REVIEW - ASTHMA
COPD	DOCLE	BRONCHITIS - CHRONIC
COPD	DOCLE	CHRONIC BRONCHITIS, INFECTIVE EXACERBATION
COPD	DOCLE	CHRONIC OBSTRUCTIVE AIRWAYS DISEASE
COPD	DOCLE	EMPHYSEMA
COPD	DOCLE	COAD - INFECTIVE EXACERBATION
COPD	DOCLE	EMPHYSEMA - INFECTIVE EXACERBATION
COPD	Pyefinch	BRONCHITIS - CHRONIC
COPD	Pyefinch	CHRONIC BRONCHITIS, INFECTIVE EXACERBATION
COPD	Pyefinch	CHRONIC OBSTRUCTIVE AIRWAYS DISEASE
COPD	Pyefinch	EMPHYSEMA
COPD	Pyefinch	COAD - INFECTIVE EXACERBATION
COPD	Pyefinch	ACUTE EXACERBATION OF COPD
COPD	Pyefinch	COAD, INFECTIVE EXACERBATION
COPD	Text	BRONCHITIS - CHRONIC
COPD	Text	BRONCHITIS, CHRONIC
COPD	Text	CHRONIC BRONCHITIS
COPD	Text	CHRONIC BRONCHITIS - INFECTIVE EXACERBATION
COPD	Text	AC/COPD
COPD	Text	ASTHMA / COPD
COPD	Text	ASTHMA/ COPD
COPD	Text	ASTHMA/COAD
COPD	Text	ASTHMA/COPD

Condition	Source	Relevant terms
COPD	Text	CAL (CHRONIC AIRWAYS LIMITATION)
COPD	Text	CHANGE MEDICATION COPD
COPD	Text	CHRONIC AIRWAYS LIMITATION
COPD	Text	CHRONIC BRONCHITIS COPD
COPD	Text	CHRONIC OBSTR PULMON DISEASE COPD
COPD	Text	CHRONIC OBSTRUCTIVE AIRWAYS DISEASE
COPD	Text	CHRONIC OBSTRUCTIVE PULMONARY DISEASE
COPD	Text	COAD
COPD	Text	COAD (CHRONIC OBSTRUCTIVE AIRWAYS DISEASE)
COPD	Text	COAD/EMPHYSEMA
COPD	Text	COPD
COPD	Text	COPD (CHRONIC OBSTRUCTIVE PULMONARY DISEASE)
COPD	Text	COPD - INFECTIVE EXACERBATION
COPD	Text	COPD - MILD
COPD	Text	COPD EXACERBATION
COPD	Text	COPD IN ACUTE EXACERBATION
COPD	Text	COPD MILD
COPD	Text	COPD REVIEW
COPD	Text	COPD SCRIPT
COPD	Text	COPD, INFECTIVE EXACERBATION
COPD	Text	COPD.
COPD	Text	COPD/ASTHMA
COPD	Text	COPD/EMPHYSEMA
COPD	Text	EARLY COPD
COPD	Text	EMPHYSEMA
COPD	Text	EXACERBATION COPD
COPD	Text	EXACERBATION OF COPD
COPD	Text	INFECTIVE EXACERBATION COPD
COPD	Text	INFECTIVE EXACERBATION OF COPD
COPD	Text	MILD COPD
COPD	Text	REVERSIBLE COPD
COPD	Text	SEVERE COPD
COPD	Text	URTI, COPD EXACERBATION
COPD	Text	ACUTE EXACERBATION OF COPD
COPD	Text	CHRONIC BRONCHITIS, INFECTIVE EXACERBATION
COPD	Text	COAD - INFECTIVE EXACERBATION
COPD	Text	COAD, INFECTIVE EXACERBATION
COPD	Text	COPD - INFECTIVE EXACERBATION
COPD	Text	COPD, INFECTIVE EXACERBATION
COPD	Text	EMPHYSEMA - INFECTIVE EXACERBATION
COPD	Text	INFECTIVE EXACERBATION OF CHRONIC BRONCHITIS
COPD	Text	INFECTIVE EXACERBATION OF COAD
COPD	Text	INFECTIVE EXACERBATION OF COPD

5.3. Appendix C: Additional analyses

5.3.1. Coprescribing of COPD medicines (asthma)

A small number of patients may be exposed to unsafe medicine use practices including double dosing and the use of regimens that include concomitant use of a SAMA and a LAMA. There may be patients with asthma only prescribed LAMA therapy despite these medicines being PBS listed for patients with COPD only.

Questions

- For patients with asthma only (no COPD):
- What combination of medicine formulations (by class) were recorded as their 'current medications' in 2016, highlighting the combinations with safety concerns?

Methods

This was a cross-sectional analysis of regular patients (all ages) at clinically representative practices with **asthma only** (without COPD).

All prescriptions for medicine classes and medicines of interest (TABLE 1**Error! Reference source not found.**) were extracted for the period from 1 January 2016 to 31 December 2016. Multiple prescriptions for the same drug prescribed on the same day were counted as a single prescription.

To investigate the use of combinations of medicine formulations we identified all "current medications" according to the Prescription History file and removed records marked as ceased or deleted. Medicine formulation combinations with potential safety concerns are identified as "duplicated therapy" in TABLE 32 and specifically detailed under TABLE 33. We did not include the SABA class of medicines in this analysis as they can be used safely with all COPD medicines.

For patients with asthma only (no COPD) we calculated:

- The proportion of patients on mono-, dual-, triple-therapy and the specific combinations of medicine formulations according to their latest "current medications"
- The proportion of patients on duplicated therapy
- The proportion of patients on both LAMA maintenance therapy and SAMA reliever therapy

Additional caveats

- Medicines may have been ceased without a record in the clinical system.
- SABA medicines are available over-the-counter, therefore SABA use may be underestimated in this report

Results

Current medications in 2016

Of the 274,208 regular patients with asthma only, 50% weren't on a reliever medication according to their current medications, 48.6% were on a SABA, 0.2% SAMA and 0.9% SABA + SAMA. (TABLE 31).

TABLE 31 SUMMARY OF RELIEVER AND MAINTENANCE THERAPY ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	ASTHMA ONLY	
Therapy	**N**	**%**
Relievers		
No current reliever	137,938	50.3
SAMA only	541	0.2
SABA only	133,193	48.57
SABA + SAMA	2,536	0.92
Total	274,208	100
Maintenance therapy		
No current maintenance therapy	158,318	57.75
At least 1 current maintenance therapy	115,890	42.27
Total	274,208	100

According to patients' current medications, of the 115,890 patients with asthma only currently on at least one maintenance therapy, 77.1% were currently on dual therapy with ICS/LABA, 17.6% were on ICS monotherapy and 1.2% were on triple therapy with ICS/LABA/LAMA (TABLE 32).

TABLE 32 COPRESCRIBING OF COPD MEDICATIONS FOR MAINTENANCE THERAPY ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	ASTHMA ONLY	
Combinations (Maintenance)	**N**	**%**
Monotherapy		
LAMA	300	0.26
LABA	274	0.24
ICS	20,414	17.61
Duplicated monotherapy		
LAMA x 2	<5	
LABA x 2	<5	
ICS x 2	215	0.19
Dual therapy		
LAMA + LABA	87	0.08
ICS + LABA	89,321	77.07
ICS & LAMA	71	0.06
Duplicated dual therapy		
ICS + (LAMA x 2)	<5	
ICS + LABA & LABA	119	0.10
(ICS x 2) & LAMA	1,415	1.22
ICS + LABA & ICS	0	0.00
LAMA + LABA & LABA	0	0.00
LAMA + LABA & LAMA	<5	
LAMA + LABA x 2	0	0.00
ICS + LABA x 2	1982	1.71

	ASTHMA ONLY	
Combinations (Maintenance)	**N**	**%**
Triple therapy		
ICS + LABA + LAMA	1431	1.23
Duplicated triple therapy		
ICS + LABA & (LAMA x 2)	9	0.01
ICS + LABA & LAMA & LABA	60	0.05
ICS + LABA & LAMA & ICS	59	0.05
ICS + LABA + LAMA & LABA & LAMA	<5	
ICS + LABA + LAMA & ICS + LABA	49	0.04
(ICS + LABA + LAMA) x 2	<5	
Other	72	0.06
TOTAL	115,890	100.00

Current medications in 2016 – combinations with safety concerns

This analysis suggests that around 3.0% of patients with asthma only who are on maintenance therapy (3,492 out of 115,890) were prescribed at least one LAMA product despite this class only being indicated for patients with COPD. 3.38% of patients with asthma only (3,920 out of 115,890) may be at risk of having duplicated therapy and only 0.1% (n=152) were currently on at least one LAMA product and at least one SAMA product. (TABLE 33)

TABLE 33 COMBINATIONS WITH POTENTIAL SAFETY CONCERNS ACCORDING TO PATIENTS' CURRENT MEDICATIONS, MEDICINEINSIGHT 2016

	ASTHMA ONLY	
Combinations with potential safety concern	**N**	**%**
Concomitant LAMA and SAMA	152	0.13
Duplicated therapy (see TABLE 30)	3,920	3.38
On at least one LAMA therapy	3,492	3.01
Total patients on at least one maintenance therapy	115,890	100

5.3.2. Initial pharmacotherapy COPD (all)

Questions

For patients with COPD (all), with or without asthma, who started therapy for the first time between 1 July 2015 and 31 December 2016:

- How many medicines were used for initial therapy?
- What medicines were used for initial therapy?
- Has the distribution of initial therapies changed in this period compared with the period 1 July 2013 to 30 June 2015?

Methods

This was a cross-sectional analysis of data for all regular patients 35 years or older diagnosed with COPD (with or without asthma) who attended clinically representative sites and who started therapy for the first time between 1 July 2015 and 31 December 2016 or between 1 July 2013 and 30 June 2015:

We excluded patients:

- with a record of a COPD medication prior to 1 July 2013, or
- who started their first COPD medicine within 12 months of their first encounter at the practice (on the basis they may have been prescribed COPD medications from other sources before joining the practice (eg, another GP practice or specialist/hospital)

We identified the first medicine class(es) and medicine(s) of interest prescribed for each patient. Please note, the previous MedicineInsight COPD Report (1 July 2013 to 30 June 2015) excluded SABA medicines from the analysis of initial therapy; to produce comparable results for this report we also excluded SABA medicines when defining initial therapy.

All prescriptions for medicine classes and medicines of interest (TABLE 1) were extracted for these patients for the period from 1 July 2013 to 31 December 2016. Patients with more than one script for the same medicine class or medicine had the relevant class or medicine only counted once as an initial therapy.

We calculated:

- The proportion of patients with 1, 2, or 3 medicines prescribed as initial therapy.
- The number and proportion of patients prescribed each medicine of interest as initial therapy.

We compared:

- The number and proportion of patients prescribed each medicine of interest as initial therapy in 1 July 2013 to 30 June 2015 versus 1 July 2015 to 31 December 2016.
- We also compared our results to those presented in the previous report for the period 1 July 2013 to 30 June 2015, noting the issues with this comparisons in Section 5.3.2.4

Additional caveats

- Specialist and hospital prescriptions are not included in MedicineInsight unless manually entered into the clinical information system by the practice staff. If the initial prescription was written by a specialist (in secondary care) the first prescription will be missing.
- Patients may have had their first diagnosis of COPD after their first COPD medication.

New methodology for defining initial therapy

In the previous MedicineInsight Report on COPD (January 2016) we identified initial therapy between 1 July 2013 and 30 June 2015. Of the 47,268 regular patients (all ages) with COPD (with or without asthma) in that report we found 28,208 patients who had not received a prescription prior to 1 July 2013 and were eligible for inclusion in the analysis. Using new methodology in this report we found 4,424 patients we define as starting therapy between 1 July 2013 and 30 June 2015.

The number and proportion of all regular patients with COPD starting therapy in the previous report was substantially greater than the number and proportion we found starting therapy in this latest report. Proposed explanations for this discrepancy are listed below:

- The previous report covered a 24-month period and this report covers an 18-month period.
- The previous report included patients with COPD of all ages, whereas this report restricted the population to patients 35 years and over.
- Since the previous report was published we have improved our methodology for defining new therapies in MedicineInsight. Our new approach is more conservative in order to improve the accuracy of the definition, leading to more patients being excluded on the

basis of uncertainty whether the medicine is really new. Differences between the methods used for these two reports are summarised below:

- In the previous report, when excluding patients prescribed a COPD medication prior to 1 July 2013, only prescriptions ordered at the practice (in the Prescription table) were analysed. We now use information from the Prescription History table as well, to exclude patients with evidence of a COPD medication from another source.
- The previous report included patients who started their first COPD medicine within 12 months of their first visit at the practice, whereas this was an exclusion criteria for the latest report, on the basis that these patients may have been prescribed COPD medications from other sources before joining the practice (prescriptions are valid for 12 months).

Results

Initial pharmacotherapy in patients with COPD (all)

Of the 3,775 patients with COPD (all) who started therapy for COPD between 1 July 2015 and 31 December 2016, 45.9% were prescribed only one medicine of interest as initial therapy, 49.0% were prescribed dual therapy and 4.5% triple therapy. The most common choice of initial therapy by class was dual therapy with ICS + LABA (41.6%; almost all were FDC), followed by LAMA monotherapy (32.6%) and LAMA + LABA dual therapy (7.0%) (TABLE 34). The most common choice of initial therapy by individual medicine(s) was tiotropium ((21.4%) followed by fluticasone + salmeterol (18.7%) and budesonide + formoterol (18.0%) (TABLE 35).

When comparing initial therapy for COPD in the period July 2013 to June 2015 versus July 2015 to December 2016 we found the following (TABLE 34):

- Initial therapy with LAMA increased from 23.6% in 2013/15 to 32.6% in 15/16
- Initial therapy with LAMA + LABA increased from 1.5% to 7%
- Initial therapy with ICS + LABA decreased from 51.7% to 41.6%
- Initial therapy with ICS + LABA + LAMA decreased slightly from 5.2% to 4.3%

TABLE 34 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD (ALL) BY MEDICINE CLASS, MEDICINEINSIGHT JUL 2015–DEC 2016 AND JUL 2013–JUN 2015

	Current Report				Previous Report*	
	Jul 2015–Dec 2016		Jul 2013–Jun 2015		Jul 2013–Jun 2015	
Initial therapy	N	%	N	%	N	%
Monotherapy						
SAMA	114	3.02	127	2.87	682	2.42
LAMA	1,232	32.63	1,047	23.67	9,480	33.64
LABA	169	4.48	271	6.13	1,127	4.00
ICS	220	5.83	327	7.39	n.a.	
Dual therapy						
LAMA + LABA	266	7.04	67	1.51	556	1.97
ICS + LABA	1,571	41.60	2,288	51.72	11,061	39.25
ICS & LAMA	7	0.19	22	0.50	n.a.	
ICS & SAMA	6	0.16	5	0.11	n.a.	
Triple therapy						
ICS + LABA & LAMA	161	4.26	232	5.24	4,843	17.18
ICS + LABA & SAMA	9	0.24	13	0.29	158	0.56
Other	20	0.53	25	0.57	277	0.98
TOTAL	3,775	100	4,424	100.00	28,184	100

**Note: The methodology for defining 'initial therapy' was less sensitive in the previous report (see Section 4.4.5)*

TABLE 35 INITIAL PHARMACOTHERAPY FOR PATIENTS WITH COPD (ALL) BY INDIVIDUAL MEDICINE(S), MEDICINEINSIGHT JUL 2015–DEC 2016 AND JUL 2013–JUN 2015

		Current Report			
Class	Medicine	Jul 2015–Dec 2016		Jul 2013–Jun 2015	
Monotherapy		N	%	N	%
SAMA	*Ipratropium*	114	3.02	127	2.87
LAMA	*Aclidinium*	193	5.11	125	2.83
	Glycopyrronium	102	2.70	81	1.83
	Tiotropium	808	21.40	814	18.40
	Umeclidinium	128	3.39	27	0.61
LABA	*Formoterol*	7	0.19	<5	
	Indacaterol	152	4.03	254	5.74
	Salmeterol	10	0.26	13	0.29
ICS	*Beclometasone*	14	0.37	19	0.43
	Budesonide	60	1.59	95	2.15
	Ciclesonide	28	0.74	37	0.84
	Fluticasone	118	3.13	176	3.98
Dual therapy					
LAMA + LABA (FDC)	*Aclidinium + formoterol*	40	1.06	0	0.00
	Glycopyrronium + indacaterol	62	1.64	25	0.57
	Umeclidinium + vilanterol	97	2.57	16	0.36
	Tiotropium + olodaterol	55	1.46	0	0.00
LAMA & LABA	*Aclidinium & indacaterol*	0	0.00	<5	
	Aclidinium & salmeterol	0	0.00	0	0.00

		Current Report			
Class	**Medicine**	**Jul 2015–Dec 2016**		**Jul 2013–Jun 2015**	
	Glycopyrronium & indacaterol	8	0.21	7	0.16
	Tiotropium & formoterol	0	0.00	0	0.00
	Tiotropium & indacaterol	< 5		21	0.47
	Tiotropium & salmeterol	< 5		<5	
ICS + LABA (FDC)	*Budesonide + formoterol*	681	18.04	926	20.93
	Fluticasone + formoterol	19	0.50	22	0.50
	Fluticasone + salmeterol	707	18.73	1,289	29.14
	Fluticasone + vilanterol	164	4.34	45	1.02
Triple therapy					
ICS + LABA & LAMA	*Budesonide + formoterol & aclidinium*	< 5		<5	
	Budesonide + formoterol & glycopyrronium	< 5		0	0.00
	Budesonide + formoterol & tiotropium	43	1.14	66	1.49
	Budesonide + formoterol & umeclidinium	< 5		0	0.00
	Fluticasone + formoterol & tiotropium	< 5		<5	
	Fluticasone + salmeterol & aclidinium	10	0.26	<5	
	Fluticasone + salmeterol & glycopyrronium	<5		7	0.16
	Fluticasone + salmeterol & tiotropium	76	2.01	152	3.44
	Fluticasone + salmeterol & umeclidinium	< 5	0.08	0	0.00
	Fluticasone + vilanterol & tiotropium	5		<5	
	Fluticasone + vilanterol & umeclidinium	11	0.29	0	0.00
ICS + LABA & SAMA	*Budesonide + formoterol & ipratropium*	< 5		5	0.11
Other		40	1.06	60	1.36
TOTAL		3,775	100.00	4,424	100.00

Comparing this report with the previous COPD report, the top two most common choices for initial therapy were the same; ICS + LABA (41.6% vs 39.3, respectively); followed by LAMA monotherapy (32.6% vs 33.6%, respectively). However in this report, the third most common choice for initial therapy was LAMA & LABA dual therapy (7.0% vs 2.0%, respectively) whereas the previous report found that triple therapy with ICS + LABA & LAMA was the third most common choice (4.3% vs 17.2%, respectively) (TABLE 34). The most common choice of initial therapy by individual medicine(s) was the same in both reports; tiotropium, followed by fluticasone + salmeterol and budesonide + formoterol. (TABLE 35). The relatively high proportion of patients apparently prescribed triple therapy as initial treatment in the previous report suggests that these patients had initial treatment elsewhere but the methodology used in the previous report was not specific enough to exclude them.

5.4. Appendix D: About MedicineInsight

The Australian Government funded NPS MedicineWise[a] in 2011 to establish and manage a longitudinal general practice data platform to improve the post-marketing surveillance of medicine use in Australia and support quality improvement activities in general practices. It is the first large-scale, national general practice data program in Australia that extracts longitudinal de-identified patient records from the software that general practices already use to manage patient records and write prescriptions.

MedicineInsight aims to:

- support quality improvement in participating general practices
- inform future policy and primary care research
- achieve better healthcare for Australians
- support sustainable Pharmaceutical Benefits Scheme (PBS) and Medicare Benefits Scheme (MBS).

By December 2016 the MedicineInsight program had recruited more than 550 general practices from around Australia to participate in the program. It currently includes administrative, clinical and prescribing records for more than 3.5 million active patients and more than 2000 GPs.

5.4.1. How MedicineInsight collects data

MedicineInsight extracts anonymised clinical data from general practices that use one of two CISs: *Best Practice* or *Medical Director 3.* The data available in these systems includes data entered directly by GPs or practice staff as well as system-generated data such as the time and date that records are accessed.

An all-of-practice data collection is conducted when a practice joins MedicineInsight. The extraction tool then collects incremental data weekly, enabling development of a longitudinal database in which patients within practices can be tracked over time.

The data MedicineInsight collects from general practices includes:

- patient demographic and clinical data entered directly by GPs and practice staff into the system
- system-generated data (eg, time and date the electronic medical records of a patient are accessed)
- practice and GP information for the administration of quality improvement activities by NPS MedicineWise
- prescriptions and pathology data. The pathology data is transferred directly into the CIS from pathology providers.

Patient level data are de-identified ‘at source’, meaning the patients’ personal identifiers such as name, exact date of birth and street address are not extracted by the tool. The data held in the MedicineInsight database are anonymous; however, each patient, practice and provider has a unique identifying number which enables patient data to be matched across multiple data tables within each practice.

FIGURE 7 provides an overview of how the MedicineInsight data flows, including how general practice reports and patients lists are provided back to a general practice, where any re-identification of patients occurs, and how data extracts and aggregated reports are provided.

[a] NPS MedicineWise is an independent, evidence-based, not-for-profit organisation established in 1998, which receives funding from the Australian Government Department of Health. Our mission is to enable the best decisions about medicines, health technologies and other health choices for better health and economic outcomes. Our vision is to lead innovation and improvement in health care by building trust, implementing change and demonstrating impact.

FIGURE 7 HOW MEDICINEINSIGHT DATAFLOW WORKS

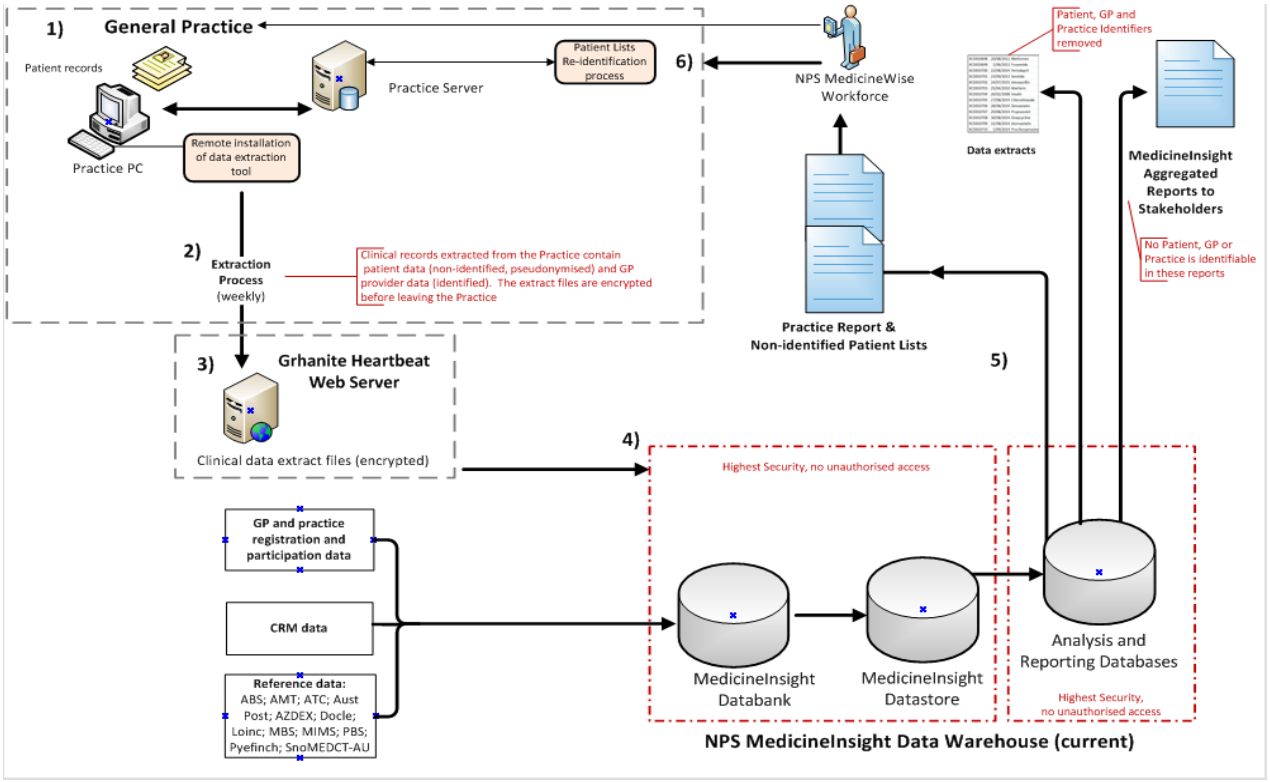
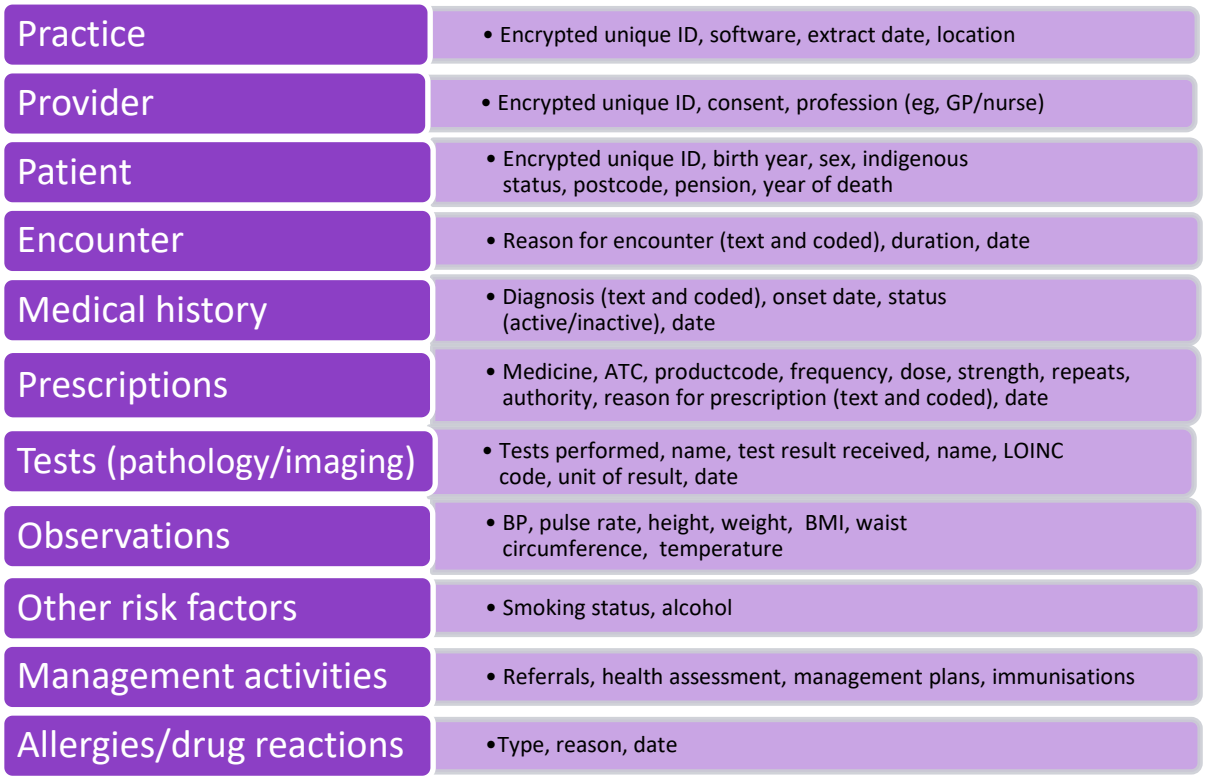


FIGURE 8 provides an overview of the data and the fields that are available from the MedicineInsight data extracted from the CISs. The data includes both coded and free-text fields. Not all the data fields contained in FIGURE 8 are currently available for inclusion in this report. For example, imaging results are saved in a general practice record in a 'report' PDF format rather than with the detailed results that are available on pathology tests. At this point MedicineInsight is unable to extract the imaging data from the PDF. Also progress notes, that could potentially identify individuals, are not collected by MedicineInsight.

Depending on the CIS at their practice, clinicians use coding systems such as 'Docle', 'Pyefinch' or 'ICPC' to enter medical terms into their system. However, it is not mandatory to use a code and clinicians can enter medical terms as free text. Some data used in this report, such as medical conditions, are derived from using a combination of different fields and analysis of the free text.

FIGURE 8 OVERVIEW OF MEDICINEINSIGHT DATA FIELDS



5.4.2. Recruitment of practices

Practices are recruited into MedicineInsight via a number of methods:

- The NPS MedicineWise Clinical Service Specialists (CSSs) who visit more than 15,000 GPs across Australia each year discuss the benefits of being involved in MedicineInsight with the GPs.
- The MedicineInsight recruitment team, and in the past other organisations that have been commissioned to assist with recruitment, make an initial phone call or email to practices in areas where recruitment is lower.
- GPs and practices may make expression of interest submissions after visiting the MedicineInsight website or hearing about MedicineInsight at conferences and other meetings and through other stakeholder groups such as Primary Health Networks (PHNs).
- Practices are recruited through specific targeted initiatives in which the PHNs are using MedicineInsight to support specific additional quality improvement initiatives (eg, Tasmania and Hunter New England and Central Coast).

After a practice agrees to participate in MedicineInsight and completes the paperwork, they are contacted by the extraction tool vendor from the University of Melbourne, who organise the remote installation of the extraction tool (GRHANITE), and by their local CSS, who organises their first MedicineInsight visit using the data extracted from the practice.

FIGURE 9 shows the geographical distribution of MedicineInsight practices and TABLE 36 describes the size and regional characteristics of MedicineInsight practices.

FIGURE 9 APPROXIMATE DISTRIBUTION OF MEDICINEINSIGHT PRACTICES.

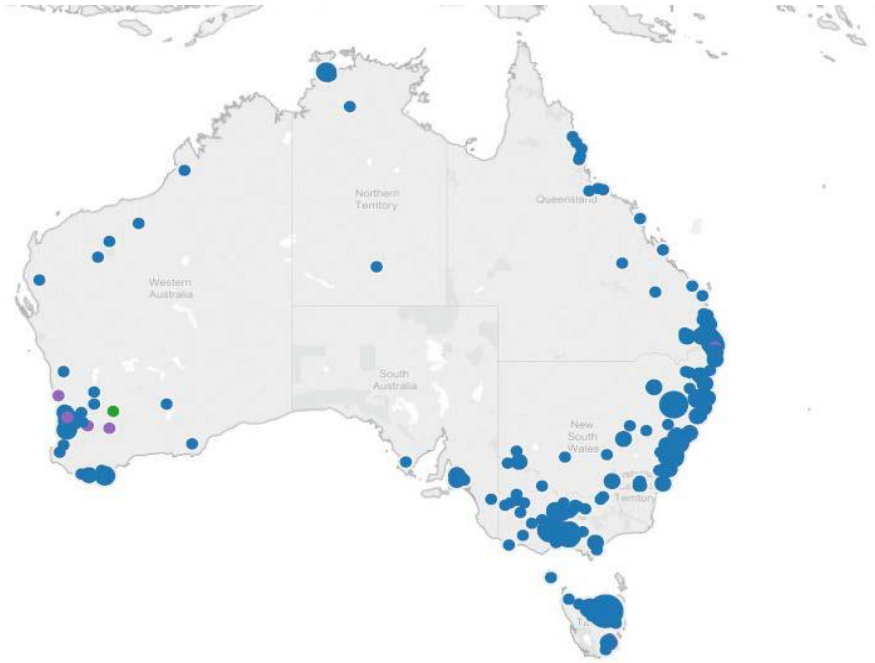


TABLE 36 CHARACTERISTICS OF MEDICINEINSIGHT PRACTICES (JUNE 2016)

Characteristic	MedicineInsight (June 2016) n = 557
	↖
Size	
1 GP	7
2–5 GPs	50
6 or more GPs (Note: 29% missing info for eMI)	44
Location (rurality)	
Major city	59
Inner/outer regional	37
Remote/very remote	3
State/Territory	
NSW	29
Vic	23
SA	4
Qld	20
Tas	8
WA	12
NT	2
ACT	2

5.4.3. How are the data used?

Increasingly there is recognition of the expanding uses for MedicineInsight data. At the end of December 2016 the data have been used for a range of activities, including:

- Post-marketing surveillance, including for drugs prescribed for chronic obstructive pulmonary disease (COPD), diabetes and asthma, antidepressants anticoagulants, testosterone, ezetimibe, quetiapine and antibiotics
- informing medicines policy, including a review of biological medicines used in general practice, monitoring the impact of changes to PBS restrictions for testosterone, and reviewing the use of antibiotics commonly used for respiratory tract infections
- supporting quality improvement activities in general practice by preparing monthly reports for each practice in areas including improving care for patients with diabetes, stroke, COPD, depression and antibiotic use. The reports compare practice activity with best practice guideline and comparable practice groups and can be accessed by practice staff and/or discussed at clinical meetings facilitated by an NPS MedicineWise Clinical Services Specialist (CSS). These meetings provide practice staff with an opportunity as a group to reflect on current practice, decide on areas for improvement and on how these may be implemented.
- primary care research, including evaluation of vaccination coverage, cardiovascular disease, chronic kidney disease, diabetes, pain, obesity and lung cancer. For more details see the NPS MedicineWise *MedicineInsight data* web page (www.nps.org.au/health-professionals/medicineinsight/interested-in-medicineinsight-data).

5.4.4. Quality improvement activities

Since 2013, NPS MedicineWise has been delivering routine practice reports from MedicineInsight for GPs, showing trends in clinical practice and prescribing to support effective educational interventions and quality improvement programs to assist GPs in delivering the best care to their patients.

In the 2015–16 financial year, more than 2000 health professionals from 318 general practices participated in MedicineInsight visits, which included a tailored practice report and facilitated meeting. Topics have included type 2 diabetes, stroke prevention, antibiotics and managing depression.

Additionally, all practices have access to an online report repository, allowing them to download their tailored updated practice reports as required. Since December 2016 more than 500 confidential practice reports are provided monthly to participating practices via an online portal and through clinical meetings facilitated by the NPS MedicineWise team of 61 CSSs. Reports are tailored for each practice and compare procedures and prescriptions between 'Your Practice 12 months ago', 'Your Practice now', and in comparison to all other MedicineInsight practices as well as information on data quality and completeness.

5.4.5. Data governance

NPS MedicineWise is the data custodian for the MedicineInsight program. Ownership of the original data remains with participating general practices, and MedicineInsight only contains anonymised patient data. The pilot MedicineInsight program was approved by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee in January 2013.

NPS MedicineWise has a data governance framework and policy to ensure rigour and transparency, and that information is collected ethically, legally, securely and confidentially. The framework complies with national and State legislation, including, but not limited to, Australian privacy laws and the Australian Privacy Principles.

NPS MedicineWise has an independent, external Data Governance Committee that was established in 2015 to provide advice to NPS MedicineWise on all aspects of the MedicineInsight data access model. The committee consists of external academics, practising

GPs, an expert on data security, the Australian Bureau of Statistics (ABS), and legal and consumer advocates.

This group provides guidance and expertise to ensure appropriate governance is in place and provides advice to NPS MedicineWise on general data governance issues, the data access framework and decisions on data access for specific projects applying for MedicineInsight data.

A further separate independent development committee has been established to advise NPS MedicineWise on transition to a 'big data' environment on topics including data storage, security, coding standards, analysis, data accessibility and record linkage.

Further information and the MedicineInsight data book are available on the NPS MedicineWise website at www.nps.org.au/health-professionals/medicineinsight/interested-in-medicineinsight-data.

5.4.6. Representativeness of MedicineInsight data

To investigate the representativeness of MedicineInsight data, we compared:

- available demographic data for MedicineInsight GPs who had consented to participate in quality improvement activities to the most recent national data from General Practice Workforce Statistics 2014.[12]
- the demographics of MedicineInsight patients to the most recent national data from MBS statistics and a range of national data.[13,14,15,16,17,18]

Participating GPs

At June 2016, 1,511 GPs in MedicineInsight practices had consented to participate in quality improvement activities. These GPs are a younger-aged cohort and more likely to be female than those in national data. GPs located in NSW, Qld, WA and NT are currently under-represented in our data. TABLE 37 provides a detailed comparison of characteristics of these GPs (when data were available) to the available national data.

TABLE 37 CHARACTERISTICS OF MEDICINEINSIGHT GPS (WHO ARE INVOLVED IN QI ACTIVITIES) COMPARED WITH NATIONAL GP DATA[12]

Characteristic	MedicineInsight (August 2016) n = 1483 %	DoH[12] (2014) n = 33,275 %
Sex (eMI missing: n = 569)		
Male	52	56
Female	48	44
Age group (eMI missing: n = 597)		
Under 35	16	13
35–44	25	24
45–54	30	26
55–64	22	23
65+	7	13
Location (eMI missing: n = 3)		
Major city	60	67

Characteristic	MedicineInsight (August 2016) n = 1483 %	DoH[12] (2014) n = 33,275 %
Inner regional	27	19
Outer regional	11	9
Remote/very remote	2	4
State/Territory		
SA	6	8
Vic	38	24
NSW	22	31
Qld	17	21
Tas	8	3
WA	8	10
NT	0	2
ACT	1	1

MedicineInsight patient cohort

MedicineInsight active patient cohort includes all patients who have visited a practice at least once in the previous 3 years. There are currently 4,354,413 patients in the patient cohort. This was based on data extracted from 506 MedicineInsight practices.

Patients presenting at MedicineInsight GP encounters in 2016 had a similar age profile to that of recipients of general practice-related MBS items[13] (FIGURE 10). The sex profile is also similar, with most MedicineInsight patients and MBS item recipients being female (54% vs 50%) (TABLE 38).

MedicineInsight has a similar proportion of Aboriginal and Torres Strait Islander patients to that in the BEACH data[15] (1.7%) but a smaller proportion compared with ABS census data[16] (2.5%). MedicineInsight has a similar representation of MedicineInsight patients across State/Territory and geographical areas, with a few exceptions: a higher proportion of patients in Tasmania and Western Australia, and fewer patients in South Australia (TABLE 38).

FIGURE 10 PATIENTS AT MEDICINEINSIGHT ENCOUNTERS (JUNE 2016) COMPARED WITH PATIENTS RECEIVING MBS GP SERVICES[13]

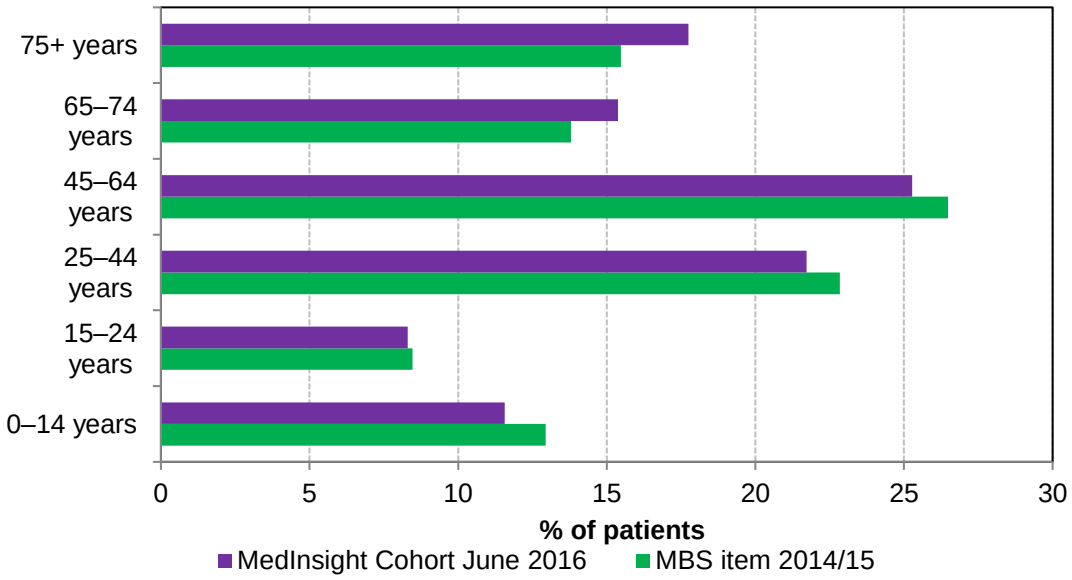


TABLE 38 CHARACTERISTICS OF MEDICINEINSIGHT PATIENT COHORT COMPARED WITH OTHER NATIONAL DATA

Sociodemographic characteristic	MedicineInsight cohort June 2016 n=4,354,413 %	National data (various sources) %
Gender		
Male	45.9	49.7[13]
Female	53.8	50.3
Missing/Other	0.4	
Aboriginal or Torres Strait Islander	1.9	1.7[15] 2.5[16]
Pension	24.5	23.1[17]
DVA	0.8	0.7[18]
Region		
Major city	66.8	70.9[14]
Inner regional	21.1	18.1
Outer regional	9.5	8.8
Remote	1.3	1.4
Very remote	0.3	0.9
State/Territory		
NSW	29.6	32.0[14]
Vic	24.3	24.8
SA	3.0	7.2
Qld	19.2	20.1
Tas	6.1	2.2
WA	13.8	11.0
NT	1.6	1.0
ACT	1.8	1.6

Weighting

Currently no weighting of the data has been undertaken to account for potential differences in the characteristics of the MedicineInsight patients and practices compared with those of national patients and practices. There are many technical considerations to be made about when and how to apply weightings to the dataset. Work is underway to determine the best approach to be undertaken in future analyses.

Completeness of MedicineInsight data

Analysis and interpretation of MedicineInsight data were limited by the accuracy and completeness of data entered, as well as the representativeness of the cohort compared with the population that usually attends Australian general practices.

To explore the completeness of the data we examined the completeness of a series of key indicators related to patient demographics, patient risk factors and condition recording in data extracted from 450 practices. TABLE 39 shows that most demographic variables are complete, and the recording of risk factors such as smoking status and blood pressure was moderately high and improving. Usually at least one diagnosis or reason for visit was recorded per visit; but there remains significant variation across the individual fields. We are working with practitioners to improve data completeness.

Progress notes within clinical records can provide richer information; however, due to privacy concerns and the inability to fully de-identify this information to date, we are not able to extract from this field. We will aim to extract from progress notes in the future when we have developed filters to securely de-identify the data.

TABLE 39 COMPLETENESS OF KEY MEDICINEINSIGHT INDICATORS IN 450 MEDICINEINSIGHT PRACTICES

Completeness indicator	Completeness assessment
Patient demographics practices	**Median (interquartile range)**
Year of birth field completeness	100% (100%–100%)
Sex field completeness	100% (100%–100%)
Indigenous status completeness	72% (47%–88%)
Patient risk factors recording practices	
Smoking status completeness	69% (58%–80%)
Patients 40+ years with a BP recording in last 12 months	42% (35%–49%)
Patients 16+ years with a BMI recording in last 12 months	15% (10%–22%)
Condition recording (last 12 months)	
History recorded at encounter (any)	77% (54%–90%)
History recorded at encounter (coded)	72% (60%–85%)
Reason for prescription (any)	33% (16%–51%)
Reason for prescription (coded)	17% (7%–29%)
Reason for visit (any)	71% (40%–88%)
Reason for visit (coded)	56% (27%–73%)

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